Preparing Spanish-Speaking Older Adults for Advance Care Planning and Medical Decision-Making—The PREPARE Trial

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TABLE OF CONTENTS

ABSTRACT ............................................................................................................................................. 5

BACKGROUND ......................................................................................................................................... 7
   Easy-to-Use ACP Tools .......................................................................................................................... 8
   Aims ..................................................................................................................................................... 10
   Significance ........................................................................................................................................ 10
   Innovation .......................................................................................................................................... 11

PARTICIPATION OF PATIENTS AND OTHER STAKEHOLDERS ......................................................... 12
   Description of the Stakeholder Advisory Board .................................................................................. 12
   Impact of the Stakeholder Advisory Board ......................................................................................... 12
      Table 1. Notable Impacts of Engaging Diverse Stakeholders ...................................................... 14

METHODS ............................................................................................................................................... 16
   Study Overview ................................................................................................................................... 16
   Study Design ...................................................................................................................................... 17
      Figure 1. PREPARE study flow diagram ......................................................................................... 18
   Study Setting ...................................................................................................................................... 19
   Participants: Forming the Study Cohort .............................................................................................. 19
      Table 2. Inclusion and Exclusion Criteria of Participants ............................................................... 22
   Interventions and Comparators ........................................................................................................ 27
      Figure 2. PREPARE welcome webpage with the 5 steps of the program in English and Spanish ................................................................................................................................. 29
      Figure 3. Easy-to-read advance directive in English and Spanish .............................................. 31
   Study Outcomes ................................................................................................................................ 33
      Table 3. Study Outcome Measures ............................................................................................... 39
   Time Frame for the Study .................................................................................................................. 43
   Data Collection, Sources, and Retention Strategies ......................................................................... 43
   Analytic and Statistical Approaches .................................................................................................. 45
      Table 4. Cumulative Loss to Follow-up at Each Time Point ............................................................ 50
   Changes to the Original Protocol ...................................................................................................... 51
      Table 5. Summary of Changes to the Original Protocol Listed by Topic ..................................... 51
      Table 6. Summary of Changes to the Statistical Analysis Plan ..................................................... 55

RESULTS .................................................................................................................................................. 56
Aim 1 Results
Table 7. Cognitive Interview Themes Obtained to Adapt and Refine PREPARE in Spanish

Aim 2 Results
Figure 4. CONSORT diagram of patients in the PREPARE trial

Characteristics of Patients
Table 8. Participant Characteristics, by Study Arms (PREPARE+AD vs AD Only)
Table 9. Characteristics of Respondents and Nonrespondents
Table 10. Reasons for Withdrawal From the Trial
Figure 5. New ACP documentation in the medical record

Table 11. New ACP at 15 Months
Figure 6. ACP Engagement Survey: Behavior Change and Action scores
Table 12. Process Measures of ACP Behavior Change
Table 13. Completion of ACP Actions
Table 14. Effect Size Estimates of ACP Behavior Change and Actions Over Time
Table 15. Interactions Effects of Patient Characteristics on ACP Documentation by Study Arm
Table 16. Ease of Use and Satisfaction Between Study Arms
Table 17. Depression and Anxiety Scores by Trial Arms
Table 18. Percentage of Participants With Increased ACP Behavior Change and Action Scores Over Time
Figure 7. Cumulative distribution function for time to ACP documentation

Aim 3 Results
Table 19. Positive Feedback About the PREPARE Program
Table 20. Constructive Feedback About the PREPARE Program
Table 21. Patient Suggestions for Dissemination
Table 22. Stakeholder Advisory Board Suggestions for Dissemination

DISCUSSION
Context for the Study Results
Generalizability of the Findings
Implementation of Study Results
Subpopulation Considerations
Study Limitations
Future Research ....................................................................................................................... 88
CONCLUSIONS ..................................................................................................................... 90
REFERENCES ....................................................................................................................... 91
RELATED PUBLICATIONS ..................................................................................................... 102
ACKNOWLEDGMENTS ......................................................................................................... 103
    Research Co-investigators (alphabetical order).............................................................. 103
    Stakeholder Advisory Board......................................................................................... 103
APPENDICES ....................................................................................................................... 105
    Appendix A: Multidisciplinary Stakeholder Team Description ........................................ 105
    Appendix B: Study Protocol ........................................................................................... 108
ABSTRACT

**Background:** Millions of older Latinos will face complex medical decisions over the course of advanced illness, yet most are unprepared. Preparation for decision-making, or advance care planning (ACP), has traditionally focused on making decisions about life-prolonging procedures (eg, cardiopulmonary resuscitation) by completing advance directives (ADs). Yet, ADs are difficult to understand; are often not completed, especially by minorities; and often fail to affect the quality of care received. Latinos account for 15% of the US population, a proportion projected to grow to 30% by 2050. Spanish-speaking patients face significant communication barriers, and literacy-appropriate ACP tools that address unique aspects of Latino culture (eg, *familismo* or strong family loyalty) are lacking. We created a patient-centered ACP website called PREPARE ([www.prepareforyourcare.org](http://www.prepareforyourcare.org)), which improves ACP engagement and is easy for English-speaking seniors to use; however, we had never tested it on Spanish-speaking patients.

**Objective:** To determine the efficacy of a patient-centered ACP website (PREPARE) in Spanish plus an easy-to-read AD compared with an AD alone to increase ACP documentation.

**Methods:** We conducted this comparative effectiveness randomized trial from November 2014 to March 2017 in multiple primary care clinics at a San Francisco safety-net hospital. Participants included patients who were Spanish speakers; were aged 55 years or older; and had at least 2 chronic or serious conditions, primary care visits, or additional clinic, hospital, or emergency department visits in the past year. We randomized patients to review the online PREPARE program plus the AD (PREPARE+AD) or the AD alone (AD only) in research offices. We provided no clinician- or system-level interventions. Staff were blinded for all follow-up assessments. The primary outcome was medical record ACP documentation at 15 months. Secondary outcomes included patient-reported ACP engagement at 1 week and at 3, 6, and 12 months using validated surveys of Behavior Change Processes (eg, self-efficacy, readiness) and actions (eg, discussing wishes with family and friends, discussing wishes with a clinician, documenting treatment preferences). We used intention-to-treat, mixed-effects logistic and linear regression, controlling for time, health literacy, baseline ACP, and clustering by physician.

**Results:** Of the 445 participants, the mean (SD) age was 64 years (± 7.0), 72% were women, and 62% had limited health literacy. The retention rate of participants at 12 months was 85.9%. New ACP documentation was higher in the PREPARE+AD arm than in the AD-only arm (adjusted 39% vs 24%; adjusted odds ratio = 1.99; 95% CI, 1.29-3.08; *P* = 0.002), and self-reported ACP engagement was higher at each follow-up period (*P* < 0.001).

**Conclusion:** Patient-facing ACP tools in Spanish, without clinician- or system-level interventions, increased documentation from 24% to 39%. Combining the PREPARE website with an AD produced higher documentation and engagement than the AD alone, suggesting usefulness among older Spanish speakers in safety-net settings.
Limitations: This study had 3 limitations: (1) Patients could not be blinded to the intervention or control to which they were randomized; (2) this study took place in only one area of the country; and (3) patients included only Spanish-speaking older populations who obtain care from a safety-net setting. These factors may affect the generalizability of our findings.
BACKGROUND

The population is aging, and the prevalence of chronic disease is increasing, especially among underserved populations. More than 37 million Americans speak Spanish at home, and Hispanics and Latinos (referred to as Latinos in this report) account for 15% of the US population; this proportion is projected to grow to 30% by 2050.

One critical gap in care for Latinos relates to advance care planning (ACP), which refers to engagement rates in the United States (less than 20%). Guidelines recommend ACP because studies have showed that it reduces stress in surrogate decision-makers and results in receipt of medical care that is better aligned with personal values. However, most older adults, including Latinos, have not engaged in ACP, and patients’ wishes are often not documented in the medical record.

In gap analysis and systematic reviews, ACP “usual care” focused on the completion of a legal advance directive form (AD) and the prespecification of preferences for life-sustaining procedures (eg, cardiopulmonary resuscitation [CPR]). Such usual practices do not, however, adequately prepare patients or surrogate decision-makers for complex, interdependent, and unanticipated decisions over the course of illness.

Most ADs are written in complex, legal language, which may explain why they are often not completed. Most studies show that ADs, without discussions, do not affect the quality of care or improve clinicians’ or surrogates’ understanding of patients’ wishes. This might be because ADs focus on life-prolonging procedures, while patients and surrogates often struggle over the course of illness with many other types of decisions that they are unprepared to make. ADs also fail to lessen the stress of decision-making or help patients communicate wishes to surrogates or clinicians. Surrogates are also often unaware of patients’ preferences and are poorly prepared to make decisions for others.

Although ACP engagement has been improving over time, rates have been less encouraging for minorities and patients with limited health literacy. Spanish-speaking patients face significant communication barriers, and literacy-appropriate ACP tools that
address unique aspects of Latino culture (eg, *familismo* or strong family loyalty) in Spanish are lacking. For minorities, including Latinos, decisions are complicated by a lack of trust and perceived racism, and often by the receipt of less information from clinicians than other patients. In addition, many Latinos prefer that family and doctors make medical decisions for them.

Furthermore, previous studies of patient-directed ACP tools in primary care have been less effective in increasing ACP documentation (5%-23%) than coaching or facilitation. The use of trained clinicians or ACP facilitators has resulted in improvements of 50% or more among English- and Spanish-speaking patients. However, many health care organizations, especially public and safety-net settings, do not have the resources to train dedicated ACP facilitators.

**Easy-to-Use ACP Tools**

To help overcome some of these barriers, we created easy-to-use, patient-facing ACP tools. First, we developed a broadened paradigm of ACP that focuses on preparing patients to identify and communicate their wishes and to make informed medical decisions over the course of illness. Then, in partnership with Spanish-speaking older patients and community stakeholders, we created an easy-to-read AD in Spanish that statistically significantly increased 6-month documentation rates.

We also created an online ACP program called PREPARE to provide a step-by-step guide through the ACP process. PREPARE includes video stories and was designed to be used at home (see pictures of the webpages below). We based our design of PREPARE, specifically the use of an online medium and video stories that model ACP behaviors, on several theoretical constructs. (For an in-depth description of the PREPARE program and the interventions and theoretical constructs we used, see the Methods section.) The PREPARE website has improved ACP engagement among older English-speaking veterans. However, no prior study has tested its effects among diverse, older Spanish-speaking patients. Therefore, we adopted and translated the easy-to-read AD and PREPARE into Spanish (PREPARE Su Cuidado Médico) to test these interventions among Spanish speakers.
PREPARE is a step-by-step program with video stories to help you:

- Have a voice in YOUR medical care
- Talk with your doctors
- Give your family and friends peace of mind

PREPARE videos help you answer questions about your medical wishes.

- You can print a summary of your wishes
- You can also fill out an easy-to-read advance directive

Click the video above to learn more.

Start PREPARE

FREE PREPARE Easy-to-read Advance Directives and other tools below.▼

PREPARE es un programa paso a paso con historias en video para ayudarle a:

- Ser participe en SU cuidado médico
- Hablar con sus doctores
- Darle tranquilidad a su familia y amigos

Los videos de PREPARE le ayudan a responder preguntas sobre sus desesos médicos.

- Usted puede imprimir un resumen de sus deseos
- Usted también puede llenar un formulario de instrucciones anticipadas de atención de salud de fácil lectura

Haga clic en el video para aprender más.

Comience a usar PREPARE

Formulario de Instrucciones Anticipadas de fácil lectura de PREPARE gratuito y otras herramientas abajo.▼
Aims

The main research question and objective of this randomized trial was to compare the efficacy of PREPARE plus the easy-to-read AD in Spanish (PREPARE+AD) with the AD alone in Spanish (AD only) to improve ACP documentation and engagement. We hypothesized that ACP documentation and self-reported ACP engagement would increase in both arms but would be greater in the PREPARE+AD arm.

**Aim 1:** Adapt and refine PREPARE in Spanish through cognitive interviews with Spanish-speaking Latinos and stakeholders.

**Aim 2:** Conduct a randomized controlled trial (RCT) to compare the efficacy of PREPARE plus a previously tested, easy-to-read AD (PREPARE+AD: intervention) vs the AD alone (control) to do the following:

2a: Engage older Spanish-speaking Latinos in multiple ACP behaviors (ie, identify and discuss wishes with surrogates and clinicians and complete ADs) measured by self-report and medical report review.

2b: Improve self-efficacy and satisfaction with medical decision-making.

2c: Determine whether PREPARE efficacy varies by literacy, decision control preferences, or clinician–patient language concordance.

**Aim 3:** Disseminate PREPARE with input from patients, caregivers, and stakeholders.

Significance

This contribution is significant because it is an incremental step along a continuum of research to develop, implement, and disseminate easy-to-access, self-sustaining interventions designed to empower older Latinos to engage in ACP in the community or clinical setting. If we find that PREPARE improves engagement in the ACP process among older Latinos, then these patients might be able to use PREPARE to help them discuss ACP with their doctors and surrogate decision-makers. This increased engagement in ACP could improve quality of and
satisfaction with medical care and result in the receipt of medical care that is aligned with patients’ wishes.5-9

Innovation

This research is innovative because it explores a new paradigm of ACP focused on preparing patients to communicate with surrogates and clinicians and to make informed decisions during their illness. PREPARE is patient-centered and culturally and linguistically appropriate. It provides video stories that model ACP behaviors and can be used and completed in the home. PREPARE is also free to the public and can be easily used and disseminated in the Latino community.
PARTICIPATION OF PATIENTS AND OTHER STAKEHOLDERS

Description of the Stakeholder Advisory Board

We engaged the Latino community in the ongoing development of our patient-centered ACP interventions. We recruited our diverse stakeholder advisory board using snowball sampling, through our research collaborators and community partners, in person, by telephone, or by letter or email. We recruited many types of stakeholders: (1) research co-investigators (4 individuals); (2) patient, caregiver, and patient advocate stakeholders (3 individuals, including 2 native Spanish-speaking patients); (3) community stakeholders (3 individuals); and (4) clinical stakeholders (7 individuals, including 2 nurses, a psychologist, and a social worker). The stakeholder advisory board roles and charter are in the protocol, and Appendix A documents the stakeholders’ names, credentials, and roles in the project.

Our stakeholders engaged in this work because they believe ACP is an important activity. They helped us with all aspects of the study, including the following:

1. Defining the study questions
2. Defining study outcomes
3. Defining the patient population and inclusion and exclusion criteria
4. Providing advice about recruitment and retention
5. Monitoring our study conduct and patient safety
6. Providing suggestions for publishing our research outcomes
7. Providing suggestions for disseminating our findings and the PREPARE materials

Impact of the Stakeholder Advisory Board

The impact of the engagement of the stakeholder advisory board was invaluable. This was particularly true with respect to ensuring transparency of the research process, protecting patient safety, obtaining buy-in and support of clinical champions to help with patient
recruitment and retention, and helping our team consider how to adapt research evidence into practice. Table 1 presents notable impacts of the stakeholder efforts.
Table 1. Notable Impacts of Engaging Diverse Stakeholders

<table>
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<tr>
<th>Category</th>
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<tbody>
<tr>
<td>Cultural competency of our materials</td>
<td>Stakeholders extensively vetted our study materials and informed consent forms and protocols for recruitment, retention, and depression assessment, enabling us to elevate the cultural competency of our materials and to ensure a high level of patient safety.</td>
</tr>
<tr>
<td>Decisions about hiring</td>
<td>Stakeholders and co-investigators agreed that we would attempt to hire native Spanish-speaking research staff when able and appropriate; consequently, all but one of our research assistants and volunteers were native Spanish-speakers. The one research assistant who was not a native speaker was fluent, had lived in Mexico for more than 5 years, and worked as a trained Spanish interpreter.</td>
</tr>
<tr>
<td>Patient recruitment</td>
<td>A specific and important example of stakeholder impact relates to recruitment. Although we allowed for recruitment by phone in our IRB applications and study protocols, we had only ever attempted in-clinic, in-person recruitment because of concerns about mistrust of research within the Latino community. However, in-clinic recruitment is time consuming and it was preventing us from reaching our increased recruitment goals to meet the PCORI milestones. Our stakeholder advisory board advised us that sending recruitment letters and cold calling to increase our recruitment would be acceptable to the Latino population. The board reviewed and helped refine our recruitment scripts, and the method worked very well. Our refusal rate remained the same, but this method took approximately 25% less time than in-clinic recruitment to enroll a study participant. The board’s advice helped us reach our milestones.</td>
</tr>
<tr>
<td>Patient follow-up</td>
<td>The stakeholder advisory board discussed how our team should best approach patients when conducting home visits or how we should change the study scripts when making repeated phone calls for difficult-to-reach study participants. One suggestion was to say that we were concerned for the patient and were checking in, as they had not been answering our calls. Our patient advisors suggested that this would show participants we care for their well-being and would help build rapport between study staff and patients.</td>
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<tr>
<td><strong>Patient safety</strong></td>
<td>The stakeholder advisory board reviewed our consent forms to ensure they were readable and understandable to our patient population. Because we assess depression in this study (as requested per our DSMB), the board also reviewed our depression algorithms and helped us create study scripts and protocols for our research assistants in the event a patient reported severe depression. We had to use this protocol only a few times, but it helped the study staff feel much more at ease with asking questions about depression and knowing the next steps.</td>
</tr>
<tr>
<td><strong>Suggestions for reporting study data</strong></td>
<td>Our stakeholder advisory board requested we quantify the number and percentage of patients who increased their ACP activities over time, not just report mean score numbers. Our stakeholders perceived any increase in an ACP activity over time as clinically meaningful. Thus, in addition to mean change in ACP Engagement scores, they wanted to know the percentage of patients who improved (ie, had an estimated slope &gt; 0) over time for Behavior Change scores, Action scores, and both combined. We therefore created this variable post hoc.</td>
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| **Dissemination**              | We received helpful suggestions for dissemination, including the following:  
  • Continue to use PREPARE and the easy-to-read advance directives because patients can use these tools on their own in resource-poor environments.  
  • Use hospital volunteers, peer mentors, and the hospital’s patient advisory boards to disseminate PREPARE materials and help start the conversation.  
  • Use the behavioral health teams at the general medicine clinic and family health centers to start the conversation.  
  • Have front desk staff hand out advance directives and the PREPARE pamphlets.  
  • Have the PREPARE videos playing in the waiting room.  
  • Consider adding PREPARE information on the hospital patient portals.  
  • Consider presenting PREPARE in group medical visits in primary care.  
  • Consider large-scale dissemination partnerships such as with our community partnerships, the ZSFG Wellness Center, and AARP and CMS and national Medical Legal Partnerships.                                                                                                                                                                                                                           |
METHODS

Study Overview

The trial used blinded outcome ascertainment to determine the efficacy of an online PREPARE ACP program compared with an easy-to-read AD to engage ethnically diverse Spanish-speaking older primary care patients in the ACP process. The conceptual framework47 and the trial protocol have been previously published.54 The protocol is also included in Appendix B.54 The study protocol includes further information about the study setting; eligibility criteria; study flowchart; recruitment, consent, randomization, blinding, and retention procedures; intervention and control conditions; analytic plan; sample size; intervention fidelity and data collection methods; and primary and secondary outcomes (including questionnaire validity, reliability, and response options). The published conceptual framework is also described in the Interventions and Comparators section.

Figure 1, the PREPARE study flow diagram, depicts the steps for this trial. We obtained a Health Insurance Portability and Accountability Act (HIPAA) waiver to identify individuals who met our inclusion and exclusion criteria and had upcoming primary care appointments. We used both administrative data and medical record review to determine potentially eligible patients. We then obtained primary care clinicians’ permission to allow the study team to inform their patients about the study. Next, we recruited patients, screened them for eligibility, and scheduled them for a baseline interview before an upcoming primary care appointment. To standardize the timing of exposure to the intervention and primary care follow-up, we scheduled study participants for baseline procedures 1 to 3 weeks before an upcoming primary care appointment.55 We then obtained informed consent and randomized those patients who provided consent to either the PREPARE intervention arm (ie, the PREPARE website with action plan exercises, an easy-to-read AD, and PREPARE materials to take home—a website login, pamphlet, booklet, and DVD) or the control arm (ie, the AD alone).

We then conducted blinded outcome ascertainment by performing medical record reviews to determine ACP documentation at baseline and at the end of the study (15 months).
We also conducted blinded outcome ascertainment using patient surveys at 1 week and 3, 6, and 12 months after the primary care appointment.

Study Design

This study was a single-blind (staff blinded), parallel-group, comparative effectiveness trial randomized at the patient level. We chose an active control arm (ie, an easy-to-read AD) because we believe that providing an AD for chronically and seriously ill older patients should be the standard of care, even if it is not often “usual” care in clinical practice. Given the potential benefits of ACP, we decided, with our stakeholder advisory board, to perform a comparative effectiveness study and provide all participants some form of ACP. The AD used in this study has been adopted by Zuckerberg San Francisco General Hospital and Trauma Center (ZSFG) and is available in its primary care clinics.

Both PREPARE and the AD are available in Spanish and are written at a fifth-grade reading level. They were designed with and for diverse older adults from several community and clinical settings and cultural backgrounds. Neither patient-facing tool requires clinician- or system-level involvement to begin the ACP process; therefore, we did not include any clinician, electronic health record, or system-level interventions in this trial.
Figure 1. PREPARE study flow diagram

- **Administrative data pull and chart review from ZSFG**
  - Language listed as Spanish
  - ≥ 55 years of age and ≥ 2 chronic illnesses
  - Seen by primary care physician ≥ 2 times in the past year + ≥ 2 additional inpatient or outpatient visits
  - Not deaf, blind, demented, or psychotic

- **Obtain clinicians’ permission to tell their patients about the study**

- **Screen for eligibility**
  - Excluded if they report not speaking Spanish “well” or “very well”
  - Excluded if they report poor vision, lack of a phone, out of the country ≥ 3 months
  - Excluded if they test positive for moderate-to-severe cognitive impairment

- **Baseline Survey: 1-3 weeks prior to primary care visit**
  - Chart review to assess ACP documentation
  - In-person survey to assess baseline ACP engagement, moderator and mediator variables, and demographic variables

- **Block randomized by health literacy level (limited vs. adequate literacy)**

- **PREPARE INTERVENTION**
  - PREPARE website in Spanish
  - Action plan created within the website
  - Easy-to-read advance directive in Spanish
  - To take home: website login and PREPARE booklet, pamphlet, and DVD

- **CONTROL**
  - Easy-to-read advance directive only
    - (Spanish)

- **Post-intervention acceptability and usability questionnaire for feasibility**

- **Reminder phone call 1-3 days prior to primary care visit**
  - **PREPARE**: Remind to discuss ACP and bring advance directive
  - **Control**: Remind about visit

- **1-week, 3-month, and 6-months follow-up interview (phone or in-person)**
  - Assess ACP engagement

- **Final follow-up**
  - Assess ACP engagement in 12 month interview (phone or in-person)
  - Chart review to assess ACP documentation at 15 months

**Abbreviations**: ACP, advance care planning; ZSFG, Zuckerberg San Francisco General Hospital
Study Setting

The San Francisco Health Network (SFHN) is the safety-net system in San Francisco. It consists of 11 federally qualified primary care clinics, including ZSFG, which has 582 licensed beds. SFHN cares for more than 105,000 patients and more than 30,000 Spanish speakers (> 90% Mexican and Central American). ZSFG is an urban, public hospital that, with SFHN, serves racially and ethnically diverse, low-income and indigent patients; 30% of patients are Spanish speakers. Recruitment for this randomized trial occurred in 4 separate primary care clinics associated with SFHN and ZSFG. These 4 clinics are housed in 3 separate physical locations in San Francisco.

Participants: Forming the Study Cohort

Target Population and Relevance to the Research Question

This is the first study to test PREPARE among Spanish-speaking older adults in safety-net, primary care settings. The inclusion and exclusion criteria are specified below.

Target Sample Size and Minimum Clinically Significant Difference Used in Calculating It

Our primary outcome is ACP documentation. Prior research demonstrates an estimated effect size of ACP interventions on ACP documentation of 0.50 standard deviations (SDs). Because both the intervention arm and the control arm received the AD, we assumed that both arms would have an AD completion rate of ≤ 15%. We estimated that PREPARE would result in a 0.5 (2-fold) increase above 15%. We estimated that a sample of 350 patients (175 per arm) would afford us 92% power (2-tailed α of 0.05) to detect a difference of ACP documentation of 15% in the control arm vs 30% in the PREPARE arm and 80% power to detect a difference of 15% vs 27%. We expected a 15% dropout rate at 12 months based on our prior RCT at ZSFG; therefore, we planned to recruit 402 patients, or 201 in each arm.

We determined that we would have adequate power to detect clinically important interactions with ACP documentation based on health literacy because a prior trial of the easy-to-read AD was able to detect an interaction with only 200 patients.
Recruitment Strategies

We used weekly administrative data pulls from the electronic health record to identify patients with upcoming primary care appointments and to target patient recruitment efforts.

We obtained permission from the medical directors of all primary care programs to contact primary care clinicians and patients. We then sent providers a letter and secure email asking permission to contact their patients to further explain the study. We had a potential pool of 125 clinicians, most of whom cared for no more than 3 to 4 eligible patients on average. We provided clinicians a list of their patients to review. Clinicians could provide a blanket consent for all patients, identify individual patients from the list who they did not want our team to contact, or refuse consent for all patients. If we did not hear back from the clinician after 3 attempts to obtain permission, we assumed assent.

Recruitment materials. We posted Spanish-language study-related flyers written at a fifth-grade reading level in approved areas in the primary care clinics. To enhance recruitment, we also mailed patients Spanish-language letters and postcards written at a fifth-grade reading level that described the study and provided a telephone number to either opt out or call to learn more about the study. If patients did not opt out within 1 week of the mailings, we deemed them eligible to be contacted so that we could assess both their willingness to participate in the study and their eligibility. We contacted potential participants by phone or in the clinic. To standardize the timing between intervention exposure and primary care follow-up, we scheduled patients for the baseline interview and exposure to either PREPARE+AD or AD only 1 to 3 weeks before their upcoming primary care appointment.

Reimbursement. Patients who consented and enrolled were paid $50 for the baseline interview and given $10 municipal transportation vouchers to help them return for in-person follow-up interviews if they desired. Participants were also reimbursed $25 for each of the 1-week and 3-, 6-, and 12-month interviews. All surrogates were paid $25 for 1 interview at 12 months.
Enhancing recruitment. We employed several strategies to enhance our recruitment of this vulnerable population. First, we attempted to hire individuals who had experience with diverse populations and individuals who were bilingual and bicultural. Second, we conducted sensitivity training with all research staff members and required them to use approved study scripts. Sensitivity training included unconscious bias training provided through the University of California, San Francisco. Topics were reviewed during weekly team meetings as needed. Study scripts and all study materials used for recruitment were vetted, updated, and approved by our stakeholder advisory board. All materials and study scripts were written at a fifth-grade reading level and were provided to patients in Spanish.

Inclusion and Exclusion Criteria

We pulled administrative data weekly to identify patients who met eligibility criteria and who had an upcoming primary care appointment. Staff members screened participants to confirm eligibility before enrollment and collected data using Research Electronic Data Capture (REDCap). Table 2 lists our inclusion and exclusion criteria.
<table>
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<th><strong>Table 2. Inclusion and Exclusion Criteria of Participants</strong></th>
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<tr>
<td><strong>Patient Participants</strong></td>
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<tr>
<td><strong>Inclusion criteria</strong></td>
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<tr>
<td>Is 55 years of age or older</td>
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<tr>
<td>Obtains care in the primary care clinics of SFHN or ZSFG</td>
</tr>
<tr>
<td>Has been seen at least twice in the past year by a primary care provider (a measure of established primary care) and had at least 2 additional visits to ZSFG in the past year (a measure of frequently accessing the medical center)</td>
</tr>
<tr>
<td><strong>Exclusion criteria</strong></td>
</tr>
<tr>
<td>Has a clinician who is the PI, Co-I, or member of the stakeholder advisory board</td>
</tr>
<tr>
<td>Was in a prior PREPARE-related study, such as a focus group or pilot study&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Has dementia determined by clinician assessment, medical record review, or self-report</td>
</tr>
<tr>
<td>Has blindness or poor vision determined by clinician assessment, medical record review, self-report of blindness, or the inability to read print on a newspaper&lt;sup&gt;57&lt;/sup&gt;</td>
</tr>
<tr>
<td>Is deaf as determined by clinician assessment, self-report, medical record review, or research staff assessment</td>
</tr>
<tr>
<td>Has cognitive impairment as assessed by research staff by deficits on the Short Portable Mental Status Questionnaire (SPMSQ)&lt;sup&gt;58&lt;/sup&gt; and the Mini-Cog&lt;sup&gt;59,60&lt;/sup&gt;</td>
</tr>
<tr>
<td>Has delirium or psychosis as assessed by a clinician or research staff</td>
</tr>
<tr>
<td>Does not report speaking Spanish “well” or “very well”</td>
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<tr>
<td>Lacks a phone for additional study contacts and follow-up interviews</td>
</tr>
<tr>
<td>Has active drug or alcohol abuse within the past 3 months determined by clinician assessment, self-report, medical record review, or research staff assessment&lt;sup&gt;a&lt;/sup&gt;</td>
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<tr>
<td>Reported being out of town during their scheduled follow-up interview dates outside a window of 3 months</td>
</tr>
<tr>
<td>Reported being a spouse or surrogate of another enrolled participant&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Was unable to answer consent teach-back questions after 3 attempts</td>
</tr>
<tr>
<td>Had 2 or more no-show baseline interview appointments without rescheduling&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

Abbreviations: Co-I, co-investigator; PI, principal investigator; SFHN, San Francisco Health Network; ZSFG, Zuckerberg San Francisco General Hospital.

<sup>a</sup> These exclusion criteria were updated after input from our stakeholder advisory board. See the Changes to the Original Protocol section.
We had no inclusion or exclusion criteria based on gender, race, or health literacy level. Although we recruited Spanish speakers, we did not exclude any participant based on ethnicity. We assessed eligibility in person or over the phone. In brief, patients were included if they were ≥55 years old, had ≥2 chronic medical conditions determined by medical record review, had ≥2 visits with a primary care provider (ie, physician, nurse practitioner, or physician assistant) in the past year (ie, a marker of established care), and had ≥2 additional outpatient or inpatient visits with any provider in the past year (ie, a marker of frequent access).

We chose to recruit patients ≥55 years of age (rather than ≥65) because adults in safety-net settings experience accelerated aging, functional decline, and sequelae of chronic disease, necessitating decision-making and ACP at a younger age than patients with higher socioeconomic status. Our goal was to start ACP early to change the trajectory of decision-making and care over the course of illness. To enhance recruitment and follow-up, we set an inclusion criterion of ≥2 primary care visits and ≥2 additional visits in the past year, which ensured that patients had established primary care and accessed care frequently.

We excluded patients if their clinician was a principal investigator, co-investigator, or clinician member of the stakeholder advisory board or if they had been enrolled in a previous pilot study of the PREPARE website. We also excluded participants if they had medical record documentation of being deaf, being blind, having dementia, or being psychotic, or were deemed by their clinician to be too mentally or physically ill to participate. In addition, we excluded participants if evidence existed of active drug or alcohol abuse within the past 3 months as determined by clinician assessment, self-report, medical record review, or research staff assessment. Through in-person or phone screening by study staff, we also excluded patients for several other reasons: if they self-reported vision too poor to read a newspaper; lacked a phone (needed for follow-up interviews and scheduling); planned to be out of the country for ≥ 3 months; screened positive for moderate-to-severe cognitive impairment using the validated Short Portable Mental Status Questionnaire (SPMSQ) followed by the Mini-Cog; or self-reported or were determined by study staff to be blind, deaf, intoxicated, or
actively psychotic. Because ACP is an iterative process,\textsuperscript{12,67} we did not exclude patients with prior ACP experiences (eg, an AD).

To minimize the risk of contamination among patients within the same physician’s practice, study staff delivered the interventions in research study offices outside the clinic. Furthermore, we provided no additional training or materials to the clinicians or to clinic staff.

To minimize the risk of contamination by fellow research participants, we excluded any spouse or partner of a currently enrolled patient who was also receiving care in the SFHN or at ZSFG, met the eligibility criteria, and therefore, was also a potential patient participant. This avoided a situation in which 2 closely related people living in the same home could be randomly assigned to different study arms. We also excluded any patients who had been enrolled in a previous PREPARE-related study or were known to have previously been exposed to PREPARE (eg, evidence of PREPARE exposure in a note in their medical record).

To save research staff considerable time and effort, we considered ineligible those potential participants who missed a baseline interview appointment (ie, no-shows) more than 2 times without prior notification and rescheduling, unless there were extenuating circumstances.

**Forming the Study Arms and Any Differences in How They Were Formed**

We used the same methods to form both the control and the intervention arms. As described previously, our point of first contact with both arms occurred 1 to 3 weeks before a primary care appointment, and we conducted recruitment through study flyers, mailed study postcards, in-clinic recruitment, or telephone calls. These methods, including the randomization procedures discussed in the Randomization Procedures and Concealing the Sequence of Random Assignment section, did not differ between arms.

**Process for Collecting Baseline Data**

As described under Study Overview, we obtained a HIPAA waiver to access patient characteristics for eligibility purposes (Protocol, Appendix B). We also collected information on
inclusion and exclusion criteria (Table 2) during the screening process in person or by phone. Other baseline data were collected in person during the baseline interview. To maintain fidelity to the study protocol, we trained study staff to use study scripts. Senior research staff also observed a 10% random sample of all interviews to ensure study fidelity.

**Consent procedures.** We used a modified consent process that several co-authors designed for vulnerable populations. Consent forms written at the fifth-grade reading level were provided and read to participants in Spanish. Participants were told there was a “50/50” chance of being in either of the 2 groups. This review of the consent form was followed by standardized “teach-to-goal” questions to ensure understanding. We deemed potential participants ineligible if they could not correctly complete the teach-back process after 3 attempts.

**Ascertainment of Reasons That Screened Individuals Declined to Participate**

We asked all potential participants who refused to enroll in the study if their decision was based on any the following factors:

- They were not interested in the study or topic.
- They would refuse to be in ANY research study (ie, they mistrust research in general).
- They were too busy due to other commitments (eg, work, caretaking).
- They could not commit to the time required for the interview or the follow-up schedule.
- They self-reported that their health was too poor to participate.
- A family member who answered the phone refused on the patient’s behalf due to poor health.
- They reported health privacy concerns (ie, concerns about privacy of medical information or distrust of the clinic or hospital).
- They declined because of travel or distance commuting for the baseline interview.
- They could not state a reason.
We also tracked the number of individuals who were interested and eligible but whom we could not schedule for a baseline interview during the study period due to scheduling issues, such as their work or caregiver responsibilities.

**Randomization Procedures and Concealing the Sequence of Random Assignment**

Randomization occurred at the patient level. A statistician not involved in recruitment or data collection used a computer-based random number generator to create a randomization scheme using block randomization by health literacy (adequate health literacy vs limited health literacy, as determined by a validated question concerning confidence with medical forms).\(^{69}\) We used random block sizes of 4, 6, and 8 to ensure an equal number of patients with limited health literacy were in each group. Randomization information was associated with a unique patient identification number and was kept separate from other patient data. We concealed randomization through the screening for eligibility process. However, we were unable to conceal randomization before informed consent due to the logistics of scheduling study rooms, a scarce resource at ZSFG. We allocated an additional 60 minutes for room scheduling for individuals who were randomized to the PREPARE arm.

**Blinding.** We were unable to blind patient participants to the intervention. However, they were told during informed consent that each research subject would review 1 of 2 guides and that they had a “50/50 chance” of getting 1 of the 2 interventions. We provided each arm with ACP materials and did not tell participants which interventions were associated with the intervention arm (PREPARE+AD) or the active control arm (AD only).

However, research staff remained blinded for all follow-up assessments. To ensure blinding of all outcome assessments, the research staff member who completed the baseline interview and randomization for a particular participant did not conduct that participant’s follow-up interviews. At the start of all follow-up interviews, we reminded participants not to discuss the study materials they reviewed. If, however, during the follow-up interview the research assistant became unblinded (ie, the participant mentioned the PREPARE website), we
noted this information in our database and we assigned the participant a new blinded research assistant for all subsequent interviews.

Interventions and Comparators

**Study Interventions and Why They Were Chosen**

*The PREPARE Online ACP Program.* PREPARE is an easy-to-use, patient-centered, interactive online educational program that is available in English or Spanish, is written at a fifth-grade reading level, and includes voice-overs of all text for the reading impaired and closed-captioning of all videos for the hearing impaired ([www.prepareforyourcare.org](http://www.prepareforyourcare.org)). The theoretical framework of PREPARE and this study was based primarily on Social Cognitive Theory, with elements from the Health Belief Model, the Theory of Planned Behavior, and Behavior Change Theory.

In these theories and in behavioral studies, modeling behaviors (ie, actually showing people how to do something) helps people change their behavior. Successful behavioral change interventions model skills, enhance self-efficacy, and address perceived barriers, especially literacy-appropriate interventions. Modeling behaviors (as in PREPARE) can also improve patients’ ability to communicate with clinicians and improve outcomes, such as increased question-asking behavior and a sense of control during a clinical visit, an increased desire to participate in decision-making, and improved affect and functional status.

PREPARE incorporates these successful teaching methods by modeling behaviors in videos. Videos and interactive websites are more powerful mediums to teach information and change behavior than written materials, especially for those with language or literacy barriers. PREPARE also includes a training and goal-setting component (ie, an action plan). Action plans are effective in changing outpatient behaviors, such as exercise, and help patients engage in other preventative and disease management activities in the outpatient setting. To ensure that PREPARE content is acceptable to individuals from diverse cultural backgrounds, we used extensive formative research and cognitive interviewing with the target
population (ie, racially and ethnically diverse older adults with limited health literacy and English proficiency).53

The PREPARE website leads people through a 5-step ACP process that ranges from choosing a surrogate decision-maker to asking their clinicians the right questions (Figure 2). PREPARE also helps them answer personal values questions about their medical care and create an action plan to engage in some form of ACP.
Figure 2. PREPARE welcome webpage with the 5 steps of the program in English and Spanish
**Active comparator.** We chose an active control arm—ie, an easy-to-read AD (Figure 3)—because we believe providing an AD for chronically and seriously ill older patients should be the standard of care, even if it is not often “usual” care in clinical practice. We created the easy-to-read AD in partnership with Spanish-speaking older patients and community stakeholders. In an RCT among older English-speaking and Spanish-speaking patients at ZSFG, this AD increased 6-month documentation rates and was overwhelmingly preferred to the standard form. ZSFG has already adopted this AD and makes it available in its primary care clinics.

**Administration and duration of the interventions.** For the intervention arm (PREPARE+AD), after the baseline interview, participants reviewed all 5 steps of the PREPARE website in Spanish in our research offices that had internet access. We asked participants to review PREPARE on their own and in its entirety. Research assistants were available to answer questions if needed but did not go through the website with the participants.

At the end of the program, a summary of the PREPARE+AD participants’ medical wishes and action plan were automatically generated from the PREPARE website in written format. We asked participants to review the easy-to-read AD for at least 5 minutes and up to 15 minutes. We then gave participants both the AD and a PREPARE pamphlet, booklet, and DVD to take with them in case they did not have internet access at home.
Figure 3. Easy-to-read advance directive in English and Spanish

California Advance Health Care Directive

This form lets you have a say about how you want to be cared for if you cannot speak for yourself.

This form has 3 parts:

Part 1 Choose a medical decision maker, Page 3
A medical decision maker is a person who can make health care decisions for you if you are not able to make them yourself.
They are also called a health care agent, proxy, or surrogate.

Part 2 Make your own health care choices, Page 6
This form lets you choose the kind of health care you want.
This way, those who care for you will not have to guess what you want if you are not able to tell them yourself.

Part 3 Sign the form, Page 11
The form must be signed before it can be used.

You can fill out Part 1, Part 2, or both.

Fill out only the parts you want. Always sign the form in Part 3.
2 witnesses need to sign on Page 12, or a notary on Page 13.
Instrucción anticipada de atención de salud

Advance Health Care Directive

Este formulario le permite indicar cómo desea ser atendido si está muy enfermo.
This form lets you have a say about how you want to be cared for if you cannot speak for yourself.

Este formulario consta de 3 partes: This form has 3 parts.

Parte 1

Escoger una persona decisora, Página 3
Part 1: Choose a medical decision maker, Page 3
Una persona decisoría es una persona que puede tomar decisiones médicas por usted si está muy enfermo para tomarlas por usted mismo.
A medical decision maker is a person who can make health care decisions for you if you are not able to make them yourself.
También se les llama un agente de salud, un representante, o un sustituto.
They are also called a health care agent, proxy, or surrogate.

Parte 2

Tomar sus propias decisiones de atención de salud, Página 6
Part 2: Make your own health care choices, Page 6
Este formulario le permite escoger el tipo de atención de salud que desea. De esta manera, las personas encargadas de su cuidado no tendrán que adivinar lo que desea si está muy enfermo para decirlo por usted mismo.
This form lets you choose the kind of health care you want. This way, those who care for you will not have to guess what you want if you are not able to tell them yourself.

Parte 3

Firmar el formulario, Página 11
Part 3: Sign the form, Page 11
El formulario se debe firmar antes de que se pueda usar.
The form must be signed before it can be used.

Usted puede llenar la Parte 1, la Parte 2, o ambas. You can fill out Part 1, Part 2, or both.
Llene sólo las partes que desee. Siempre firme el formulario en la Parte 3.
Fill out only the parts you want. Always sign the form in Part 3.
Es necesario que 2 testigos firmen en la página 12, o que un notario firme en la página 13.
2 witnesses need to sign on page 12, or a notary on page 13.

Su Nombre: Your Name
For participants in the control arm (AD only), we gave them only the easy-to-read AD, asked them to review it for at least 5 minutes and up to 15 minutes in study offices, and gave them the form to take home if they wished. Research assistants were available to answer questions if needed but did not go through the form with the participants.

For participants in both arms, we made reminder phone calls 1 to 3 days before their next scheduled primary care appointment. For participants in the PREPARE+AD arm, we reminded them to bring their study materials (ie, action plan and AD) and to talk to their clinician about ACP. For participants in the AD-only arm, research staff members reminded them only about their upcoming appointment and did not provide additional encouragement about ACP.

Study Outcomes

In this section, we describe all outcomes for the 3 study aims. We also provide a full description of all primary and secondary outcomes, including the validity, reliability, references, and the schedule of administration, in the Study Protocol (Appendix B).

Aim 1

Adapt and refine PREPARE in Spanish through cognitive interviews with Spanish-speaking Latinos and stakeholders.

The outcomes for aim 1 included obtaining qualitative input from patients about what we needed to update on the PREPARE website in Spanish for it to be appropriate for use with diverse older adults. Through cognitive interviews, we gathered information about what participants liked and did not like overall, and what they liked and did not like about the wording of PREPARE, the instructions, the colors, the pictures, and the formatting:

- What did you like about these materials? What did you not like? Why?
- Were there any pictures/actors/videos, words, or instructions that you liked or did not like? Why?
Aim 2

Conduct an RCT to compare the efficacy of PREPARE plus an easy-to-read AD (intervention) vs the AD alone (control).

Outcome Overview

Because ACP ideally is a process that occurs over time, our team decided that assessing a full range of ACP measures was important. These included ACP documentation over time (the primary outcome) as well as several behavior change constructs and several additional ACP actions over a 12-month period (secondary outcomes). All study measures used in this analysis, including validity and reliability of information and the schedule of administration (ie, baseline; 1 week; and 3, 6, and 12 months), are described in the following sections and in a previously published protocol.54

Primary Outcome

The primary outcome is documentation of ACP wishes in the ZSFG/SFHN medical record from enrollment to 15 months. ACP documentation included 4 categories: (1) the easy-to-read AD or other valid ADs or living wills; (2) a durable power of attorney for health care document; (3) a Physician Orders for Life-Sustaining Treatment form; or (4) other documentation that demonstrated a discussion concerning patients’ surrogate or wishes for medical care (ie, notes describing patients’ goals for medical care by clinicians). Staff members reviewed 100% of participants’ medical records by hand, and 2 independent and blinded research assistants reviewed all records. Training materials concerning how to code ACP documentation were created and provided to all research staff. This training included a PowerPoint training curriculum and extensive examples from participants’ records. The trainer directly observed the staff’s coding of ACP documentation for the first 10% of coding and continued observation until the trainer and the staff reached agreement in coding. Coding questions and examples were also presented at weekly meetings. The ACP documentation was double coded for all participants. The principal investigator reviewed any discrepancies and the study team discussed all cases until 100% agreement was obtained.
We assessed baseline and 15-month ACP documentation rates. Patients in our study were enrolled, randomized, and exposed to the intervention 1 to 3 weeks before a primary care appointment. We timed ACP documentation to the date of intervention exposure because patients might have engaged in ACP before seeing their primary care provider. The patient-reported outcomes in the follow-up surveys (1 week and 3, 6, and 12 months), however, were timed to the primary care visit because those questions addressed engagement in discussions with clinicians (see the Main Patient-reported Secondary Outcomes section). This time frame for ACP documentation was determined from a prior PREPARE trial conducted within the Department of Veterans Affairs to standardize the expected time from intervention exposure to the primary care visit and the anticipated time to schedule and complete the final patient interview.52

Because legal forms and documented discussions can be used to direct medical care, we created a composite variable of any ACP documentation (ie, forms and discussions). We also reported the percentages of forms and discussions separately. Two independent research assistants double-coded all medical review data. The principal investigator adjudicated discrepancies.

**Main Patient-reported Secondary Outcomes**

The main patient-reported secondary outcome is the validated ACP Engagement Survey,53,55,92 measured at baseline, at 1 week, and at 3, 6, and 12 months. We chose this outcome to measure the full process of ACP, and it contains both a Behavior Change Process component and an Action component. The survey measures ACP Behavior Change Processes, such as knowledge, contemplation, self-efficacy, and readiness, on a validated 57-item scale. We measured the ACP Behavior Change Process on a 5-point Likert scale and calculated average 5-point scores. The survey also measures ACP Actions on a validated 25-item Action scale. It assesses ACP activities (yes or no) such as identifying a surrogate decision-maker, identifying values and goals for medical care (categorized as “Quality of Life”), choosing the level of leeway in surrogate decision-making, discussing one’s wishes with clinicians and surrogates, and documenting one’s wishes in an AD. The ACP Engagement Survey’s validity and
reliability, as well as its ability to detect change in response to an ACP intervention, have been described previously.53,55,92

Feasibility: Ease-of-Use and Satisfaction Secondary Outcomes

To evaluate whether and how PREPARE may be used in clinical practice and in the community, we assessed ease of use and satisfaction of the PREPARE website compared with an AD alone, using validated scales. These questions were asked immediately after reviewing the interventions; therefore, staff were not blinded. Ease of use was measured on a 10-point scale: “On a scale of 1 to 10, with 1 being very hard and 10 being very easy, how easy was it to use this guide?” Satisfaction was measured as comfort (“How comfortable were you viewing this guide?”), helpfulness (How helpful was this guide?”), and recommendations (“How likely are you to recommend this guide to others?”). All 3 items were assessed on a 5-point Likert scale (from 1 = not at all to 5 = extremely).18

Adverse Event Secondary Outcomes

To ensure that the PREPARE program did not cause undue harm, we assessed both depression93,94 and anxiety.95,96 We measured depression using the validated Patient Health Questionnaire-8 (PHQ-8; scores 0-24) and anxiety using the Generalized Anxiety Disorder-7 (GAD-7; scores 0-21) at baseline and each follow-up.94,95 Scores of 5, 10, 15, and 20 represent mild, moderate, moderately severe, and severe depression or anxiety, respectively.

Participant Characteristics and Potential Mediating or Moderating Variables

Based on the previously published conceptual framework of PREPARE,53 we hypothesized that PREPARE efficacy may vary across (ie, have a heterogeneous effect among) several moderator or mediator variables. These included, for instance, health literacy97 dichotomized to limited and adequate, clinician–patient language concordance (concordant vs discordant), and the patient’s desired role in decision-making using the validated Decision Control Preferences Scale with family and doctors (wants to make his or her own decision vs wants doctors or family to make decisions for him or her).98
We also hypothesized that several confounding variables may affect PREPARE efficacy; these include self-rated health\textsuperscript{99,100} and past experiences with ACP, such as prior documentation of legal forms and documented discussions. We also assessed a full range of patient-reported characteristics, as these factors may affect patient–clinician communication\textsuperscript{37,101}; among them were age, self-reported gender, finances, education, access to the internet at home, and religiosity and spirituality. We also controlled all outcomes for potential clustering by physician.

**Post Hoc Outcomes**

*Stakeholders’ suggested post hoc secondary outcomes.* Our stakeholder advisory board requested that we quantify the numbers and percentages of patients who increased their ACP activities over time. Our stakeholders perceived any increase in an ACP activity over time as clinically meaningful.

Thus, in addition to mean change in ACP Engagement Survey scores, stakeholders wanted to know the percentages of patients who improved (ie, had an estimated slope $> 0$) over time for the Behavior Change scores, the Action scores, and both combined. We created this variable post hoc.

*PCORI reviewer’s requested post hoc secondary outcomes.* A PCORI reviewer requested we conduct an analysis to determine when ACP documentation took place over the 15-month follow-up by study intervention.

All key outcomes, including validity and reliability of information and the schedule of administration (ie, baseline; 1 week; and 3, 6, and 12 months), are included in Table 3 and have been described in a previously published protocol.\textsuperscript{54} All results from these outcomes are included in this report.

Mediator variables, measured at baseline, may explain how or why a particular effect or relationship occurs, but these variables may also be affected by the intervention and are
therefore also considered secondary outcome variables measured over time (ie, knowledge, self-efficacy, and readiness, as well as barriers and attitudes).
Table 3. Study Outcome Measures

<table>
<thead>
<tr>
<th>Construct</th>
<th>Measure</th>
<th>No. of Items</th>
<th>English Reliability/Validity</th>
<th>Spanish Reliability/Validity&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Baseline</th>
<th>1 Week</th>
<th>3 Months</th>
<th>6 Months</th>
<th>12 Months</th>
<th>15 Months</th>
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<td>New ACP documentation</td>
<td>Medical record review: ACP documentation (ie, legal forms and documented goals of care discussions)&lt;sup&gt;52,54&lt;/sup&gt;</td>
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<td><strong>Secondary Outcomes</strong></td>
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<td>The full ACP process</td>
<td>ACP Engagement Survey&lt;sup&gt;53&lt;/sup&gt;</td>
<td>57</td>
<td>Behavior Change measures:</td>
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<td>Behavior Change Process measures (knowledge, contemplation, self-efficacy, readiness)</td>
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<td>Percentage increase in ACP activities</td>
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<sup>a</sup> Information on reliability and validity provided where available.
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<th>English Reliability/Validity</th>
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<th>15 Months</th>
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<td>Implementation: acceptability</td>
<td>Acceptability and usability:</td>
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<td>1 factor explained 81% to 85% of variance/scale; Kuder-Richardson &gt; 0.75&lt;sup&gt;18&lt;/sup&gt;</td>
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<td></td>
<td>(1) Ease of use and understanding</td>
<td>6</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(2) Usefulness in decisions and discussions</td>
<td>6</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>(3) Attitudes about norms or expectations</td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<td></td>
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<tr>
<td>Adverse Event Secondary Outcomes</td>
<td></td>
<td></td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>Depression</td>
<td>PHQ-8</td>
<td>8</td>
<td>Scores ≥ 10: 100% sensitive and 95% specific for major depressive disorder&lt;sup&gt;93,94&lt;/sup&gt;</td>
<td>Scores ≥ 10: 77% sensitive and 100% specific for major depressive disorder&lt;sup&gt;102&lt;/sup&gt;</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Anxiety</td>
<td>GAD-7&lt;sup&gt;95&lt;/sup&gt;</td>
<td>7</td>
<td>Cronbach α = 0.92&lt;sup&gt;95&lt;/sup&gt; ICC* = 0.83</td>
<td>Cronbach α = 0.88&lt;sup&gt;96&lt;/sup&gt; ICC* = 0.64</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Demographic Information</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Demographic information</td>
<td>Age, gender, race and ethnicity,&lt;sup&gt;103&lt;/sup&gt; marital status, and education</td>
<td></td>
<td></td>
<td></td>
<td>NA</td>
<td>NA</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Construct</td>
<td>Measure</td>
<td>No. of Items</td>
<td>English Reliability/Validity</td>
<td>Spanish Reliability/Validitya</td>
<td>Baseline</td>
<td>1 Week</td>
<td>3 Months</td>
<td>6 Months</td>
<td>12 Months</td>
<td>15 Months</td>
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<tr>
<td>-------------------------------</td>
<td>------------------------------------------------------------------------</td>
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</tr>
<tr>
<td>Finances</td>
<td>“In general, how do your finances usually work out at the end of the month?”</td>
<td>1</td>
<td>Associated with functional impairment and comorbidity104</td>
<td>NA</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Socioeconomic social standing</td>
<td>Social standing ladder (ie, “place an x where you think you stand relative to other people in society”)</td>
<td>1</td>
<td>Associated with functional decline105</td>
<td>NA</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Health literacy</td>
<td>S-TOFHLA (scores 0-36)97: continuous and dichotomized to limited = 0 to 22 and adequate = 23 to 36</td>
<td>36</td>
<td>Cronbach α = 0.97; correlation coefficient with other literacy tests &gt; 0.8097</td>
<td>Cronbach α &gt; 0.95106</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient–clinician language concordance</td>
<td>To clinicians: “How well do you speak Spanish?107 Fluent, very well (concordant) vs well, fair, or poor”</td>
<td>1</td>
<td>AUROC† 94% (95% CI, 90%-98%)107</td>
<td>AUROC† 94% (95% CI, 90%-98%)107</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Desired role in decision-making</td>
<td>CPS with clinician98</td>
<td>2</td>
<td>Correlation between preferred and actual role in decision-making40,108,109</td>
<td>Correlation between preferred and actual role in decision-making110</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Internet access</td>
<td>“Do you have access to the internet in your home?”</td>
<td>1</td>
<td>NA</td>
<td>NA</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Construct</td>
<td>Measure</td>
<td>No. of Items</td>
<td>English Reliability/Validity</td>
<td>Spanish Reliability/Validity&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Baseline</td>
<td>1 Week</td>
<td>3 Months</td>
<td>6 Months</td>
<td>12 Months</td>
<td>15 Months</td>
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<tr>
<td>----------------------------</td>
<td>-------------------------------------------------------------------------</td>
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</tr>
<tr>
<td>US acculturation</td>
<td>Based on acculturation scale (USAS): “How many years have you lived in the US?”</td>
<td>1</td>
<td>Associated with desire to know prognosis&lt;sup&gt;111&lt;/sup&gt;</td>
<td>NA</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Functional status</td>
<td>ADL (0- to 16-point scale) and IADL measure (0- to 12-item scale)&lt;sup&gt;112,113&lt;/sup&gt;</td>
<td>13</td>
<td>Morbidity/mortality correlation&lt;sup&gt;126,127&lt;/sup&gt;</td>
<td>Cronbach α = 0.94&lt;sup&gt;114&lt;/sup&gt;</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Self-rated health status</td>
<td>“How would you rate your health?” (5-point Likert)&lt;sup&gt;99,100&lt;/sup&gt;</td>
<td>1</td>
<td>Morbidity/mortality correlation&lt;sup&gt;99,100&lt;/sup&gt;</td>
<td>NA</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prior ACP experience</td>
<td>Prior ACP experiences (eg, “Ever had to make life-threatening medical decisions?”)&lt;sup&gt;18&lt;/sup&gt;</td>
<td>5</td>
<td>NA</td>
<td>NA</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Social support</td>
<td>Modified MOS-SS (scores 11-55)&lt;sup&gt;115&lt;/sup&gt;</td>
<td>11</td>
<td>Cronbach α = 0.88-0.93&lt;sup&gt;115&lt;/sup&gt;</td>
<td>Cronbach α = 0.94&lt;sup&gt;116&lt;/sup&gt;</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Presence of a possible surrogate decision-maker</td>
<td>11</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Religion and spirituality</td>
<td>Self-reported extent to which spirituality or religion (5-point Likert) and play a role in decision-making&lt;sup&gt;117&lt;/sup&gt;</td>
<td>4</td>
<td>Spirituality is associated with quality of life. Religiosity is associated with wanting all measures to extend life&lt;sup&gt;117&lt;/sup&gt;</td>
<td>NA</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

Abbreviations: ADL, activities of daily living; AUROC, area under the receiver operating curve; CPS, Control Preference Scale; GAD-7, Generalized Anxiety Disorder-7; IADL, instrumental activities of daily living; ICC, intraclass correlation; MOS-SS, Medical Outcomes Study Social Support; NA, not applicable; PHQ-8, Patient Health Questionnaire-8; S-TOFHLA, Short Test of Functional Health Literacy in Adults; USAS, United States Acculturation Scale.

<sup>a</sup>If a validated Spanish-language version of a survey was not available, we translated the English version into Spanish.
Aim 3

Disseminate PREPARE with input from patients, caregivers, and stakeholders.

We obtained input from PREPARE+AD arm participants about how we could improve the online ACP program, using an open-ended question at the 12-month follow-up interview. We also conducted 2 focus groups that included our multidisciplinary patient, surrogate, patient advocate, and clinician stakeholders (ie, clinic directors, nurse practitioners, nurses, primary care physicians, social workers, psychologists, and palliative and geriatrics specialists). In the focus groups, we asked about workflow in the clinic; feedback about use; and the impact that PREPARE had on discussions, documentation, and length of primary care visits. We also asked for advice about incorporating PREPARE into the clinic workflow, identifying barriers and facilitators, and obtaining logistic input about when and where patients should review the materials and who should introduce ACP.

Time Frame for the Study

We conducted the trial from November 1, 2014, to March 31, 2017.

Data Collection, Sources, and Retention Strategies

Process for Making Follow-up Contact

We conducted follow-up interviews 1 week and 3, 6, and 12 months after the primary care visit in the clinic, by phone, or in the home if needed to accommodate patients’ functional limitations; we reimbursed participants $25 for each of these interviews. We used several measures to help ensure follow-up. Each follow-up interview took between 30 and 45 minutes.

Upon enrollment, we asked participants to provide alternative phone numbers (eg, cell or work numbers) and 1 to 3 additional phone numbers of close contacts who would know how to contact patients if our study staff was unable to reach them. Many patients in safety-net settings are marginally housed, have intermittent phone access, and may change locations and phone numbers during the study period. We also asked participants whether they preferred a text message or an email to schedule follow-up visits, and we used their preferred mode of
communication. If these other modes of communication failed, we mailed reminder letters. If needed, we also attempted to contact patients during scheduled clinic visits or made home visits.

*Participant appointment reminder sheet.* We created an appointment reminder sheet as a reference for patient participants, which showed the dates and times for their upcoming appointments.

*Reminders for the primary care visit.* Participants received a brief reminder call 1 to 3 days before their next primary care visit. Participants in the AD-only arm were reminded to come to their scheduled appointment, while participants in the PREPARE+AD arm were reminded of their appointment and to bring the PREPARE materials to the visit.

*Reminders for study interviews.* For all follow-up interviews, participants in both arms received reminders of their upcoming study interview by phone or in person. To help participants follow along during the interview, we sent them a version of the survey via mail or email, as preferred. No survey responses or information were collected by mail or email. We used 14-point font and color-coded, standardized, large-font response options to aid readability.

*Participants who missed their primary care appointment.* Participants who canceled or missed their primary care appointments and did not reschedule within 30 days of the canceled appointment received a courtesy call reminding them to reschedule in order to continue with the study schedule. We had 2 main strategies for participants who canceled or missed their primary care appointments after they had been enrolled and randomized:

- If they rescheduled and attended their primary care appointment within 6 months from the date they were randomized, they received a brief reminder call 1 to 3 days before their primary care appointment date. We conducted follow-up assessments at 1 week and 3, 6, and 12 months from this primary care appointment date.
• If they did not reschedule or attend their primary care appointment within 6 months from the date they were randomized, they received a brief reminder call 1 to 3 days before their primary care appointment date. We conducted follow-up assessments at 6 and 12 months from the primary care appointment date.

**Procedures for Ascertaining Reasons for Loss to Follow-up and Withdrawal**

We tracked the number of individuals who did not complete their 12-month interview. For those who did not complete it, we conducted medical record review to determine whether they were deceased. For participants who wanted to withdraw, we asked them why in open-ended questions. If they could not provide an answer for why they wanted to withdraw, we prompted them from a list of reasons we obtained from prior ACP trials (eg, the study is too long, they are too busy, the study topic is too upsetting, they are too ill to participate).52

**Analytic and Statistical Approaches**

**Analytic Methods**

For aims 1 and 3, we used qualitative analysis. Aim 1 included cognitive interviews and aim 3 included focus groups. Through qualitative (thematic) content analysis,118,119 for aim 1, we identified themes concerning improvements, changes, or additional domains or content that should be added to PREPARE to ensure its usability. For aim 3, we obtained suggestions for PREPARE improvement and dissemination. Themes were identified through coding, in which passages of transcripts were marked according to their substantive content to facilitate retrieval, review, and consolidation into overarching themes. The coding scheme followed the cognitive interview guide or focus group. Two independent reviewers coded the data; a third party resolved any discrepancies.

Aim 2 was the RCT, randomized at the patient level, comparing PREPARE+AD with the AD alone. We assessed all variables for distributional and outlier values using standard summary statistics, including percentages and means and SDs. We compared baseline participant characteristics between arms using unpaired t tests, chi-square tests, or Fisher exact tests as confirmation of successful randomization. Using t tests or chi-square tests, we also
compared patients’ age and gender between those who refused vs those who enrolled and between those who withdrew vs those who remained in the study.

We used intention-to-treat analysis using SAS, version 9.4 (SAS Institute) and STATA 15.0 (StataCorp). All $P$ values were 2 tailed and set at a significance level of 0.05 for the primary outcome and Bonferroni adjusted to a level of $P < 0.025$ for secondary patient-reported outcomes.

For the primary and main secondary outcomes, we used mixed-effects logistic regression for dichotomous variables and linear regression for continuous variables. The mixed-effects models included fixed effects for the primary modeling terms of time. For the primary outcome of ACP documentation, we based time on the baseline assessment and 15-month follow-up. For ACP Engagement Surveys, we based time on the baseline assessment and the 1-week, 3-month, 6-month, and 12-month follow-up periods. We modeled time using dummy variables to allow for nonlinearity. We included the standard error (SE) where appropriate (confidence intervals are $\pm 1.96$ times the SE).

**Dealing With Confounding**

The mixed-effects models included fixed effects for the primary modeling terms of study arm (AD only vs PREPARE+AD), an interaction term of study arm and time, and a random effect for subjects. In the models, we also adjusted for factors we hypothesized a priori might affect study outcomes, which included the randomization blocking factor of limited vs adequate literacy\textsuperscript{120} and baseline ACP documentation. In addition, we included random physician intercepts to account for nesting (clustering) of patients within physicians. We anticipated very low intra-clinician correlations due to clustering or contamination, because randomization is at the patient level and intra-clinician correlation values for patient outcomes are typically quite low even in physician-level cluster randomized trials (eg, 0.015).\textsuperscript{121} Furthermore, because we had a potential pool of 125 clinicians, most clinicians cared for no more than 3 to 4 eligible patients on average, so there would be negligible loss of effective sample size accounting for
clustering and contamination. We used standardized, clinically meaningful effect sizes (ie, 0.20-0.49 small, 0.50-0.79 medium, and ≥0.80 large).122

**Analysis of Other Secondary Outcomes**

We assessed ease of use and satisfaction using the Wilcoxon rank-sum test. We assessed depression and anxiety measures using analysis of variance (ANOVA).

**Identifying Heterogeneity of Treatment Effects**

As part of the PCORI Methodology Standards, we planned, a priori, to test for interactions and heterogeneity of treatment effects of ACP documentation by study arm by adding interaction terms to the group-by-time variable in mixed-effects models. The purpose was to explore whether the efficacy of the materials differed by patient arm. This information is important both for further refinement of the tool and for dissemination of the materials. We assessed heterogeneity effects for the following variables:

- Health literacy (ie, limited vs adequate literacy)
- Patient–clinician language (concordance vs discordance)
- Control preferences for decision-making (ie, patient makes his or her own decisions vs doctor makes decisions and patient makes own decisions vs family makes decisions)
- Age (ie, < 65 years vs 65 years of age)
- Gender (ie, self-reported man vs woman)
- Race/ethnicity (ie, White, Latino vs non-White, Latino)
- Education (high school or less vs more than high school)
- US acculturation (ie, born in the United States vs born outside the United States)
- Finances (ie, able to make ends meet at the end of the month vs unable to make ends meet)
- Religious/spiritual (fairly to extremely vs somewhat to not at all)
• Health status (ie, good to excellent vs fair to poor)
• Presence of a potential surrogate (ie, yes vs no)
• Internet access at home (ie, yes vs no)

Almost all (more than 98%) participants identified as White, Latino; reported being born outside the United States; and reported having a potential surrogate decision-maker (see the Results section). Therefore, we did not assess interactions for these variables given the small number of non-Latinos. A P value for interaction < 0.05 was considered statistically significant.

Missing Data
We did not have any missing data for the primary outcome because 2 independent coders reviewed the medical records for all patients. In addition, we had less than 10% missing data for all other variables of interest; 93% of all participants had follow-up data for at least 1 time point (Table 4). For these secondary outcomes, all available data were included in mixed-effects models, and we used a mean imputation approach.123

Unblinding. We assessed whether any research staff member became unblinded during follow-up assessment by asking staff to report whether the participant disclosed information that would allow the staff member to identify the study arm allocation. We planned to conduct sensitivity analysis as needed; however, no staff member became unblinded.

Post Hoc Statistical Analysis
Per stakeholder request, we conducted post hoc mixed-effects regression to calculate the percentages of participants who increased their Behavior Change scores, Action scores, or both Behavior Change and Action scores from baseline (ie, estimated slope > 0) by study arm. P values were Bonferroni adjusted to a significance level of < 0.017.
A PCORI reviewer also requested we conduct an analysis to determine when ACP documentation took place. To do this, we determined the absolute number of patients with ACP documentation from their baseline over the course of 15-month follow-up by study arm.
Table 4. Cumulative Loss to Follow-up at Each Time Point

<table>
<thead>
<tr>
<th>Lost to Follow-up&lt;sup&gt;a&lt;/sup&gt;</th>
<th>PREPARE+AD Arm</th>
<th></th>
<th>AD-only Arm</th>
<th></th>
<th>Total lost to follow-up</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 Wk</td>
<td>3 Mo</td>
<td>6 Mo</td>
<td>12 Mo</td>
<td>Total N (%)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1 Wk</td>
<td>3 Mo</td>
<td>6 Mo</td>
<td>12 Mo</td>
</tr>
<tr>
<td>Withdraw</td>
<td>14</td>
<td>9</td>
<td>3</td>
<td>1</td>
<td>27 (77%)</td>
<td>6</td>
<td>7</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Removed</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1 (3%)</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Unable to contact</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td>4 (11%)</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Deceased</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>3 (9%)</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Total lost to follow-up</td>
<td>14</td>
<td>12</td>
<td>4</td>
<td>5</td>
<td>35 (100%)</td>
<td>8</td>
<td>9</td>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td>Unavailable for this interview&lt;sup&gt;c&lt;/sup&gt;</td>
<td>29</td>
<td>25</td>
<td>13</td>
<td>n/a</td>
<td></td>
<td>20</td>
<td>25</td>
<td>13</td>
<td>n/a</td>
</tr>
</tbody>
</table>

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<sup>a</sup> “Lost to follow-up” includes any individual who died or withdrew from the study.

<sup>b</sup> Total may not add to 100 due to rounding at the second decimal place.

<sup>c</sup> “Unavailable for this interview” meant participants completed subsequent interviews and were not lost to follow-up.
Changes to the Original Protocol

Between early January 2014 and early 2017, we made some changes to the original protocol and to our statistical analysis plan. Tables 5 and 6, respectively, summarize these changes.

Table 5. Summary of Changes to the Original Protocol Listed by Topic

<table>
<thead>
<tr>
<th>Topic</th>
<th>Date</th>
<th>Summary of Changes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eligibility screening</td>
<td>1/16/2014</td>
<td>Eligibility screening in busy outpatient clinics was often difficult. With our stakeholder advisory board, we decided to include the ability to recruit and screen by telephone. See “Patient recruitment” in Table 1.</td>
</tr>
<tr>
<td>Exclusion criteria</td>
<td>1/16/2014</td>
<td>To minimize the risk of unblinding by fellow research participants, any spouse or partner of a currently enrolled patient or an individual who was named as an enrolled patient’s potential surrogate decision-maker (regardless of cohabitation or spousal status), was excluded from being a patient participant. This avoided a situation in which 2 closely related people living in the same home could be randomized to different study arms, which could result in unblinding.</td>
</tr>
<tr>
<td>Exclusion criteria</td>
<td>1/27/2014</td>
<td>To save research staff considerable time and effort, potential participants who initially scheduled but then missed the baseline interview (ie, no-shows) more than 2 times without prior notification and rescheduling with study staff would be considered ineligible, unless there were significant extenuating circumstances.</td>
</tr>
<tr>
<td>Exclusion criteria</td>
<td>7/15/2014</td>
<td>To minimize potential contamination, we excluded participants who might have been exposed to the PREPARE website from other sources, such as being in a PREPARE-related focus group or pilot study.</td>
</tr>
<tr>
<td>Exclusion criteria</td>
<td>10/3/2014</td>
<td>To ensure the safety of our research staff, we excluded potential participants with evidence of active drug or alcohol abuse within the past 3 months determined by clinician assessment, self-report, medical record review, or research staff assessment.</td>
</tr>
<tr>
<td>Topic</td>
<td>Date</td>
<td>Summary of Changes</td>
</tr>
<tr>
<td>--------------------------</td>
<td>---------</td>
<td>----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Recruitment methods</td>
<td>11/13/2013</td>
<td>We initially sent opt-out letters to potential participants. However, many SFHN/ZSFG patients are marginally housed, had incorrect mailing addresses, or have limited literacy. We also discovered that many patients were confusing the opt-out letters for hospital bills. With input from our stakeholder advisory board and DSMB, we switched to more engaging recruitment letters and postcards that allowed patients to call and hear more about the study or to opt out. They could also opt out at any time.</td>
</tr>
<tr>
<td>Recruitment methods</td>
<td>1/16/2014</td>
<td>Our stakeholder advisory board determined that recruiting patients by telephone (in addition to in-clinic recruitment) would be acceptable. In addition, because we were attempting to enroll patients 1 to 3 weeks before a primary care visit, we had difficulty approaching patients in the clinic ahead of their primary care appointments. In addition, our primary care stakeholders felt it would be better for their clinic workflow if research staff were not in the clinic at all times. Therefore, we expanded our recruitment options—after receiving permission from the clinician and sending recruitment letters—to approaching potential participants in the clinic as well as recruiting by phone.</td>
</tr>
<tr>
<td>Consent forms</td>
<td>1/27/2014</td>
<td>For staff safety and the need to exclude or withdraw participants who were intoxicated, psychotic, or threatening, the consent form also explained, “We also may ask you to stop taking part in this study if we feel it is in your best interest or if you do not follow the study rules.”</td>
</tr>
</tbody>
</table>
| Consent forms            | 1/27/2014 | Clinicians needed to be contacted if their patients reported severe depression or anxiety. We updated our consent forms to fully explain this to participants:  
“We would need to contact your regular doctor or a medical provider for the following reasons: You report or we observe that you are having:  
• A medical emergency such as a serious medical illness  
• A serious mental illness, such as major depression  
• You report that you may harm yourself, you may harm someone else, or someone is harming you” |
<table>
<thead>
<tr>
<th>Topic</th>
<th>Date</th>
<th>Summary of Changes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Randomization</td>
<td>1/16/2014</td>
<td>We initially planned to block randomize by both health literacy and patient–clinician language concordance. We decided not to block randomize by patient–clinician language discordance because we thought that the high prevalence of discordance would result in equal distribution across both arms. Furthermore, this study allowed us to add Spanish speakers to an established, ongoing R01 trial, which only block randomized by health literacy.</td>
</tr>
<tr>
<td>Follow-up and retention</td>
<td>1/16/2014</td>
<td>Because many of our patients had functional limitations, we expanded the options for follow-up interviews to be not only in the clinic or by phone but also in the home if needed.</td>
</tr>
<tr>
<td>Follow-up and retention</td>
<td>1/16/2014</td>
<td>All data capture occurred by verbal survey administration and many of our follow-up interviews occurred over the phone. To help participants follow along during the interview, we mailed them a Participant Version of the survey to be used during the phone call if desired. No data were collected by mail.</td>
</tr>
<tr>
<td>Follow-up and retention</td>
<td>5/28/2014</td>
<td>To help with retention, we created an appointment reminder sheet to show the dates and times for upcoming primary care appointments as well as upcoming study appointments.</td>
</tr>
<tr>
<td>Follow-up and retention</td>
<td>7/15/2014</td>
<td>For all participants who missed their primary care appointment and did not reschedule, we provided a courtesy call to remind them to reschedule the appointment.</td>
</tr>
<tr>
<td>Follow-up and retention</td>
<td>7/15/2014</td>
<td>We enrolled patients based on upcoming primary care appointments. We timed all follow-up interviews to this primary care appointment. Some primary care appointments were subsequently missed or canceled. In consultation with our stakeholder advisory board and the DSMB, we decided that for participants who rescheduled and attended their primary care appointment within 6 months, we would still conduct interviews at 1 week and 3, 6, and 12 months from the primary care appointment date. If participants did not reschedule within 6 months, we conducted follow-up assessments at 6 and 12 months from the primary care appointment date.</td>
</tr>
<tr>
<td>Topic</td>
<td>Date</td>
<td>Summary of Changes</td>
</tr>
<tr>
<td>------------------------------</td>
<td>------------</td>
<td>-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td><strong>Measures and data collection</strong></td>
<td>2/12/2013</td>
<td>Correction: A priori, we planned to collect ACP documentation data at 15 months (not 12 months as stated in our original and published protocol) to mirror the methods used in our previously published trial of PREPARE in the VA setting. We fixed this typo in our final protocol. From the previous VA trial, we estimated that the time from the intervention to the primary care visit and the average time to schedule and conduct the final patient interview would be 3 months. Therefore, we standardized this window for all participants in this and our previous published trial.</td>
</tr>
<tr>
<td><strong>Measures and data collection</strong></td>
<td>3/24/2017</td>
<td>We had planned to send surveys to clinicians to obtain feedback about PREPARE implementation and dissemination. Of PREPARE patients, 85 had ACP documentation facilitated by only 40 clinicians, more than half of whom were resident trainees who had left the clinic by the end of the study. Our multidisciplinary stakeholder advisory board suggested we instead conduct an in-depth focus group with the board. The board believed this information would be more robust and insightful than sending surveys to approximately 20 clinicians who had not been educated about PREPARE in this patient-facing–only trial.</td>
</tr>
<tr>
<td><strong>Measures and data collection</strong></td>
<td>9/20/2017</td>
<td>Our stakeholder advisory board requested we quantify the number and percentage of patients who increased their ACP activities over time. Our stakeholders perceived any increase in an ACP activity over time as clinically meaningful. Thus, in addition to mean change in ACP Engagement scores, they wanted to know the percentage of patients who improved over time for Behavior Change scores, Action scores, and both combined. We defined improvement as an estimated overall slope &gt; 0. Therefore, we created this variable post hoc and used Bonferroni corrections to set the $P$ value of significance at 0.017.</td>
</tr>
</tbody>
</table>

Abbreviations: DSMB, data safety and monitoring board; SFHN, San Francisco Health Network; ZSFG, Zuckerberg San Francisco General Hospital; VA, Veterans Administration.

aThe R01 is a type of NIH Research Project Grant (see https://grants.nih.gov/grants/funding/r01.htm).
## Table 6. Summary of Changes to the Statistical Analysis Plan

<table>
<thead>
<tr>
<th>Topic</th>
<th>Date</th>
<th>Summary of Changes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Models</td>
<td>9/30/2016</td>
<td>We explained more fully the modeling terms in the mixed-effects models.</td>
</tr>
<tr>
<td>Effect size definitions</td>
<td>9/30/2016</td>
<td>We added information and references concerning clinically meaningful effect sizes.</td>
</tr>
<tr>
<td>Post hoc secondary outcome</td>
<td>9/30/2016</td>
<td>Based on a stakeholder advisory board request, we included a description of an added post hoc outcome to calculate the percentage of participants who increased their ACP Engagement scores. Bonferroni-adjusted $P$ values for this post hoc analysis were adjusted to a significance level of 0.017.</td>
</tr>
<tr>
<td>Interactions</td>
<td>9/30/2016</td>
<td>We more clearly defined the variables used to test for interactions and how these variables were dichotomized for analysis.</td>
</tr>
<tr>
<td>Bonferroni corrections</td>
<td>9/30/2017</td>
<td>We added Bonferroni-adjusted $P$ values for all secondary outcomes.</td>
</tr>
</tbody>
</table>
RESULTS

Results are presented by study aim.

Aim 1 Results

*Aim 1: Adapt and refine PREPARE in Spanish through cognitive interviews with Spanish-speaking Latinos and stakeholders.*

We completed key cognitive interviews with patients from North America, including Mexico (n = 8), Cuba (n = 1), and Puerto Rico (n = 1); Central America, including Nicaragua (n = 2); South America, including Chile (n = 3); and Spain (n = 1). We continued to conduct interviews until we reached thematic content saturation. The study staff compiled the results of these cognitive interviews and reviewed them over several study meetings to identify terms and concepts that would need to be further updated and culturally adapted to meet the needs of the broadest Spanish-speaking population.

Overall, the responses were very positive. Because we had several native Spanish speakers on our staff, most participants reported that PREPARE in Spanish was culturally appropriate and easy to understand. Table 7 summarizes the key refinements.
Table 7. Cognitive Interview Themes Obtained to Adapt and Refine PREPARE in Spanish

<table>
<thead>
<tr>
<th>Theme</th>
<th>Patient Input and Quotations</th>
<th>Changes to PREPARE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Wording</strong></td>
<td>“Advance care planning (ACP) is a difficult term for Spanish speakers not only because [of] its lack of use in everyday language, but also culturally, since ACP is not the usual practice.”</td>
<td>We realized that many terms we used are not well known in Spanish for people with minimal or no literacy. We translated <em>advance care planning</em> as “planificación anticipada de atención de salud” to help break down the term and make it more descriptive.</td>
</tr>
<tr>
<td><strong>Wording</strong></td>
<td>“La traducción de ‘advance directive’ es ‘directiva anticipada’, pero los pacientes que son de baja lectura no sabrán esa palabra o lo que quiere decir. Debemos de usar diferentes palabras para describir lo que es.”</td>
<td>The translation for <em>advance directive</em> is not an easy term for patients with low literacy to understand. We had many conversations about what to use as an alternative. We decided to use “Instrucción anticipada de atención de salud”—which translates literally as “instructions for anticipated health care.” This term clarified the meaning and purpose of an advance directive for Spanish speakers.</td>
</tr>
<tr>
<td><strong>Wording</strong></td>
<td>“You need to clarify ‘familiares’ and include ‘CERCANOS’ making the term ‘familiares cercanos’ so people understand the importance of their selection.”</td>
<td>Because Latinos often have large extended families, we clarified the term <em>family</em> early on within the site when describing who might be a good decision-maker. We made sure to say “close family” when asking if someone had close family or friends who could make medical decisions if the patient were unable to do so.</td>
</tr>
<tr>
<td><strong>Wording</strong></td>
<td>“Modify ‘asilo’ to ‘asilo de ancianos.’ Many users might think it’s for crazy people, not old folks. Also need to add ‘en’ to say ‘en un asilo, en un hospital’ since we are speaking about a place.”</td>
<td>We made a universal change to say “en un asilo de ancianos” and used this wording in our new advance directives.</td>
</tr>
<tr>
<td>Theme</td>
<td>Patient Input and Quotations</td>
<td>Changes to PREPARE</td>
</tr>
<tr>
<td>-------</td>
<td>-----------------------------</td>
<td>-------------------</td>
</tr>
<tr>
<td><strong>Wording</strong></td>
<td>“‘Como otras personas lo lograron que sea más fácil’ we need to change to ‘. . . lo lograron fácilmente’ making it ‘cómo otras personas lo lograron fácilmente’ because current translation is wordy.”</td>
<td>Throughout the steps within PREPARE, we included many videos to show users “how other people made it easier.” Our original Spanish translation was wordy and unclear. We simplified the language and made a universal change throughout to say “Cómo otras personas lo lograron más fácilmente.”</td>
</tr>
<tr>
<td><strong>Wording</strong></td>
<td>“The sentence ‘No podrán tomar algumas o todas sus decisiones’ is a double negative in Spanish, so we need to change so it is grammatically correct and does not confuse users.”</td>
<td>We changed the wording for clarity: “No podrán tomar algunas decisiones médicas o incluso ninguna.”</td>
</tr>
<tr>
<td><strong>Wording</strong></td>
<td>“Instead of ‘es posible que su situación sea diferente.’ What about: ‘su situación puede ser diferente.’”</td>
<td>We made a universal change to “Su situación puede ser diferente.” We used this every time we showed an example video or script.</td>
</tr>
<tr>
<td><strong>Wording</strong></td>
<td>“Regarding the word ‘cualquier,’ we should change to ALGUN because it matters who you choose. This makes the question: ¿Puede pensar en ALGÚN familiar o amigo que PODRÍA llegar a ayudarle a tomar decisiones médicas en su nombre si está demasiado enfermo para tomar sus propias decisiones?”</td>
<td>We changed “cualquier” to “algun” because “cualquier” implied that it did not matter who the patient chose as a decision-maker; in reality, we wanted patients to think of and choose a good decision-maker since this person would be able to make medical decisions on the patient’s behalf.</td>
</tr>
<tr>
<td>Theme</td>
<td>Patient Input and Quotations</td>
<td>Changes to PREPARE</td>
</tr>
<tr>
<td>------------</td>
<td>---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td>-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Wording</td>
<td>“On the webpage where I need to write my decision-maker’s name, I am confused because it feels like I have to write the name of the group making decisions for me. Reorder sentences for clarity, and then have the field to type in the user’s decision-maker. ‘Si ya eligió a una persona decisor, escriba su nombre a continuación. O, si prefiere elegir a un grupo de personas, escriba el nombre de una persona que hablará en nombre del grupo:’”</td>
<td>We moved the order of sentences on the page in step 1 where we instruct users to write the name of their decision-maker or, if they prefer a group, to write the name of the spokesperson.</td>
</tr>
<tr>
<td>Buttons</td>
<td>“Do I click ‘siguiente’ or click on menu?”</td>
<td>While navigating the pages, participants had trouble understanding where to click. We placed all instructions inside yellow headers/fields so that they would be easier to see. In addition, we changed the color of the buttons to blue.</td>
</tr>
<tr>
<td>Buttons</td>
<td>“Unsure of the use of the word ‘boton’ for button. Buttons are on clothes, and it is hard to show the same meaning on a screen. I think many users may be confused and look for an actual button, and they may not know how to move forward or back (especially since many will probably not be savvy computer users). I am concerned they can get lost while trying to navigate the website.”</td>
<td>In English, we instructed users to “click on the NEXT button to move on.” We decided it would be difficult at first for Spanish users to understand that our blue outlined boxes were buttons that would move them forward or back within the website. For Spanish we decided to not use the word “button,” but simply use the word “SIGUIENTE” or “VOLVER” to instruct them to move forward or back, respectively: “Haga clic en SIGUIENTE para avanzar.” In this way, they would see the word “SIGUIENTE” (which would be in our blue outlined “button” layout) and click that word (aka the button) to move forward. We also made sure to describe the use of our buttons and other instructions for navigating the website in our Spanish video, “How to Use PREPARE,” which all users saw prior to starting the 5 steps.</td>
</tr>
<tr>
<td>Theme</td>
<td>Patient Input and Quotations</td>
<td>Changes to PREPARE</td>
</tr>
<tr>
<td>-------</td>
<td>------------------------------</td>
<td>-------------------</td>
</tr>
<tr>
<td>Buttons</td>
<td>“Many buttons are not translated. Change ‘click to play’ to ‘haga clic para reproducir’; change ‘DONE’ to ‘hecho’; and change ‘click to watch’ to ‘haga clic para ver.’”</td>
<td>We made changes to translations throughout the website for clarity. Again, we used the actual words on the button when saying “click on X to move on.”</td>
</tr>
<tr>
<td>Pictures</td>
<td>“En donde están las caras de los Latinos? Hacen falta en los videos y pasos.”</td>
<td>We received a comment about the lack of Latino faces and characters in the videos and steps. To address this, we added more pictures of Latinos throughout the website.</td>
</tr>
<tr>
<td>New Content</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Explain why many of the actors in the videos are not Latino</td>
<td>“Ese video solo es importante para pacientes asiáticos, no aplica para mí. Prefiero ver los videos de Latinos y costumbres Latinas.”</td>
<td>Several individuals felt that if the video included people from other cultures, then it was not pertinent to them or their families. We included a new webpage that said, “In the videos you will see people from many different cultures. But, all of the stories are still very important for Spanish-speaking people.”</td>
</tr>
<tr>
<td>Explain why the videos show a range of illness states</td>
<td>“This is first time (in step 2) you talk about death. You might want to be more transparent in the beginning and say this is about decisions for end of life.”</td>
<td>We added this statement to the beginning of the welcome step: “You will see stories of people who are making all kinds of decisions. Some of these people are healthy and some are ill. Some decisions are about medicine or surgery. Some decisions are about the care they would want if they were very ill.”</td>
</tr>
<tr>
<td>Include information about how quality of life may differ</td>
<td>“‘Calidad de vida’ means different things to everyone.”</td>
<td>We updated PREPARE to use this very language to say that quality of life is different for each person. We also updated this language in the Spanish advance directive.</td>
</tr>
</tbody>
</table>
Aim 2 Results

Aim 2: Conduct an RCT to compare the efficacy of PREPARE plus a previously tested, easy-to-read AD vs the AD alone.

Of 849 eligible Spanish-speaking patients, 445 (55.6%) enrolled in the trial. We randomized 219 to the PREPARE+AD intervention group and 226 to the AD-only control group. Figure 4 (ie, the CONSORT diagram) documents the flow of participants from the original potential pool of patients through analysis. It also describes the reasons for ineligibility, including the lack of clinician permission, and the reasons for refusal.

Retention and Loss to Follow-up

At 12 months, 181 PREPARE+AD participants and 197 AD-only participants completed follow-up interviews. Total retention rate of survivors (n = 440) was 85.9%; there were 5 decedents. Therefore, the overall loss to follow-up rate was 14.1% (Figure 4). The PREPARE+AD arm retention rate was 83.8%; there were 3 decedents. The AD-only arm retention rate was 87.9%; there were 2 decedents.
Figure 4. CONSORT diagram of patients in the PREPARE trial

* Patient had concerns about privacy of medical information or distrust of the clinic or hospital.

\* Patient was willing to participate, but logistical issues (e.g., work, caretaking, travel, or illness) prevented scheduling.

\* Patient was removed from the study for staff’s safety.

\* Unavailable participants completed subsequent interviews and were not lost to follow-up.
Characteristics of Patients

The mean age of enrolled participants was 64.1 ± 7.0 years; 71.9% were women; 61.5% had limited health literacy (including 8.1% of participants considered illiterate with S-TOFHLA [Short Test of Functional Health Literacy in Adults] scores of 0); 57.2% reported fair-to-poor health; and 24.3% had any prior evidence of ACP documentation. Participant characteristics did not differ between the PREPARE+AD and AD-only groups, except for any (ever) prior ACP documentation (PREPARE+AD 20% vs AD only 28%, \( P = 0.04 \); Table 8).

The median number of enrolled patients per clinician was 2 (interquartile range [IQR] 1-4; range, 1-13).

The gender of patients who refused did not differ from those who enrolled; however, those who refused were older than those who enrolled: 67.9 years (SD ± 8.4 years vs 64.1 ± 7.0 years, \( P < 0.001 \); Table 9).
Table 8. Participant Characteristics, by Study Arms (PREPARE+AD vs AD Only)

<table>
<thead>
<tr>
<th>Participant Characteristics, N = 445&lt;sup&gt;a&lt;/sup&gt;</th>
<th>PREPARE+AD</th>
<th>AD Only</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 219</td>
<td>n = 226</td>
</tr>
<tr>
<td>Age, mean (SD)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>64 (6.8)</td>
<td>64 (7.2)</td>
</tr>
<tr>
<td>Women, no. (%)</td>
<td>157 (71.7)</td>
<td>163 (72.1)</td>
</tr>
<tr>
<td>Race and ethnicity, no. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White, Latino/Hispanic</td>
<td>216 (98.6)</td>
<td>224 (99.1)</td>
</tr>
<tr>
<td>White, non-Latino/Hispanic</td>
<td>1 (0.5)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>African American</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Asian/Pacific Islander</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Multiethnic/other</td>
<td>2 (0.9)</td>
<td>2 (0.9)</td>
</tr>
<tr>
<td>US acculturation: place of birth, no. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>United States</td>
<td>1 (0.5)</td>
<td>3 (1.3)</td>
</tr>
<tr>
<td>South America</td>
<td>10 (4.6)</td>
<td>13 (5.7)</td>
</tr>
<tr>
<td>Central America</td>
<td>147 (67.1)</td>
<td>152 (67.3)</td>
</tr>
<tr>
<td>North America (Mexico, Cuba, and Puerto Rico)</td>
<td>61 (27.8)</td>
<td>58 (25.7)</td>
</tr>
<tr>
<td>If born outside United States, years in the United States, mean (SD)</td>
<td>26 (11.7)</td>
<td>26 (11.9)</td>
</tr>
<tr>
<td>Education ≤ high school, no. (%)</td>
<td>187 (85.4)</td>
<td>185 (81.9)</td>
</tr>
<tr>
<td>Limited health literacy, no. (%)</td>
<td>129 (59.7)</td>
<td>142 (63.1)</td>
</tr>
<tr>
<td>S-TOFHLA (0-36), range, mean (SD)</td>
<td>0 to 36, 18.8 (11.3)</td>
<td>0 to 36, 17.7 (12.1)</td>
</tr>
<tr>
<td>Patient–doctor language discordance, no. (%)</td>
<td>65 (32.2)</td>
<td>86 (41.2)</td>
</tr>
<tr>
<td>Finances, not enough to make ends meet, no. (%)</td>
<td>63 (29.4)</td>
<td>59 (26.5)</td>
</tr>
<tr>
<td>Financial social standing 1 to 10 score, mean (SD)</td>
<td>5.3 (2.3)</td>
<td>5.8 (8.1)</td>
</tr>
<tr>
<td>Religious, fairly to extremely, no. (%)</td>
<td>105 (48.4)</td>
<td>117 (52.0)</td>
</tr>
<tr>
<td>Spiritual, fairly to extremely, no. (%)</td>
<td>123 (56.4)</td>
<td>142 (63.1)</td>
</tr>
<tr>
<td>Social support</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married/in a long-term relationship, no. (%)</td>
<td>86 (39.5)</td>
<td>81 (35.8)</td>
</tr>
<tr>
<td>Have adult children, no. (%)</td>
<td>194 (88.6)</td>
<td>201 (88.9)</td>
</tr>
<tr>
<td>Have a potential surrogate, no. (%)</td>
<td>217 (99.5)</td>
<td>219 (96.9)</td>
</tr>
<tr>
<td>Participant Characteristics, N = 445&lt;sup&gt;a&lt;/sup&gt;</td>
<td>PREPARE+AD n = 219</td>
<td>AD Only n = 226</td>
</tr>
<tr>
<td>-----------------------------------------------</td>
<td>---------------------</td>
<td>-----------------</td>
</tr>
<tr>
<td><strong>Health and functional status</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Self-rated health, fair to poor, no. (%)</td>
<td>127 (58.3)</td>
<td>127 (56.2)</td>
</tr>
<tr>
<td>Instrumental activities of daily living difficulty score 0 to 16, mean (SD)</td>
<td>2.4 (3.4)</td>
<td>2.5 (3.6)</td>
</tr>
<tr>
<td>Activities of daily living difficulty score 0 to 12, mean (SD)</td>
<td>1.6 (1.8)</td>
<td>1.9 (2.2)</td>
</tr>
<tr>
<td>Depression, moderate to severe, no. (%)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>27 (12.3)</td>
<td>29 (13.0)</td>
</tr>
<tr>
<td>Anxiety, moderate to severe, no. (%)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>21 (9.6)</td>
<td>26 (11.5)</td>
</tr>
<tr>
<td><strong>Desired role in decision-making</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low decision control with doctors (ie, doctors make all medical decisions), no. (%)</td>
<td>33 (15.3)</td>
<td>33 (14.8)</td>
</tr>
<tr>
<td>Low decision control with family (ie, family makes all medical decisions), no. (%)</td>
<td>5 (2.3)</td>
<td>8 (3.6)</td>
</tr>
<tr>
<td><strong>Access to the internet in the home, no. (%)</strong></td>
<td>57 (26.1)</td>
<td>78 (34.5)</td>
</tr>
<tr>
<td><strong>History of ACP activities</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Completed a will, no. (%)</td>
<td>20 (9.2)</td>
<td>20 (8.9)</td>
</tr>
<tr>
<td>Made funeral arrangements, no. (%)</td>
<td>54 (24.7)</td>
<td>56 (25.1)</td>
</tr>
<tr>
<td>Any prior ACP documentation,&lt;sup&gt;c&lt;/sup&gt; no. (%)</td>
<td>44 (20.1)&lt;sup&gt;d&lt;/sup&gt;</td>
<td>64 (28.3)&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>Legal forms</td>
<td>29 (13.2)</td>
<td>44 (19.5)</td>
</tr>
<tr>
<td>Documented discussions about ACP</td>
<td>21 (9.6)</td>
<td>29 (12.8)</td>
</tr>
<tr>
<td><strong>ACP documentation rate 12 months before intervention exposure, no. (%)</strong></td>
<td>13 (5.9)</td>
<td>22 (9.7)</td>
</tr>
</tbody>
</table>

Abbreviation: S-TOFHLA; Short Test of Functional Health Literacy in Adults.

<sup>a</sup> Results are presented as means with SDs and as numbers (no.) and percentages (%).

<sup>b</sup> Depression is measured with the 8-item Patient Health Questionnaire (PHQ-8; scores 0-24) and anxiety is measured with the 7-item Generalized Anxiety Disorder screening measure (GAD-7; scores 0-21). Moderate-to-severe depression and anxiety are defined by scores greater than 10 on both assessments.<sup>54</sup>

<sup>c</sup> Includes any prior legal forms (ie, advance directives, durable power of attorney for health care, and Physician Orders for Life-Sustaining Treatment form) and documented ACP discussions in the past 5 years (ie, oral directives or goals of care notes by clinicians).<sup>54</sup>

<sup>d</sup> No patient characteristic, overall, displayed any between-group differences, except for any previous ACP documentation, <i>P</i> = 0.04.
Table 9. Characteristics of Respondents and Nonrespondents

<table>
<thead>
<tr>
<th>Patient characteristics</th>
<th>Respondents, n = 445</th>
<th>Nonrespondents (refused), n = 267</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD)</td>
<td>64.1 (7.0)</td>
<td>67.9 (8.4)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Women, no. (%)</td>
<td>320 (71.9)</td>
<td>200 (74.9)</td>
<td>0.38</td>
</tr>
<tr>
<td>White, Latino/Hispanic, no. (%)</td>
<td>440 (98.9)</td>
<td>224 (97.4)</td>
<td>0.08</td>
</tr>
</tbody>
</table>

As documented in Table 10, the overall withdrawal rates did not differ between arms; 29 participants (13.4%) withdrew from the PREPARE+AD arm and 21 (9.3%) from the AD-only arm (P = 0.44). The arms did not differ significantly in the rates of, or reasons for, withdrawal.

Table 10. Reasons for Withdrawal From the Trial

<table>
<thead>
<tr>
<th>Reason</th>
<th>PREPARE+AD</th>
<th>AD Only</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 29 n (%)</td>
<td>n = 21 n (%)</td>
<td></td>
</tr>
<tr>
<td>Lost interest, no. (%)</td>
<td>7 (24.1)</td>
<td>5 (23.8)</td>
<td>0.44a</td>
</tr>
<tr>
<td>Too sick, no. (%)</td>
<td>1 (3.5)</td>
<td>2 (9.5)</td>
<td></td>
</tr>
<tr>
<td>Study too long, no. (%)</td>
<td>9 (31.0)</td>
<td>3 (14.3)</td>
<td></td>
</tr>
<tr>
<td>Study upsetting, no. (%)</td>
<td>4 (13.8)</td>
<td>1 (4.8)</td>
<td></td>
</tr>
<tr>
<td>Too busy, no. (%)</td>
<td>3 (10.3)</td>
<td>2 (9.5)</td>
<td></td>
</tr>
<tr>
<td>Other, no. (%)</td>
<td>5 (17.3)</td>
<td>8 (38.1)</td>
<td></td>
</tr>
</tbody>
</table>

* Fisher exact test. Test of significance set at P < 0.05.

**Primary Outcome**

The ACP documentation rate 12 months before intervention exposure did not differ between arms and was 7.9% overall: 5.9% in the PREPARE+AD arm and 9.7% in the AD-only arm, P = 0.14 (Table 8).

For our primary outcome, new overall ACP documentation by medical record review at 15 months was statistically significantly higher in the PREPARE+AD arm than in the AD-only arm. In unadjusted analyses, the rates of new ACP documentation were 38% for the
PREPARE+AD arm and 26% for the AD-only arm ($P = 0.004$). In mixed-effects models—adjusted for literacy, baseline ACP documentation, and clustering by physician—the rates of new ACP documentation were 39% for the PREPARE+AD arm and 24% for the AD-only arm (adjusted odds ratio = 1.99; 95% CI, 1.29-3.08; $P = 0.002$; Figure 5).

**Figure 5. New ACP documentation in the medical record**

<table>
<thead>
<tr>
<th>Percentage</th>
<th>PREPARE</th>
<th>AD-only</th>
</tr>
</thead>
<tbody>
<tr>
<td>45%</td>
<td>![Red Bar]</td>
<td>![Blue Bar]</td>
</tr>
<tr>
<td>40%</td>
<td>![Red Bar]</td>
<td>![Blue Bar]</td>
</tr>
<tr>
<td>35%</td>
<td>![Red Bar]</td>
<td>![Blue Bar]</td>
</tr>
<tr>
<td>30%</td>
<td>![Red Bar]</td>
<td>![Blue Bar]</td>
</tr>
<tr>
<td>25%</td>
<td>![Red Bar]</td>
<td>![Blue Bar]</td>
</tr>
<tr>
<td>20%</td>
<td>![Red Bar]</td>
<td>![Blue Bar]</td>
</tr>
<tr>
<td>15%</td>
<td>![Red Bar]</td>
<td>![Blue Bar]</td>
</tr>
<tr>
<td>10%</td>
<td>![Red Bar]</td>
<td>![Blue Bar]</td>
</tr>
<tr>
<td>5%</td>
<td>![Red Bar]</td>
<td>![Blue Bar]</td>
</tr>
<tr>
<td>0%</td>
<td>![Red Bar]</td>
<td>![Blue Bar]</td>
</tr>
</tbody>
</table>

**Abbreviation:** AD, advance directive.

*a New ACP documentation during the 15 months following the intervention was determined by objective electronic medical record review by 2 independent reviewers. Percentages reflect predicted values from mixed-effects models adjusted for literacy, baseline ACP documentation, and clustering by physician. Statistical significance set at $P < 0.05$.

Increased documentation included higher rates of legal forms (adjusted 25% in the PREPARE+AD arm vs 9% in the AD-only arm; $P < 0.001$) and a nonsignificant trend for documented discussions (adjusted 26% vs 19%; $P = 0.09$). Of those with ACP discussions ($n = 106$), 19.8% had discussions about goals of care and 15.3% had discussions about surrogates (Table 11).
Table 11. New ACP at 15 Months

<table>
<thead>
<tr>
<th></th>
<th>Overall, N = 445</th>
<th>PREPARE+AD</th>
<th>AD Only</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total ACP documentation</td>
<td>142 (31.9)</td>
<td>84 (38.4)</td>
<td>58 (25.7)</td>
<td>0.004</td>
</tr>
<tr>
<td>Forms and orders</td>
<td>79 (17.8)</td>
<td>56 (25.6)</td>
<td>23 (10.2)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Discussions</td>
<td>106 (23.8)</td>
<td>59 (26.9)</td>
<td>47 (20.8)</td>
<td>0.13</td>
</tr>
<tr>
<td>Goals of care and AD forms</td>
<td>88 (19.8)</td>
<td>49 (22.4)</td>
<td>39 (17.3)</td>
<td>0.18</td>
</tr>
<tr>
<td>Surrogate</td>
<td>68 (15.3)</td>
<td>41 (18.7)</td>
<td>27 (12.0)</td>
<td>0.047</td>
</tr>
</tbody>
</table>

Abbreviations: ACP, advance care planning; AD, advance directive.

Secondary Outcomes

Main self-reported secondary outcome. The ACP Engagement Survey. Self-reported ACP engagement, including mean Behavior Change Process and Action scores in the validated ACP Engagement Survey, increased significantly more in the PREPARE+AD arm than in the AD-only arm (group by time \( P < 0.001 \)).

Figure 6 shows both the Behavior Change and Action scores of the ACP Engagement Survey. \( P \) values reflect significance for overall group by time interactions using repeated measures, mixed-effects linear regression models adjusted for health literacy, baseline ACP documentation, and clustering by physician. \( P \) values for group were nonsignificant, suggesting no differences between groups at baseline. \( P \) values for time were highly significant \( (P < 0.001) \), suggesting overall improvement in both groups over time.

The ACP Engagement Survey comprises both the Behavior Change Process and Action Measures. Both measures have validated subscales.

Table 12 shows the difference in Behavior Change Process subscales. Both PREPARE+AD and AD-only activities increased the Behavior Change Process subscales of knowledge, contemplation, self-efficacy, and readiness to engage in ACP across a range of ACP behaviors. However, PREPARE+AD resulted in statistically significantly higher gains.
Figure 6. ACP Engagement Survey: Behavior Change and Action scores

Abbreviations: ACP, advance care planning; AD, advance directive.

a Behavior Change scores were measured on a 5-point Likert scale.

b Action scores were measured on a 0- to 25-point scale.
Table 12. Process Measures of ACP Behavior Change

<table>
<thead>
<tr>
<th>Score, 0 to 5&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Study Arm</th>
<th>Percentage Change Over Time</th>
<th>Mixed-Effects Models&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PREPARE+AD, Mean (SE)&lt;sup&gt;c&lt;/sup&gt;</td>
<td>AD Only, Mean (SE)&lt;sup&gt;c&lt;/sup&gt;</td>
<td>P value&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>BL 1 Wk 3 Mo 6 Mo 12 Mo</td>
<td>BL 1 Wk 3 Mo 6 Mo 12 Mo</td>
<td>PREPARE+AD AD Only Group Time Group × Time&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Total Process score</td>
<td>2.3 (0.05) 2.9 (0.07) 3.0 (0.07) 3.1 (0.07) 3.2 (0.07)</td>
<td>2.4 (0.05) 2.6 (0.06) 2.7 (0.07) 2.8 (0.07) 2.9 (0.07)</td>
<td>39% 21% 0.57 &lt;0.001 &lt;0.001</td>
</tr>
<tr>
<td>Knowledge</td>
<td>2.7 (0.07) 3.1 (0.07) 3.3 (0.08) 3.4 (0.08) 3.5 (0.07)</td>
<td>2.8 (0.07) 2.9 (0.07) 3.1 (0.07) 3.2 (0.07) 3.3 (0.07)</td>
<td>30% 18% 0.20 &lt;0.001 &lt;0.001</td>
</tr>
<tr>
<td>Contemplation</td>
<td>2.2 (0.05) 2.7 (0.07) 2.9 (0.08) 3.0 (0.08) 3.0 (0.07)</td>
<td>2.3 (0.06) 2.4 (0.06) 2.6 (0.07) 2.7 (0.07) 2.8 (0.07)</td>
<td>36% 22% 0.90 &lt;0.001 0.001</td>
</tr>
<tr>
<td>Self-efficacy</td>
<td>2.6 (0.06) 2.9 (0.08) 3.1 (0.08) 3.0 (0.08) 3.1 (0.08)</td>
<td>2.6 (0.06) 2.7 (0.07) 2.8 (0.08) 2.8 (0.08) 3.0 (0.08)</td>
<td>19% 15% 0.68 &lt;0.001 0.006</td>
</tr>
<tr>
<td>Readiness</td>
<td>2.5 (0.06) 3.2 (0.08) 3.3 (0.09) 3.4 (0.08) 3.5 (0.08)</td>
<td>2.6 (0.06) 2.8 (0.07) 3.0 (0.08) 3.0 (0.08) 3.2 (0.08)</td>
<td>40% 23% 0.49 &lt;0.001 &lt;0.001</td>
</tr>
</tbody>
</table>

Abbreviations: ACP, advance care planning; AD, advance directive.

<sup>a</sup>Average score on a 5-point Likert scale.

<sup>b</sup>Analysis of differences by study group at baseline (Group), differences over time (Time), or differences by study group over time (Group × Time) using mixed-effects models. The percentage change is the difference between the 12-month minus the baseline value divided by the baseline value × 100.

<sup>c</sup>Confidence intervals are ± 1.96 times the SE.

<sup>d</sup>P value is based on mixed-effects models adjusted for literacy, any ACP documentation at baseline, and clustering within physician.
Table 13 shows the difference in ACP Action Measure subscales. Both the PREPARE+AD and the AD-only interventions increased the Action subscales of decision-makers, quality of life, flexibility for surrogate decision-making, and asking doctors questions. However, PREPARE+AD produced statistically significantly higher gains.

**Effect Size Estimates of the ACP Engagement Survey: Behavior Change and Action Scores**

We calculated clinically meaningful effect sizes from changes based on standardized criteria (ie, 0.20-0.49 small, 0.50-0.79 medium, and ≥0.80 large). Table 14 includes the calculated effect sizes from baseline (ie, mean PREPARE+AD scores minus mean AD-only scores divided by pooled baseline SDs). Effect size estimates were medium to large for PREPARE+AD across the 4 follow-up time points (0.70-1.16 SDs for Behavior Change Process scores, 0.57-1.18 SDs for Action scores) and small to medium for AD only (0.21-0.63 SDs for Behavior Change Process scores, 0.24-0.74 SDs for Action scores).
### Table 13. Completion of ACP Actions

<table>
<thead>
<tr>
<th>Score, 0 to 25&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Study Arm</th>
<th>Percentage Change Over Time</th>
<th>Mixed-Effects Models&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>PREPARE+AD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Total Action score</td>
<td>80%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>BL</td>
<td>1 Wk</td>
</tr>
<tr>
<td>PREPARE+AD, Mean (SE)&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
<td>6.9 (0.31)</td>
<td>9.5 (0.45)</td>
</tr>
<tr>
<td>AD Only, Mean (SE)&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
<td>8.0 (0.30)</td>
<td>9.5 (0.45)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Decision-maker</td>
<td>88%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>BL</td>
<td>1 Wk</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.6 (0.09)</td>
<td>2.5 (0.11)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>QOL</td>
<td>173%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>BL</td>
<td>1 Wk</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.5 (0.13)</td>
<td>2.8 (0.20)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Flexibility</td>
<td>156%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>BL</td>
<td>1 Wk</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.9 (0.08)</td>
<td>1.7 (0.11)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Asking questions</td>
<td>4%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>BL</td>
<td>1 Wk</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2.8 (0.12)</td>
<td>2.5 (0.14)</td>
</tr>
</tbody>
</table>

Abbreviations: ACP, advance care planning; AD, advance directive; BL, baseline; QOL, quality of life.

<sup>a</sup>Total score is 0 to 25 points. The decision-maker subscale had a total of 0 to 5 possible points, quality of life 0 to 10 points (ie, identifying values and goals for medical care), flexibility 0 to 5 points, and asking doctors questions 0 to 5 points.

<sup>b</sup>Analysis of differences by study group at baseline (Group), differences over time (Time), or differences by study group over time (Group × Time) using mixed-effects models.

<sup>c</sup>Confidence intervals are ± 1.96 times the SE.

<sup>d</sup>P value is based on mixed-effects models adjusted for literacy, any ACP documentation at baseline, and clustering within physician.
### Table 14. Effect Size Estimates of ACP Behavior Change and Actions Over Time

<table>
<thead>
<tr>
<th>Time Points for Measurement</th>
<th>Spanish Speakers, n = 445</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PREPARE+AD</td>
</tr>
<tr>
<td>ACP Behavior Change</td>
<td></td>
</tr>
<tr>
<td>1 week</td>
<td>0.70</td>
</tr>
<tr>
<td>3 months</td>
<td>0.93</td>
</tr>
<tr>
<td>6 months</td>
<td>1.00</td>
</tr>
<tr>
<td>12 months</td>
<td>1.16</td>
</tr>
<tr>
<td>ACP Actions</td>
<td></td>
</tr>
<tr>
<td>1 week</td>
<td>0.57</td>
</tr>
<tr>
<td>3 months</td>
<td>0.86</td>
</tr>
<tr>
<td>6 months</td>
<td>0.90</td>
</tr>
<tr>
<td>12 months</td>
<td>1.18</td>
</tr>
</tbody>
</table>

Abbreviations: ACP, advance care planning; AD, advance directive.

**Interactions (Heterogeneity of Intervention Effects)**

After adjustment, we observed no significant interaction effects for ACP documentation as a function of gender, health literacy, health status, access to the internet, or doctor–patient language discordance (Table 15; $P > 0.05$). For age, the $P$ value for interaction equaled 0.04; for participants less than 65 years of age, the ACP documentation rate was 40.2% in the PREPARE+AD arm and 21.0% in the AD-only arm; and for participants 65 years or older, the documentation rate was 35.9% in the PREPARE+AD arm and 33.0% in the AD-only arm.
Table 15. Interactions Effects of Patient Characteristics on ACP Documentation by Study Arm

<table>
<thead>
<tr>
<th>Participant Characteristics</th>
<th>PREPARE+AD</th>
<th>AD Only</th>
<th>P value&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 219 (%)</td>
<td>n = 226 (%)</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 65 years</td>
<td>42.1</td>
<td>21.2</td>
<td>0.04</td>
</tr>
<tr>
<td>≥ 65 years</td>
<td>35.7</td>
<td>32.5</td>
<td>0.54</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>37.3</td>
<td>22.2</td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>44.3</td>
<td>33.4</td>
<td></td>
</tr>
<tr>
<td>Health literacy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adequate</td>
<td>44.3</td>
<td>26.4</td>
<td>0.56</td>
</tr>
<tr>
<td>Limited</td>
<td>37.1</td>
<td>25.2</td>
<td></td>
</tr>
<tr>
<td>Role in decision-making with doctor</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Makes own decisions</td>
<td>39.0</td>
<td>25.2</td>
<td>0.97</td>
</tr>
<tr>
<td>Doctor decides</td>
<td>43.4</td>
<td>29.3</td>
<td></td>
</tr>
<tr>
<td>Role in decision-making with family</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Makes own decisions</td>
<td>38.5</td>
<td>25.6</td>
<td>0.20</td>
</tr>
<tr>
<td>Family decides</td>
<td>75.5</td>
<td>22.6</td>
<td></td>
</tr>
<tr>
<td>Doctor–patient language</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Concordant</td>
<td>38.7</td>
<td>29.8</td>
<td>0.13</td>
</tr>
<tr>
<td>Discordant</td>
<td>44.0</td>
<td>21.1</td>
<td></td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ high school</td>
<td>37.3</td>
<td>20.5</td>
<td>0.16</td>
</tr>
<tr>
<td>&gt; high school</td>
<td>50.7</td>
<td>48.0</td>
<td></td>
</tr>
<tr>
<td>Finances</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Able to make ends meet</td>
<td>35.0</td>
<td>24.1</td>
<td>0.46</td>
</tr>
<tr>
<td>Unable to make ends meet</td>
<td>48.4</td>
<td>28.4</td>
<td></td>
</tr>
<tr>
<td>Health status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Good to excellent</td>
<td>30.2</td>
<td>24.1</td>
<td>0.22</td>
</tr>
<tr>
<td>Fair to poor</td>
<td>45.6</td>
<td>26.8</td>
<td></td>
</tr>
<tr>
<td>Religious</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fairly to extremely</td>
<td>39.6</td>
<td>29.7</td>
<td>0.30</td>
</tr>
<tr>
<td>Not at all to somewhat</td>
<td>39.2</td>
<td>21.4</td>
<td></td>
</tr>
<tr>
<td>Spiritual</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fairly to extremely</td>
<td>39.4</td>
<td>29.7</td>
<td>0.15</td>
</tr>
<tr>
<td>Not at all to somewhat</td>
<td>40.1</td>
<td>18.9</td>
<td></td>
</tr>
<tr>
<td>Internet access at home</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>37.5</td>
<td>32.7</td>
<td>0.13</td>
</tr>
<tr>
<td>No</td>
<td>40.2</td>
<td>21.8</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: ACP, advance care planning; AD, advance directive.

<sup>a</sup> Percentages represent stratified, adjusted analysis. Interactions were tested by adding interaction terms to the group-by-time variable in adjusted mixed-effects models. All dichotomous interaction terms are defined in the protocol. All models were adjusted for health literacy, prior ACP documentation, and clustering by clinician; however, the health literacy interaction model was adjusted only for prior ACP documentation and clustering by clinician. The P value significance level was set at < 0.05. Only 5 (1.1%) participants were non-White/Latino; 4 (0.9%) were born in the United States and 8 (1.8%) reported no close family or friends; therefore, we were unable to assess for interactions for these variables.
Ease-of-Use and Satisfaction Secondary Outcomes

We found no significant differences in the 10-point self-reported ease-of-use scales for the PREPARE+AD intervention arm vs the AD-only control arm (7.5 [7.2-7.8] vs 7.3 [7.0-7.7]; \( P = 0.38 \); Table 16). We also found no significant differences for the 5-point satisfaction scales, including comfort reviewing the interventions (3.8 [3.8-3.9] vs 3.7 [3.5-3.8]; \( P = 0.01 \)) and likelihood of recommending the guides (4.1 [4.0-4.2] vs 4.0 [3.9-4.1]; \( P = 0.19 \)), respectively. However, PREPARE+AD was perceived as being more helpful than AD only (4.2 [4.1-4.3] vs 3.9 [3.8-4.0]; \( P < 0.001 \)).

Table 16. Ease of Use and Satisfaction Between Study Arms

<table>
<thead>
<tr>
<th></th>
<th>PREPARE+AD</th>
<th>AD Only</th>
<th>( P ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ease of use, 10-point scale</strong></td>
<td>7.5 (0.15)</td>
<td>7.3 (0.16)</td>
<td>0.72</td>
</tr>
<tr>
<td><strong>Satisfaction, 5-point scale</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Comfort viewing</td>
<td>3.8 (0.04)</td>
<td>3.7 (0.06)</td>
<td>0.09</td>
</tr>
<tr>
<td>Helpfulness</td>
<td>4.2 (0.04)</td>
<td>3.9 (0.05)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Recommend</td>
<td>4.1 (0.04)</td>
<td>4.0 (0.05)</td>
<td>0.26</td>
</tr>
</tbody>
</table>

Abbreviation: AD, advance directive.

a Confidence intervals are ± 1.96 times the SE.
b Ease of use was measured on a scale of 1 (very hard) to 10 (very easy).
c Satisfaction was measured with the question, “How comfortable were you viewing this guide?”; helpfulness, “How helpful was this guide?”; and recommendations, “How likely are you to recommend this guide to others?” assessed on a 5-point Likert scale (1 = not at all to 5 = extremely) from our prior work.54

Adverse Event Secondary Outcomes

No adverse events were reported. As shown in Table 17, after controlling for baseline scores, adjusted mean depression scores at 12 months were 3.9 for PREPARE+AD and 4.5 for AD only; \( P = 0.10 \). Adjusted mean anxiety scores were 3.0 for PREPARE+AD (< 5 considered no anxiety) and 3.7 for AD only; \( P = 0.05 \).
Table 17. Depression and Anxiety Scores by Trial Arms

<table>
<thead>
<tr>
<th>Adverse Event Outcome</th>
<th>PREPARE+AD, n = 219</th>
<th>AD Only, n = 219</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depression: PHQ-8 score (0-24)</td>
<td>3.9 (0.28)</td>
<td>4.5 (0.27)</td>
<td>0.10</td>
</tr>
<tr>
<td>Anxiety: GAD-7 score (0-21)</td>
<td>3.0 (0.25)</td>
<td>3.7 (0.24)</td>
<td>0.05</td>
</tr>
</tbody>
</table>

Abbreviation: AD, advance directive; GAD-7, Generalized Anxiety Disorder-7; PHQ-8, Patient Health Questionnaire-8.

a Adjusted for baseline depression and anxiety scores. Adjusted mean and 95% CI. Depression was measured using the validated PHQ-8 (scores 0-24) and anxiety was measured with the GAD-7 (scores 0-21). Scores less than 5 represent no clinically meaningful anxiety or depression and scores of 5, 10, 15, and 20 represent mild, moderate, moderately severe, and severe depression or anxiety, respectively.94,95

b Confidence intervals are ± 1.96 times the SE.

Post Hoc Secondary Outcomes

As noted earlier, the stakeholder advisory board requested these analyses after we had established the original protocol. In the PREPARE+AD arm, 97.3% of participants increased their self-reported ACP Engagement Behavior Change (eg, self-efficacy and readiness) or Action scores from baseline compared with 83.6% of those randomized to the AD-only arm (P < 0.001; Table 18).

As documented in Table 18, for Behavior Change scores, 96.8% of participants in the PREPARE+AD arm increased their scores, as did 81.0% in the AD-only arm (P < 0.001). For the Action scores, 94.1% of participants in the PREPARE+AD arm increased their scores, as did 76.6% in the AD-only arm (P < 0.001; Table 18).

For documentation-specific activities (eg, documenting a surrogate decision-maker or completing an AD), 98.2% of participants in the PREPARE+AD arm vs 81.4% in the AD-only arm increased their Behavior Change or Action scores (P < 0.001). For discussion-specific ACP activities (eg, talking with surrogate decision-makers or medical providers about their wishes), 98.6% of participants in the PREPARE+AD arm vs 86.7% in the AD-only arm increased their scores (P < 0.001). These documentation-specific and discussion-specific significant findings remained when we separated them by Behavior Change survey items and Action score survey items (P < 0.001 for all; Table 18).
Table 18. Percentage of Participants With Increased ACP Behavior Change and Action Scores Over Time

<table>
<thead>
<tr>
<th>ACP Activities</th>
<th>Improvement in Behavior Change and ACP Actions&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Improvement in ACP Behavior Change Only</th>
<th>Improvement in ACP Actions Only</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PREPARE+AD</td>
<td>AD Only</td>
<td>PREPARE+AD</td>
</tr>
<tr>
<td></td>
<td>n (%)</td>
<td>n (%)</td>
<td>P value</td>
</tr>
<tr>
<td>All ACP activities</td>
<td>213 (97.3%)</td>
<td>189 (83.6%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Documentation</td>
<td>215 (98.2%)</td>
<td>184 (81.4%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Discussions</td>
<td>216 (98.6%)</td>
<td>196 (86.7%)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Abbreviations: ACP, advance care planning; AD, advance directive.

<sup>a</sup>The validated ACP Engagement Survey includes both Behavior Change and Action scores. Percentages reflect participants with positive slopes over time, adjusted for health literacy, baseline ACP documentation, and clustering by physician. “All ACP activities” is a composite measure of Behavior Change and Action scores. We present slopes for all reported ACP activities as well as ACP documentation-specific and ACP discussion-specific activities. Statistical significance set at $P = 0.017$. 
Timing of ACP Documentation

A PCORI reviewer also requested we conduct a post hoc analysis to determine when ACP documentation took place. Figure 7 plots the absolute number of patients with ACP documentation from their baseline over the course of 15-month follow-up by study arm. The largest rate of completion occurred within the first 3 months and was larger for the PREPARE+AD arm than the AD-only arm. However, ACP documentation continued to increase over the 15-month period in both arms.

Figure 7. Cumulative distribution function for time to ACP documentation

Abbreviations: ACP, advance care planning; AD, advance directive.
Aim 3 Results

Aim 3: Disseminate PREPARE with input from patients, caregivers, and stakeholders.

At the end of the study, we asked the participants in the PREPARE+AD arm how we could improve PREPARE and whether they had any suggestions for dissemination. Although we asked patients for constructive feedback about what we could do better, we continued to hear themes of positive feedback (translated from Spanish into English for this report; Table 19). We also heard some constructive feedback from patient participants that has allowed us to update and improve PREPARE (Table 20).

Additionally, patients gave very helpful suggestions for dissemination (Table 21), which we will incorporate into our dissemination plans. The stakeholder advisory board focus groups also produced several themes for dissemination (Table 22).
<table>
<thead>
<tr>
<th>Theme</th>
<th>Patient Quotation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Easy to use</td>
<td>“I think it’s a great guide to make the right decisions. I liked everything, and I thought it was easy, even though I’d never used a computer before.”</td>
</tr>
<tr>
<td>Well translated and culturally appropriate</td>
<td>“I think this is very useful, very interesting, and the language was very easy to understand. I liked the questions asked and that here I learned about what is important to me and how that will affect others. The translation was very well done. People of different nationalities and from different countries can all understand the word choices. Very respectful language, accessible, and understanding was not hard at all.”</td>
</tr>
<tr>
<td>Fills a gap for Spanish materials</td>
<td>“I have been looking and asking around for this type of information, but I did not find the resources. I did not want to leave this to my kids, for them to suffer. God answered my prayers.”</td>
</tr>
<tr>
<td>Videos help with learning</td>
<td>“I learned a lot of new things. I liked what I watched; the videos were good. I liked that I saw videos that talked about choices that I prefer.”</td>
</tr>
<tr>
<td>Helps individuals define or change their mind about their values or goals</td>
<td>“I came in having some original thoughts but [the content] really made me understand certain things and made me change my mind. Thought I wanted to give my daughter limited flexibility and ended with total flexibility.”</td>
</tr>
<tr>
<td>Decreases anxiety about advanced care planning</td>
<td>“It gives a lot of advice on how to communicate to your family about this topic. It gives you the information to not feel nervous about talking about this topic to your family. It’s very good. I have never seen any information about advance care planning in the hospital before and this was my first time learning about this topic.”</td>
</tr>
<tr>
<td>Helps people talk to their doctors</td>
<td>“It motivates us to be more well aware of our health and decisions that we may have to make. It takes away the fear and motivates us to ask doctors questions to help us understand how our health is doing.” “It is very important, happy to be here; it will help me to speak to my doctor and family. I will recommend it to my friends and family. It will help me confide with my doctor.”</td>
</tr>
</tbody>
</table>
### Table 20. Constructive Feedback About the PREPARE Program

<table>
<thead>
<tr>
<th>Theme</th>
<th>Patient Quotation</th>
<th>Changes to PREPARE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scenarios</td>
<td>“I don’t agree with some of the ideas in the videos, like when people decide that it’s okay to be put on a feeding tube and breathing machine for a long time.”</td>
<td>We added “your situation may be different” to every scenario.</td>
</tr>
<tr>
<td>Language</td>
<td>“I feel like if I am terminally ill or sick and I have to decide what I have to do with myself in the next 3 or 6 months, ‘States worse than death’ is hard to hear.”</td>
<td>We have since removed all mention of that phrase from the PREPARE website, advance directive, and materials.</td>
</tr>
<tr>
<td>Shorten</td>
<td>“The interviewing sessions are too long and too intense. Making those simpler would make it more accessible to people.”</td>
<td>Participant watched the PREPARE videos and had the baseline interview all on the same day, which made for a very long interviewing session. In subsequent studies, we will separate these activities. In addition, we have shortened several of the videos and cut out 20 minutes from the PREPARE steps. We also make clear on the public-facing website that people can do one step or all steps based on their preferences.</td>
</tr>
</tbody>
</table>

### Table 21. Patient Suggestions for Dissemination

<table>
<thead>
<tr>
<th>Theme</th>
<th>Patient Quotation About Dissemination</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disseminate in the community</td>
<td>“The PREPARE material was developed with the focus of using in a hospital setting, but I believe the material needs to be modified so it can be implemented towards society. The issue of advance care planning is a bigger issue that won’t be fixed at a hospital. This is a social issue that needs to be addressed as one.”</td>
</tr>
<tr>
<td>Put on community events</td>
<td>“Organize a public meeting where groups receive information about this study and about the advance directive form and the other materials.”</td>
</tr>
<tr>
<td>Consider a group medical visit</td>
<td>“To have like a mini-seminar of, like, 10 individuals or so and invite them to come in either at the clinic, in a nice place. Possibly have a projector and explaining the importance of these things.”</td>
</tr>
<tr>
<td>Use technology</td>
<td>“People are too into technology; try texting or any other form of social media to get their interest because they get the papers and forget about them.”</td>
</tr>
</tbody>
</table>
Table 22. Stakeholder Advisory Board Suggestions for Dissemination

<table>
<thead>
<tr>
<th>Theme</th>
<th>Suggestion From Members of the Stakeholder Advisory Board</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marketing</td>
<td>The stakeholder advisory board concluded that, even though PREPARE was more efficacious than the advance directive (AD) alone, marketing and disseminating the website and the AD together “as one PREPARE program” would be important. We had created a “Thanks Mom” video with foundation funding; it is currently available on the PREPARE website. Stakeholders felt that something like this in Spanish would also be helpful for marketing to the Spanish community.</td>
</tr>
<tr>
<td>Target resource-poor public health systems</td>
<td>Because PREPARE and the AD can be used outside the clinic environment to prepare patients to have conversations with clinicians, and because PREPARE is free to the public, stakeholders suggested that we target marketing and dissemination to public health systems.</td>
</tr>
<tr>
<td>Non–clinic-based dissemination partners</td>
<td>Stakeholders suggested, with hospital approval, using hospital volunteers, lay health navigators, and peer mentors to help distribute the materials. Several patient advisors offered to sit at tables outside the clinic and hand out PREPARE pamphlets and ADs. Several stakeholders commented that hearing and accepting the information from someone from their own background and culture might be easier than from someone outside their culture.</td>
</tr>
<tr>
<td>Clinic-based dissemination partners</td>
<td>Social work and behavioral health teams were discussed as staff that may be able to start the conversation and at least provide the materials. Other stakeholders felt this should be normalized by having front desk staff hand out PREPARE pamphlets and ADs to patients.</td>
</tr>
<tr>
<td>Waiting room videos</td>
<td>Because the PREPARE steps can be played as videos in addition to the interactive components on the website, stakeholders recommended having the videos playing on a loop in the waiting room while patients are waiting.</td>
</tr>
<tr>
<td>Group medical visits</td>
<td>Several of the clinics engage in group medical visits for patients with chronic illness (eg, diabetes management). Again, video versions of PREPARE can be used, even by untrained clinical staff, to share during group advance care planning (ACP) visits.</td>
</tr>
<tr>
<td>Using the patient portal</td>
<td>Stakeholders agreed that most patients in public hospitals are not using the patient portal. That said, they stated that its use will likely increase over the years, and it may be an avenue for some patients to access the ACP information and the PREPARE website.</td>
</tr>
<tr>
<td>Theme</td>
<td>Suggestion From Members of the Stakeholder Advisory Board</td>
</tr>
<tr>
<td>-------------------------------------------</td>
<td>--------------------------------------------------------------------------------------------------------------------------</td>
</tr>
</tbody>
</table>
| **Organization and community dissemination partners** | Suggestions of groups to work with include the following:  
• Zuckerberg San Francisco General Wellness Center, which offers health education courses on a variety of topics  
• AARP, which has been trying to create more materials for Spanish-speaking older adults  
• Centers for Medicare & Medicaid Services, because ACP has been part of reimbursement programs such as the Merit-based Incentive Payment Program  
• Medical Legal Partnerships, which are legal organizations that work with disenfranchised populations in close collaboration with medical centers |
| **Ethnic media**                          | Several stakeholders recommended reaching out to Spanish-language radio and print media.                                  |
DISCUSSION

Context for the Study Results

Historically, studies demonstrate limited engagement of Spanish-speaking older adults in ACP and a lack of culturally appropriate, patient-facing ACP materials in Spanish.\(^4,15-18\) This trial, which focused on Spanish-speaking older adults with a high prevalence of limited health literacy who receive care in a safety-net health care setting, demonstrated marked increases in ACP documentation in the medical record and self-reported engagement in the process of ACP. In the absence of clinician- or system-level interventions, the easy-to-read AD in Spanish (AD only) resulted in a new ACP documentation rate of 24%. The PREPARE website plus the AD (PREPARE+AD) led to an ACP documentation rate of 39%.

This level of new ACP documentation is higher than that seen in a prior PREPARE and easy-to-read AD trial among English-speaking veterans (35%),\(^52\) and higher than prior studies of patient-directed ACP tools in primary care (5%-23%).\(^10,43,44\) And, although the level of ACP documentation in the medical record was lower than 50%, documentation in the medical record, as described in the Background section, may not provide a full picture of the ACP activities occurring over the trajectory of behavior change. For example, 97.3% of participants in the PREPARE+AD arm increased their self-reported ACP engagement, as did 83.6% of participants in the AD-only arm.

It also appears that these interventions help patients complete ACP over time. Although the largest gains in ACP documentation occur soon after the intervention, with the PREPARE arm having higher early gains, both the easy-to-read AD and PREPARE continued to increase ACP documentation over time. We created the PREPARE program to address ACP as an ongoing process over time because patients are in differing readiness stages to engage in ACP.\(^53\) We also created PREPARE to address the ongoing ACP process because patients’ wishes and values have been shown to change over time.\(^125-127\) Furthermore, the stability of AD preferences appears to be approximately 3 years.\(^125-127\) PREPARE was specifically designed to help address changing preferences by providing a framework for patients to have ongoing discussions and to update their preferences when needed.
Both tools were rated highly for ease of use and satisfaction. This finding suggests that PREPARE and the easy-to-read AD could serve as scalable, easy-to-disseminate tools to improve the ACP process, especially in busy and resource-poor primary care clinics. Unlike English-speaking veterans in a prior trial, Spanish-speaking older adults rated Spanish PREPARE as more helpful than the AD alone. This may reflect the need for a step-by-step guide for members of this population who have very high rates of limited health literacy.

The large gains in ACP engagement for both Spanish PREPARE and the easy-to-read AD may be explained by their attention to literacy and cultural considerations designed with and for diverse Spanish-speaking populations. PREPARE also models ACP behavior, based on Behavior Change and Social Cognitive theories, by using “how to” video stories. Using videos and stories has been shown to help patients make ACP and medical decisions. In prior studies, passive ACP education with written materials has been less effective than discussions with trained clinicians or facilitators. One reason may be the use of materials written at or beyond a 12th-grade reading level that have not been culturally adapted for this population.

Using trained ACP facilitators has improved communication and ACP documentation more than 50% among English- and Spanish-speaking patients. Because most health care organizations lack the resources for dedicated, trained ACP facilitators, PREPARE and the AD in Spanish, as demonstrated in this study, may allow patients to begin and, in many cases, complete the ACP process on their own.

Nevertheless, a medical provider should review and discuss all care plans with patients within the context of their current health situation and prognosis. In addition, some individuals will need a facilitator or navigator to begin to engage in ACP. However, in resource-limited, safety-net health systems in which using a trained facilitator is not feasible, gains in ACP engagement prompted by both Spanish PREPARE and the AD could have significant implications for population health. This is particularly true given the paucity of literacy- and language-appropriate materials for this vulnerable patient population, and the growing guidelines and reimbursement mechanisms for ACP. Combining the patient-facing ACP interventions in Spanish with evidenced-based clinician- and system-level interventions (eg, Vital Talk,
Jumpstart,45,132-134 Respecting Choices, the Serious Illness Checklist) will likely produce even larger gains, but further research is needed.

Generalizability of the Findings

These findings may be generalized to our study population—older Spanish-speaking patients with highly limited health literacy rates who receive care from primary care clinics in a safety-net, public hospital system. Our participants were able to use the AD and the PREPARE online program with limited to no support from research staff. Therefore, we believe that the ACP interventions can be used in diverse outpatient settings, including specialty settings, primary care, and possibly the community. However, the generalizability of our findings may be limited to patients who agreed to be in a research study about ACP. Those who refused were on average 3 years older than those who agreed to be in the study. This might have been because older adults were more seriously ill or were less interested in an online ACP tool. Generalizability is also limited to one area of the United States and one health care system and may not apply to Spanish-speaking patients in different geographical locations or within other health care systems.

Implementation of Study Results

Our engaged stakeholder advisory board and study participants discussed the lack of time and resources in a public delivery system for ACP and the important gap that PREPARE and our AD can fill. Our stakeholders concluded that providing these materials outside the clinic visit, as was done in this trial, is a good model for widespread dissemination. We also learned in this trial that any dissemination efforts will require the support of the health care systems and their clinical leadership as well as backing from clinical and community champions.

Some features of PREPARE and the AD may help with implementation in real-world settings. Among the more salient factors are the following: The materials are written at a fifth-grade reading level and are accessible to most patients; the PREPARE website (www.prepareforyourcare.org) can be played as a “movie” and can be used in group medical
visits\textsuperscript{135}; and the easy-to-read PREPARE pamphlets can be distributed in clinics and community settings to start the engagement process.

**Subpopulation Considerations**

When looking for interactions, we did not find differences in the effect of the PREPARE intervention by many patient characteristics. These included health literacy, education, gender, race or ethnicity, presence of a potential surrogate, and patient–clinician language concordance. With the many variables assessed, it is not surprising that we found one (age) to be nominally significant. Given the low computer literacy of this disenfranchised Spanish-speaking cohort, the effect may be larger among younger adults (those aged 65 and under) with higher computer literacy than older age groups, although the treatment effect was still positive for both age groups. Also, younger patients with a chronic illness might have had less opportunity to reflect on their values related to ACP, so the intervention might have been more activating for them. Power might have limited our ability to detect heterogeneity of treatment effects for some of the factors examined. In particular, only 15% of participants expressed low decision control with doctors and only 3% expressed low decision control with family. In addition, only 16% had more than a high school education. All other factors were present in at least 25% of the population. Examining the magnitude of effect suggests that, in addition to younger age, the intervention might have been especially beneficial to those who prefer that the family decide, have doctor–patient language discordance, have less than a high school education, have lower levels of spirituality or religiosity, or have no internet access at home. However, these differences were not statistically significant. Additional studies are needed to help identify which patient populations are more or less likely to respond to PREPARE.

**Study Limitations**

This study has several important limitations. Although we conducted the study in 4 primary care clinics within the San Francisco safety net, it was limited to one region of the United States and to a public health delivery system. For these reasons, our results may not be generalizable to other geographical locations, health systems, or clinical settings, or to patient populations that do not choose to participate in research.
Selection bias could have occurred among patients who were willing to participate. Specifically, we did not include individuals who had moderate-to-severe cognitive impairment, or those who reported they were too ill to participate. Nonresponse bias also might have occurred. This might have represented passive refusal or potentially further exclusion of participants who were too ill to participate. Therefore, our results may not be generalizable to patients with cognitive impairment or a serious medical illness. Nevertheless, we found no differences in reasons for refusal or patient characteristics between the intervention and control arms in the trial. In addition, all study materials were viewed in research offices, potentially limiting generalizability to viewing PREPARE at home or outside a clinical environment.

As explained, we were not able to blind patients to their random intervention assignment (PREPARE+AD vs AD only). However, clinicians and all staff who conducted follow-up interviews were blinded to group allocation. Furthermore, study interviews and reminder calls, often a routine part of primary care, may be activating to patients and encourage them to engage in ACP. Conducting telephone reminders to engage in ACP, in addition to providing the ACP interventions, may also be needed to obtain results similar to those of our trial. Finally, we were unable to do medical record review in health systems outside the SFHN and ZSFG; participants might have had additional ACP documentation in other settings.

Future Research

Several avenues for future research are promising. Although this trial demonstrated strong efficacy, the next step would be to conduct real-world effectiveness studies, allowing patients to view the materials on their own and at their own pace. This type of viewing could be studied in clinic waiting rooms or outside the clinical environment, such as in peoples’ homes, in malls, or at health fairs. It is also important to explore how health care systems might integrate PREPARE into their standard operating procedures and whether it would still be as effective in that context. Furthermore, research should be conducted in other geographic areas and with differing Spanish-speaking populations.
PREPARE and the AD can also be tested in other clinical settings, including specialty clinics, inpatient settings, and nursing homes. Researchers should consider testing these interventions among patient populations with more advanced or serious illnesses than we were able to study in this trial. Although this patient population had a high illness and comorbid disease burden, future studies could include persons with terminal conditions who may be at the end of life or receiving hospice care.

In addition, both PREPARE and the easy-to-read AD are likely to be synergistic with other clinician-level, electronic health record–level, or health system–level ACP interventions. Thus, exploring a study in which patients receive both a patient-level intervention, such as PREPARE+ AD, and an evidenced-based clinician-level intervention, such as education for clinicians or clinician reminders (eg, Vital Talk, Jumpstart, Respecting Choices, the Serious Illness Checklist), would be another good next step.

Future studies should also assess downstream outcomes of ACP. This efficacy study was designed to increase engagement in the ACP process among patients with a broad range of chronic illness. Therefore, we were unable to assess downstream outcomes such as health care utilization, cost, the type of end-of-life care received, and whether the care provided was consistent with patients’ goals at the time of hospitalization or death.
CONCLUSIONS

To our knowledge, this is the largest trial of patient-facing ACP interventions among Spanish-speaking patients. Our trial aimed to compare the efficacy of the online ACP PREPARE program plus an easy-to-read advance directive (PREPARE+AD: intervention arm) with that of an AD alone (AD only: control arm). Among Spanish-speaking older adults from a safety-net health care system, these easy-to-use ACP tools in Spanish, without system or clinician input, increased ACP documentation 24% in the AD-only arm and 39% in the PREPARE+AD arm. Combining Spanish PREPARE plus an easy-to-read AD resulted in higher ACP documentation and engagement than using the AD alone. Almost all patients in the PREPARE+AD arm reported engaging in some form of ACP.

This trial suggests that PREPARE and the easy-to-read AD may be useful ACP interventions for Spanish-speaking patient populations, especially in safety-net settings. More research is needed to determine the combined effects with other clinician- or system-level interventions. More work is also needed to determine the best ways to disseminate these freely available, easy-to-use materials to the public. These tools may be easily scalable on a broad population level because they are free to the public.

The results of our trial will be helpful to Spanish-speaking older adults in primary care and their families and to the primary care providers who care for them. Because of the ability to disseminate PREPARE and the AD to large populations, our results will also be important for health systems, especially safety-net and public hospital systems. Health systems and insurers may also be interested in PREPARE and the AD because these interventions helped increase ACP documentation in the medical record; this quality indicator has recently been tied to reimbursements from the Centers for Medicare & Medicaid Services and value-based purchasing.

Finally, our results may also be of interest to libraries, places of worship, senior centers, and other health care systems that are interested in promoting ACP and providing their members ACP information that is appropriate in terms of literacy, culture, and the Spanish language.
REFERENCES


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ACKNOWLEDGMENTS

The statements in this publication are solely the responsibility of the authors and do not necessarily represent the views of PCORI, its Board of Governors, or its Methodology Committee.

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- Deborah E. Barnes, PhD
- W. John Boscardin, PhD
- Dean Schillinger, MD
- Janet Shim, PhD

Stakeholder Advisory Board

a. Patient, Caregiver, Patient Advocate Stakeholders (alphabetical order)

- Irene Conway
- Araceli Medina
- Dora Morales

b. Community Stakeholders (alphabetical order)

- Purba Chaterjee, MPH
- Carmen Ortiz, PhD
- Michael Villaire, MSLM

c. Clinical Stakeholders (alphabetical order)

- Rosaly Ferrer, RN, MS
• Halle Hammer, MD
• Heather Harris, MD
• Claire Horton, MD
• Olga Ivanco, RN, MS
• Anne Kinderman, MD
• Lydia Leung, MD
• Laura Pullen, MSW
• Judith Sansone, RN
• Christina Weyer-Jamora, PhD
APPENDICES

Appendix A: Multidisciplinary Stakeholder Team Description

Research co-investigators (alphabetical order)

- **Dr. Deborah E. Barnes, PhD, Co-Investigator**, is an epidemiologist and trialist. She is a professor in the Departments of Psychiatry and Epidemiology & Biostatistics at UCSF, a research health science specialist for the San Francisco Veterans Affairs Health Care System, and a senior investigator for the UCSF Tideswell program. Dr. Barnes’ research focuses on the development and testing of both cognitive and exercise-based interventions to preserve cognitive function in diverse, vulnerable elders. She has experience conducting randomized trials, behavioral measurement, the design and testing of multimedia behavioral interventions, and the dissemination and implementation of these interventions.

- **Dr. W. John Boscardin, PhD, Co-Investigator**, is a professor of medicine and epidemiology & biostatistics at UCSF and a research PI at the San Francisco Veterans Affairs Medical Center (SFVAMC). He has a strong background in planning and analyzing RCTs, repeated measures, longitudinal data, hierarchical modeling, the treatment of missing data, and the use of multivariate models.

- **Dr. Dean Schillinger, MD, Co-Investigator**, is a professor of medicine in residence at UCSF, chief of the UCSF Division of General Internal Medicine at Zuckerberg San Francisco General Hospital and Trauma Center (ZSFG), and director of the Health Communications Research Program. He is a practicing primary care physician at ZSFG, an urban public hospital, where he sees patients, teaches in the primary care residency program, and conducts research; he previously directed the General Medicine Clinic. Dr. Schillinger also serves as chief of the Diabetes Prevention and Control Program for the California Department of Public Health and directs the ZSFG Center for Vulnerable Populations Health Communications Program. Drs. Sudore and Schillinger have a long working relationship, including on an RCT of an easy-to-read AD at ZSFG and on several other papers assessing the effects of health literacy and race/ethnicity on health outcomes and communication.

- **Dr. Janet Shim, PhD, Co-Investigator**, is a professor in the UCSF Department of Social and Behavioral Sciences in the School of Nursing. She has methodological expertise in qualitative methods as well as substantive expertise in medical sociology, social studies
of science, technology, and aging; and methodological experience in qualitative methods, including in-depth individual and group interviews of clinicians and patients.

Patient-Clinician Advisory Board (alphabetical order)

a. Patient, Caregiver, Patient-Advocate Stakeholders

- Irene Conway is a patient, caregiver, and patient-advocate stakeholder. Mrs. Conway has been a primary care patient at ZSFG for over 20 years and has served as a patient advocate and on the ZSFG Family Health Center (FHC) advisory board for over 10 years.

- Araceli Medina is a Spanish-speaking patient, caregiver, and patient-advocate stakeholder. She was born in Nicaragua, is a primary care patient at ZSFG, and has served as a patient advocate on the ZSFG FHC advisory board.

- Dora Morales is a Spanish-speaking patient and caregiver stakeholder. She was born in Guatemala and has served as a primary caregiver for frail older adults, is a primary care patient at ZSFG, and has served as a patient advocate on the ZSFG FHC advisory board.

b. Community Stakeholders (alphabetical order)

- Purba Chaterjee, MPH, was the program manager of the UCSF Center for Vulnerable Populations, with deep ties to the San Francisco Latino community. She acted as a liaison between Dr. Sudore’s study staff, the research community at ZSFG, and primary care clinics, and the Latino community in San Francisco. The CVP study coordinator provided guidance on recruitment of vulnerable populations and ensured Dr. Sudore’s study team had access to patient medical records, clinic schedules, patients’ upcoming appointments, and interviewing space.

- Carmen Ortiz, PhD is a patient navigator stakeholder. She is a Latina breast cancer survivor, patient and community activist, researcher, psychologist, and executive director of a nonprofit community-based organization called Círculo de Vida Cancer Support and Resource Center (http://www.circulodevida.org).

- Michael Villaire, MSLM, is chief executive officer of the Institute for Healthcare Advancement (https://www.iha4health.org/), a not-for-profit, 501(c)(3) public benefit charity whose mission is to empower diverse communities to better health. Mr. Villaire has a strong commitment to the Latino community and has extensive experience creating and providing literacy and linguistically appropriate health education material to Spanish-speakers, including the easy-to-read AD on which he and Dr. Sudore collaborated.
c. Clinical Stakeholders (alphabetical order)

- **Rosaly Ferrer RN, MS**, nurse manager of the ZSFG General Medicine Clinic and Adult Medicine Center

- **Halle Hammer, MD**, and **Lydia Leung, MD**, directors of the Family Health Center at ZSFG and director of the Family Medicine Residency Program

- **Claire Horton, MD**, director of the General Medicine Clinic at ZSFG and associate director of the Internal Medicine Residency Program

- **Olga Ivanco, RN, MS**, nurse manager of the ZSFG Family Health Center

- **Anne Kinderman, MD** and **Heather Harris, MD**, director of the Symptom Management and Palliative Care Service at ZSFG

- **Laura Pullen, MSW**, ZSFG Family Health Center medical social worker

- **Christina Weyer-Jamora, PhD**, director of Behavioral Health for Primary Care, ZSFG
Appendix B: Study Protocol

This trial protocol has been provided by the authors to give readers additional information about their work for this report. The original trial protocol has been previously published.
Final Research Protocol Table of Contents

SPIRIT Checklist
ClinicalTrials.gov Information
Introduction and Rationale
Preliminary Studies
Overview of the Trial Design
Study Setting
Participants and Eligibility and Exclusion Criteria
Recruitment Methods
Consent Procedures
Intervention and Comparison Conditions
Randomization Procedures
Blinding
Intervention Fidelity
Data Collection Methods
Follow-up and Retention
Measures
Statistical Analysis Plan
Sample Size and Power Calculations
Ethics and Advisory Committees
Human Subjects Protections
Data Safety Monitoring Plan
Charter of the Data and Safety Monitoring Board
Patient-Clinician Stakeholder Advisory Committee Role
References
### SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

<table>
<thead>
<tr>
<th>Section/item</th>
<th>Item No</th>
<th>Description</th>
<th>Addressed on page number</th>
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<tbody>
<tr>
<td><strong>Administrative information</strong></td>
<td></td>
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<tr>
<td>Title</td>
<td>1</td>
<td>Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym</td>
<td>12</td>
</tr>
<tr>
<td>Trial registration</td>
<td>2a</td>
<td>Trial identifier and registry name. If not yet registered, name of intended registry</td>
<td>12</td>
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<tr>
<td></td>
<td>2b</td>
<td>All items from the World Health Organization Trial Registration Data Set</td>
<td>N/A</td>
</tr>
<tr>
<td>Protocol version</td>
<td>3</td>
<td>Date and version identifier</td>
<td>12</td>
</tr>
<tr>
<td>Funding</td>
<td>4</td>
<td>Sources and types of financial, material, and other support</td>
<td>12</td>
</tr>
<tr>
<td>Roles and responsibilities</td>
<td>5a</td>
<td>Names, affiliations, and roles of protocol contributors</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>5b</td>
<td>Name and contact information for the trial sponsor</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>5c</td>
<td>Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities</td>
<td>NA</td>
</tr>
<tr>
<td>Section</td>
<td>Item</td>
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<tr>
<td>5d</td>
<td>Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)</td>
<td>53</td>
<td></td>
</tr>
<tr>
<td>Introduction</td>
<td>Background and rationale</td>
<td>Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention</td>
<td>12</td>
</tr>
<tr>
<td>6b</td>
<td>Explanation for choice of comparators</td>
<td>17</td>
<td></td>
</tr>
<tr>
<td>Objectives</td>
<td>7</td>
<td>Specific objectives or hypotheses</td>
<td>18</td>
</tr>
<tr>
<td>Trial design</td>
<td>8</td>
<td>Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)</td>
<td>17</td>
</tr>
</tbody>
</table>

**Methods: Participants, interventions, and outcomes**

<table>
<thead>
<tr>
<th>Section</th>
<th>Item</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study setting</td>
<td>9</td>
<td>Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained</td>
</tr>
<tr>
<td>Eligibility criteria</td>
<td>10</td>
<td>Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)</td>
</tr>
<tr>
<td>Interventions</td>
<td>11a</td>
<td>Interventions for each group with sufficient detail to allow replication, including how and when they will be administered</td>
</tr>
<tr>
<td></td>
<td>11b</td>
<td>Criteria for discontinuing or modifying allocated interventions for a given trial participant (e.g., drug dose change in response to harms, participant request, or improving/worsening disease)</td>
</tr>
<tr>
<td></td>
<td>11c</td>
<td>Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (e.g., drug tablet return, laboratory tests)</td>
</tr>
<tr>
<td></td>
<td>11d</td>
<td>Relevant concomitant care and interventions that are permitted or prohibited during the trial</td>
</tr>
<tr>
<td>Outcomes</td>
<td>12</td>
<td>Primary, secondary, and other outcomes, including the specific measurement variable (e.g., systolic blood pressure), analysis metric (e.g., change from baseline, final value, time to event), method of aggregation (e.g., median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended</td>
</tr>
<tr>
<td>Participant timeline</td>
<td>13</td>
<td>Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)</td>
</tr>
<tr>
<td>Sample size</td>
<td>14</td>
<td>Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations</td>
</tr>
<tr>
<td>Recruitment</td>
<td>15</td>
<td>Strategies for achieving adequate participant enrolment to reach target sample size</td>
</tr>
</tbody>
</table>

Methods: Assignment of interventions (for controlled trials)
### Allocation:

<table>
<thead>
<tr>
<th>Topic</th>
<th>Description</th>
<th>Reference</th>
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<tbody>
<tr>
<td><strong>Sequence generation</strong></td>
<td>Method of generating the allocation sequence (e.g., computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (e.g., blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions.</td>
<td></td>
</tr>
<tr>
<td><strong>Allocation concealment</strong></td>
<td>Mechanism of implementing the allocation sequence (e.g., central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned.</td>
<td>31</td>
</tr>
<tr>
<td><strong>Implementation</strong></td>
<td>Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions.</td>
<td>31</td>
</tr>
<tr>
<td><strong>Blinding (masking)</strong></td>
<td>Who will be blinded after assignment to interventions (e.g., trial participants, care providers, outcome assessors, data analysts), and how. <strong>17b</strong> If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant’s allocated intervention during the trial</td>
<td>31</td>
</tr>
</tbody>
</table>

### Methods: Data collection, management, and analysis

<table>
<thead>
<tr>
<th>Topic</th>
<th>Description</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Data collection methods</strong></td>
<td>Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (e.g., duplicate measurements, training of assessors) and a description of study instruments (e.g., questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol</td>
<td>32</td>
</tr>
</tbody>
</table>
18b Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols

Data management 19 Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol

Statistical methods 20a Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol

20b Methods for any additional analyses (eg, subgroup and adjusted analyses)

20c Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)

Methods: Monitoring

Data monitoring 21a Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed

21b Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial
### Harms
22 Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct

### Auditing
23 Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor

### Ethics and dissemination

<table>
<thead>
<tr>
<th>Topic</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Research ethics approval</td>
<td>24</td>
</tr>
<tr>
<td>Protocol amendments</td>
<td>25</td>
</tr>
<tr>
<td>Consent or assent</td>
<td>26a</td>
</tr>
<tr>
<td></td>
<td>26b</td>
</tr>
<tr>
<td>Confidentiality</td>
<td>27</td>
</tr>
<tr>
<td>Declaration of interests</td>
<td>28</td>
</tr>
<tr>
<td>Access to data</td>
<td>29</td>
</tr>
</tbody>
</table>

- **Research ethics approval**
  Plans for seeking research ethics committee/institutional review board (REC/IRB) approval

- **Protocol amendments**
  Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)

- **Consent or assent**
  Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)

- **Confidentiality**
  How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial

- **Declaration of interests**
  Financial and other competing interests for principal investigators for the overall trial and each study site→ *No investigators have COI*

- **Access to data**
  Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators

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**Notes:**

- **Harms:** Page 52
- **Auditing:** Page 55
- **Research ethics approval:** Page 48
- **Protocol amendments:** Page 57
- **Consent or assent:** Page 27
- **Confidentiality:** Page 50
- **Declaration of interests:** Page N/A
- **Access to data:** Page 58
### Ancillary and post-trial care

30 Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation

____ N/A _____

### Dissemination policy

31a Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (e.g., via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions

____ 58 _____

31b Authorship eligibility guidelines and any intended use of professional writers

____ N/A _____

31c Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code

____ 58 _____

### Appendices

#### Informed consent materials

32 Model consent form and other related documentation given to participants and authorised surrogates

____ 14 _____

#### Biological specimens

33 Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable

____ N/A _____

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons “Attribution-NonCommercial-NoDerivs 3.0 Unported” license.*
INTRODUCTION AND RATIONALE

Background

The population is aging,1,2 and the prevalence of chronic disease is increasing, especially among underserved and vulnerable populations (i.e., economically disadvantaged, racial and
A critical aspect of chronic and serious disease management is advance care planning (ACP), a process whereby patients plan for their future medical care. Traditionally, advance directives have been the main focus of ACP, but unfortunately, most are written with complex, legal language. This lack of attention to limited health literacy and limited English proficiency may explain why advance directives are often not completed and may explain, in part, why less than 20% of racially and ethnically diverse, older adults engage in advance care planning (ACP) by the end-of-life.

Furthermore, for ethnic minorities, a population rapidly increasing in the U.S., medical decisions are often complicated by a lack of trust and perceived racism. Ethnic minorities are also more likely to prefer aggressive treatment, mistrust advance directives, and have non-autonomous views on decision making (i.e., prefer that family and doctors make medical decisions for them). Hispanics/Latinos account for 15% of the U.S. population, a proportion projected to grow to 30% by 2050. Spanish-speaking patients face significant communication barriers, and literacy- and language-appropriate ACP tools that address unique aspects of Latino culture (e.g., *familismo* or a strong commitment and orientation to the family) are lacking. In addition, the mean reading level in the U.S. is only at the 8th grade level, and for adults over 65 years of age it is only at the 5th grade level. Patients with limited literacy often lack self-efficacy to communicate their wishes or ask questions, and the combination of limited literacy and limited English-proficiency results in low satisfaction with doctor-patient communication and decision making. However, studies show that patients can be motivated to take action in response to culturally- and linguistically-appropriate information they trust and can understand.

To address these gaps in advance care planning and shortcomings of advance directives, we developed a novel, comprehensive paradigm of ACP focused on preparing patients to identify their wishes, communicate with surrogate decision makers and clinicians, and make complex,
decisions over the course of chronic and serious illness. This approach recognizes patients’
wishes change based on changing clinical contexts and that advance directives are but one tool
to be used to inform in-the-moment decision making. To address the gaps in advance care
planning for racially and ethnically diverse older adults, and based on the new comprehensive
ACP paradigm, we created the interactive, patient-centered PREPARE website
(prepareforyourcare.org) in English and Spanish that is culturally, linguistically, and literacy-
appropriate. PREPARE has been shown in pilot studies among English-speakers to help older
adults engage in the ACP process, but it has yet to be tested in a randomized trial of Spanish-
speaking older adults. Both the new ACP paradigm and the PREPARE intervention have been
described in detail elsewhere. In addition, a description of a related trial of the efficacy of
PREPARE among U.S. Veterans describes the theoretical framework underlying the PREPARE
website.

PRELIMINARY STUDIES

We have experience conducting RCTs among diverse, older adults at the San Francisco
Health Network (SFHN) primary care clinics. Dr. Sudore designed and tested an AD written
at a 5th grade reading level among 205 chronically ill, diverse, older adults from Zuckerberg San
Francisco General Hospital (ZSFG) with a 6-month follow-up of 85%. The AD was preferred
over a standard AD, with significant interactions for limited literacy (e.g., higher preference rates
in patients with limited literacy). It also resulted in greater 6-month AD completion rates (15% vs.
7%, p = .03), doubling the rates from baseline. This AD has been adopted as the official AD for
ZSFG and is being disseminated in California. It will serve as the active control.

We designed and tested an informed consent process for diverse, older adults with
limited literacy. We found that many patients do not understand simplified consent
information and were unsure how to ask questions. But, informed decisions can be improved by
providing both easy-to-read materials and a teach-back method. We will use this interactive consent method for this study.

**Multiple steps of the ACP process:** We found that most patients go through a series of ACP behavioral steps. Six months after exposure to the easy-to-read AD, 61% of older adults contemplated ACP, 56% discussed ACP with family or friends and 22% with clinicians, and 13% completed an AD. This work shows that measuring a full range of ACP outcomes, in addition to ADs, and associated behavior change steps (contemplation to action) is important and informs our study outcomes. Previously described barriers to ACP, such as not wanting to burden family, are addressed in PREPARE.

**Evidence supporting the new ACP paradigm and content of PREPARE:** We completed 13 focus groups with 69 diverse, English- and Spanish-speaking older patients (mean age 78 +/- 8, 61% non-White) and surrogates (mean age 57 +/- 10, 91% non-White) from safety-net settings who reported making serious medical decisions. We used semi-structured interviews to ask about what best prepared them for decision making. Qualitative analysis identified 5 overarching themes, beyond ADs, that prepared patients and surrogates for decision making: (1) choose surrogates wisely and verify they know their role, (2) identify goals based on past experiences and personal values, (3) decide whether to grant leeway in surrogate decision making, (4) inform other family and friends of one’s wishes to prevent conflict, and (5) ask clinicians questions. These themes have been incorporated as educational domains of PREPARE.

**Validity and reliability of the survey to measure ACP engagement:** Surveys were designed with input from Co-Is and extensive cognitive interviews to measure discrete ACP actions (i.e., main outcomes: ACP discussions, AD completion,) and ACP behavior change (e.g., contemplation, self-efficacy, readiness). We recruited 50 older adults, aged ≥ 60 years with ≥ 2 illnesses (32% female, 42% non-White). Internal consistency 7-day test-retest reliability, and discriminant validity (scores compared to healthy young adults – 50% female, 75% non-White)
was high. Scores did not differ by race/ethnicity or literacy, p>.05. We will also use validated surveys on ACP attitudes and methods to classify patients into behavior change categories.33,34

**Preliminary evidence that PREPARE is beneficial.** In a recent pilot,27 we recruited 43 diverse, older adults from low-income senior centers. All subjects rated PREPARE easy to use (mean 9/10-point scale). Pre to post ACP behavior change scores from our validated surveys (0-124 points) increased from 72 ± 33 SD to 87 ± 22, a 15-point increase and an effect size of 0.5.

**Vulnerable populations have unique needs.** The aforementioned pilot demonstrated that, unlike our work with Veterans, patients in safety-net settings are less trustful of research and require in-person recruitment. In addition, these patients are often socially isolated and require tailored ACP for persons without surrogates or families. They also lack ready access to health information and ancillary support such as social workers or nurses necessitating access to ACP outside of the clinical environment. These findings add further evidence for the need to tailor PREPARE for vulnerable populations and to test PREPARE within safety-net settings.

**PREPARE has been shown to increase ACP Documentation and Engagement among Veterans.** A prior trial of PREPARE was conducted among 414 Veterans.35 The mean age of the cohort was 71.1 (7.8) years, 91% were men, 57% were white, 20% had limited literacy, 29% reported fair-to-poor health status, and 51% had evidence of prior ACP documentation. The follow-up time point was 6 months and there was a 90% retention rate. There were no differences in demographic characteristics between study arms. In this VA population, advance care planning documentation 6 months after enrollment was higher in the PREPARE arm vs the AD-alone arm (adjusted 35% vs 25%; odds ratio, 1.61 [95%CI, 1.03-2.51]; P = .04). PREPARE also resulted in higher self-reported ACP engagement at each follow-up, including higher process and action scores; P <.001 at each follow-up). These findings add further evidence of the validity of PREPARE. However, PREPARE has never been tested among diverse, Spanish-speaking older adults in a safety-net setting.
OVERVIEW OF THE TRIAL DESIGN

Study overview:

This study is a randomized, controlled trial that uses blinded outcome ascertainment to determine the efficacy of the ACP PREPARE website to engage ethnically diverse Spanish-speaking older primary care patients in the ACP process. First, we obtained a Health Insurance Portability and Accountability Act waiver to identify individuals who meet our inclusion/exclusion criteria and have upcoming primary care appointments. Administrative data and chart review are used to determine potentially eligible patients (Figure, Study Flow Chart).

Then primary care clinicians' permission is obtained to allow the study team to inform their patients about the study. Patients are then recruited, screened for eligibility and scheduled for a baseline interview before an upcoming primary care appointment. To standardize the timing of exposure to the intervention and primary care follow-up, study participants are scheduled for baseline procedures 1-3 weeks prior to an upcoming primary care appointment.

Next, informed consent is obtained, and those patients who provide consent are randomized to the PREPARE intervention arm (i.e., the PREPARE website with action plan exercises plus an easy-to-read advance directive plus PREPARE materials to take home, which include a website login, and a PREPARE pamphlet, booklet, and DVD) or the control arm (i.e., an easy-to-read advance directive alone). See Study Flow Figure and a full description of the intervention below.

We then conduct blinded outcome ascertainment by performing chart reviews to determine ACP documentation at baseline and at the end of the study. We also conduct blinded outcome ascertainment using patient surveys at 1 week, and 3, 6, and 12 months after the primary care appointment. We are choosing an active control arm (i.e., an easy-to-read advance directive)
because we believe provision of an advance directive for chronically and seriously ill older patients should be the standard of care, even if it is not often "usual" care in clinical practice. In addition, the easy-to-read advance directive used in this study has been adopted by the San Francisco Health Network (SFHN) and Zuckerberg San Francisco General Hospital (ZSFG) and is available in the primary care clinics.

Research Aims and Study Hypotheses:

The aims of this study are to (1) To determine the efficacy of PREPARE to engage diverse, Spanish-speaking older adults with chronic illness in advance care planning (ACP) compared to controls (AD only) and (2) To determine whether PREPARE efficacy varies by race/ethnicity, literacy, clinician-patient language concordance, and patient’s desired role in decision making.

Our primary hypothesis is that the PREPARE program plus an easy-to-read advance directive will result in greater documentation of ACP wishes, including advance directives and documentation of ACP discussions in the medical record, than an easy-to-read advance directive alone in elderly populations with chronic illness.

Our secondary hypotheses are that, compared to an advance directive alone, PREPARE will result in more engagement in behavior change processes concerning ACP, including increased self-efficacy and readiness, as well as greater engagement in a full range of ACP actions, including discussions with surrogate decision makers and other trusted family and friends. Secondary outcomes will be ascertained using validated surveys. We also hypothesize that PREPARE efficacy may vary across moderator variables such as patient health literacy, clinician-patient language concordance, and patients’ desired role in decision making.
Figure 1: PREPARE Study Flow Diagram

Administrative data pull and chart review from ZSFG
- Language listed as Spanish
- ≥ 55 years of age and ≥ 2 chronic illnesses
- Seen by primary care physician ≥ 2 times in the past year + ≥ 2 additional inpatient or outpatient visits
- Not deaf, blind, demented, or psychotic

Obtain clinicians' permission to tell their patients about the study

Screen for eligibility
- Excluded if they report not speaking Spanish "well" or "very well"
- Excluded if they report poor vision, lack of a phone, out of the country ≥ 3 months
- Excluded if they test positive for moderate-to-severe cognitive impairment

Baseline Survey: 1-3 weeks prior to primary care visit
- Chart review to assess ACP documentation
- In-person survey to assess baseline ACP engagement, moderator and mediator variables, and demographic variables

Block randomized by health literacy level (limited vs. adequate literacy)

**PREPARE INTERVENTION**
- PREPARE website in Spanish
- Action plan created within the website
- Easy-to-read advance directive in Spanish
- To take home: website login and PREPARE booklet, pamphlet, and DVD

**CONTROL**
- Easy-to-read advance directive only (Spanish)

Post-intervention acceptability and usability questionnaire for feasibility

Reminder phone call 1-3 days prior to primary care visit
**PREPARE**: Remind to discuss ACP and bring advance directive  
**Control**: Remind about visit

1-week, 3-month, and 6-months follow-up interview (phone or in-person)
- Assess ACP engagement

Final follow-up
- Assess ACP engagement in 12 month interview (phone or in person)
- Chart review to assess ACP documentation at 15 months

Abbreviations: ACP, advance care planning, ZSFG, Zuckerberg San Francisco General Hospital

**STUDY SETTING**
Recruitment for this randomized trial is occurring in 4 separate primary care clinics associated with the San Francisco Health Network (SFHN) and the Zuckerberg San Francisco General Hospital (ZSFG) in San Francisco, California. These 4 clinics are housed in 3 separate physical locations in San Francisco. ZSFG is an urban, public hospital that, with the SFHN, serves racially and ethnically diverse, low-income and indigent patients; 30% of patients are Spanish-speaking.8

PARTICIPANTS AND ELIGIBILITY AND EXCLUSION CRITERIA

There are no inclusion or exclusion criteria based on gender, race or ethnicity. We assess eligibility in person or over the phone. Older adults are included in this study if they self-report speaking Spanish “well” or “very well”; are 55 years of age or older; have ≥ 2 chronic illnesses determined by chart review; have seen a primary care clinician (physician, nurse practitioner, or physician assistant) at ZSFG/SFHN-affiliated primary care clinics ≥ 2 times in the past year (an indication of established primary care); and have had ≥ 2 additional outpatient or inpatient visits in the past year (an indication of severity of illness). Their primary care clinician must also give us permission to contact them to tell them about the study.

We are recruiting patients ≥ 55 years of age (rather than ≥ 65) because adults in safety net settings experience accelerated aging, functional decline, and sequelae of chronic disease, necessitating decision making and ACP at a younger age than patients with higher socioeconomic status.39,40 The goal is to start ACP early to change the trajectory of decision making and care over the course of illness. Our inclusion criteria of ≥ 2 primary care visits and ≥ 2 additional visits in the past year ensures patients have established primary care and access care frequently. This will enhance recruitment and follow-up.

Patients will be excluded if their clinician is a principal investigator, co-investigator or clinician-member of the Patient-Clinician Advisory Board or they had been enrolled in a previous pilot
study of the PREPARE website or been exposed to the PREPARE study materials. They will also be excluded if they have medical record documentation of being deaf, blind, having dementia, or being psychotic or are deemed by their clinician to be too mentally or physically ill to participate. Participants will also be excluded if they have evidence of active drug or alcohol abuse within the past 3 months determined by clinician assessment, self-report, chart review or research staff assessment. Through in-person or phone screening by study staff, patients are also excluded if they self-report vision too poor to read a newspaper, lack of a phone (needed for follow-up interviews and scheduling), or plans to be out of the country for ≥ 3 months; if they screen positive for moderate-to-severe cognitive impairment using the validated Short Portable Mental Status Questionnaire followed by the Mini-Cog,41-43 or self-report or are determined by study staff to be blind, deaf, intoxicated or actively psychotic. Because ACP is an iterative process and people may change their preferences over time,24,44 subjects with prior ACP experiences (e.g., an advance directive) are not excluded.

To minimize the risk of unblinding by fellow research participants, any spouse/partner of a currently enrolled patient who is also a patient at SFHN/ZSFG, meets the eligibility criteria, and therefore, is also a potential patient participant, will be excluded from being a patient participant. This will avoid a situation where 2 closely related people living in the same home could be randomized to different study arms and result in unblinding. In addition, an individual who is named as an enrolled patient’s potential surrogate decision maker (regardless of cohabitation or spousal status), who is also a patient at SFHN/ZSFG, meets the eligibility criteria, and therefore, is also a potential patient participant, will only be eligible to be a surrogate participant in our study and will be excluded from being a patient participant. In addition, we are excluding any patient who has been enrolled in a previous PREPARE-related study or is known to have previously been exposed to PREPARE (e.g. note in medical record).
To save research staff considerable time and effort, potential participants who miss an interview (i.e. no show) more than 2 times (for the same baseline interview appointment) without prior notification and rescheduling with study staff will be considered ineligible, unless there are extenuating circumstances.
### Table 2. Inclusion and Exclusion Criteria of Participants

<table>
<thead>
<tr>
<th>Patient Participants</th>
<th>Inclusion Criteria</th>
<th>Exclusion Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Inclusion Criteria</strong></td>
<td>Is 55 years of age or older</td>
<td>Has a clinician who is the PI, Co-I or member of the Stakeholder Advisory Board</td>
</tr>
<tr>
<td></td>
<td>Obtains care in the primary care clinics in the San Francisco Health Network (SFHN) and/or Zuckerberg San Francisco General Hospital (ZSFG)</td>
<td>Was in a prior PREPARE-related study, such as a focus group or pilot study*</td>
</tr>
<tr>
<td></td>
<td>Has been seen at least twice in the last year by a primary care provider (a measure of established primary care) and had at least two additional visits to ZSFG in the past year (a measure of frequent the medical center)</td>
<td>Has dementia determined by clinician assessment, chart review or self-report</td>
</tr>
<tr>
<td><strong>Exclusion Criteria</strong></td>
<td>Has blindness or poor vision determined by clinician assessment, chart review, self-report of blindness or the inability to read print on a newspaper⁵⁷</td>
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</tr>
<tr>
<td></td>
<td>Is deaf as determined by clinician assessment, self-report, chart review or research staff assessment</td>
<td>Is deaf as determined by clinician assessment, self-report, chart review or research staff assessment</td>
</tr>
<tr>
<td></td>
<td>Has cognitive impairment as assessed by research staff by deficits on the Short Portable Mental Status Questionnaire (SPMSQ)⁵⁸ and the mini-Cog⁵⁹,⁶⁰</td>
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</tr>
<tr>
<td></td>
<td>Has delirium or psychosis as assessed by a clinician or research staff</td>
<td>Has delirium or psychosis as assessed by a clinician or research staff</td>
</tr>
<tr>
<td></td>
<td>Does not report speaking Spanish “well” or “very well”</td>
<td>Does not report speaking Spanish “well” or “very well”</td>
</tr>
<tr>
<td></td>
<td>Lacks a phone for additional study contacts and follow-up interviews</td>
<td>Lacks a phone for additional study contacts and follow-up interviews</td>
</tr>
<tr>
<td></td>
<td>Has active drug or alcohol abuse within the past 3 months determined by clinician assessment, self-report, chart review or research staff assessment*</td>
<td>Has active drug or alcohol abuse within the past 3 months determined by clinician assessment, self-report, chart review or research staff assessment*</td>
</tr>
<tr>
<td></td>
<td>Reported being out of town during their scheduled follow-up interview dates outside of a window of 3 months</td>
<td>Reported being out of town during their scheduled follow-up interview dates outside of a window of 3 months</td>
</tr>
<tr>
<td></td>
<td>Reported being a spouse or surrogate of another enrolled participant*</td>
<td>Reported being a spouse or surrogate of another enrolled participant*</td>
</tr>
<tr>
<td></td>
<td>Were unable to answer consent teach-back questions after three attempts</td>
<td>Were unable to answer consent teach-back questions after three attempts</td>
</tr>
<tr>
<td></td>
<td>Had 2 or more no-show baseline interview appointments without rescheduling*</td>
<td>Had 2 or more no-show baseline interview appointments without rescheduling*</td>
</tr>
</tbody>
</table>
Abbreviations: Co-I, Co-Investigator; PI, Principal Investigator; SFHN, San Francisco Health Network; ICD, International Classification of Diseases; ZSFG, Zuckerberg San Francisco General Hospital
RECRUITMENT METHODS

Data Extraction:
To facilitate recruitment, we obtained a Health Insurance Portability and Accountability Act waiver to access patients’ names, age, primary language, phone numbers, addresses, medical record numbers, as well as dates of outpatient primary care clinic appointments in the past year and up to 3 months in the future, other appointments and hospitalizations and emergency room visits in the past year, and the name of patients’ outpatient primary care providers. From these data, we obtain a list of potentially eligible patient participants and send a secure email to their primary care providers asking for permission for our study team to tell their patients about the study through a recruitment opt-out study letter, followed by phone or in-person recruitment. Weekly administrative data pulls from the electronic health record identify patients with upcoming primary care appointments and are used to target patient recruitment efforts.

Clinician Permission to Contact Patients:
Upon completion of the administrative data pulls, providers from all recruitment sites are sent a letter or secure e-mail informing them about the research study and asking them to review a list of their patients, to refer patient(s) on their patient list who would be appropriate for the study, and to obtain permission to contact their patients to tell them more about the study. Clinicians are also informed that if the study team receives their approval, their eligible participants will receive a letter describing the research study and offering them the opportunity to decline to be contacted by research personnel and/or will be contacted in clinic. Additionally, clinicians are informed that if they do not respond one week after the 3rd attempt to contact them by the study team (including by email, phone, and/or in-person), we will assume assent to contact their patients and a letter describing the study will be sent to patients on behalf of the study team. We obtain permission from all of the Service Chiefs before their clinicians are contacted.
Recruitment Methods and Materials:

Study-related fliers written at a 5th-grade reading level in Spanish are posted in approved areas in SFHN/ZSFG-affiliated primary care clinics. Because many patients may be too ill to come to frequent clinic appointments and to be interviewed or hear about the study in busy clinic waiting rooms, we include several recruitment strategies. Therefore, in addition, recruitment letters and postcards written at a 5th grade reading level in Spanish are mailed and describe the research study as well as provide a telephone number to either opt-out or to hear more about the study. Although patients can opt out at any time, those who do not call study staff to decline participation within 1 week of the mailings are deemed eligible to be contacted to describe the study, assess willingness to participate and assess study eligibility. To standardize the timing between intervention exposure and primary care follow-up, we schedule patients for the baseline interview and exposure to PREPARE or the control intervention 1 to 3 weeks prior to their upcoming primary care appointment. Weekly administrative data pulls from the electronic health record identify patients with upcoming primary care appointments and are used to target patient recruitment efforts. Potential participants are then contacted by phone or in the clinic.

Patients who consent and enroll are paid $50 for the baseline interview and given $10 in MUNI (municipal transportation vouchers) to help participants come back to follow-up interviews in person if they desire. Participants are also reimbursed $25 for each of the 1-week, 3, 6, and 12-month interviews.

Diverse, vulnerable populations are often difficult to recruit for research studies. We employ several strategies to enhance our recruitment. First, we attempt to hire individuals who have experience with diverse populations and individuals who are bilingual (native Spanish-speaking) and bicultural. Furthermore, we conduct extensive sensitivity training with all research staff and require staff to use approved study scripts when speaking to patients. These study scripts and
CONSENT PROCEDURES

We use a modified consent process that several co-authors designed for vulnerable populations.\textsuperscript{28,29} Consent forms written at the 5\textsuperscript{th} grade reading level are provided and read to participants in Spanish. This review is then followed by standardized “teach-to-goal” questions to ensure understanding. If potential participants cannot correctly complete the teach-back process after 3 attempts, the patient is deemed ineligible.

The consent form is approved by the UCSF and ZSFG Institutional Review Boards, the patient/clinical advisory board, and the Data and Safety Monitoring Board (DSMB). The consent form states the following for the purpose of the study: “Why is this study being done? Sometimes patients and their families have to make hard medical decisions. We want to design and test an easy-to-understand handout to help. This handout will help people think about their values, or what is most important to them in their life. It will also help prepare patients to make medical decisions.” We use the word “handout” because, in pilot testing, both groups are given handout materials and written advance directives. For randomization we explain, “We will ask you to look over a handout and answer some questions about your experience with making medical decisions. There will be two groups that will be given different handouts. You will have a 50/50 chance of being in either group.”

Due to exclusions based on several missed baseline appointments and for staff safety and the need to exclude or withdraw participants who were intoxicated, psychotic, or threatening, the
consent also explains, "We also may ask you to stop taking part in this study if we feel it is in your best interest or if you do not follow the study rules."

It was determined with our Patient-Clinician Advisory Board that clinicians of patients should be contacted in the event that the patient reports severe depression or anxiety. Our DSMB agreed and our consent forms explain:

“We would need to contact your regular doctor or a medical provider for the following reasons:

- You report, or we observe that you are having a medical emergency,
- Such as a serious medical illness
- Or, a serious mental illness, such as major depression
- You report that you may harm yourself, you may harm someone else, or someone is harming you.”

**INTERVENTION AND COMPARISON CONDITIONS**

**PREPARE arm**

As previously described, PREPARE is an easy-to-use, patient-centered, interactive website that is available in Spanish, is written at a 5th grade reading level, includes voice-overs of all text for the reading-impaired and closed-captioning of all videos for the hearing impaired (www.prepareforyourcare.org).27,28 The conceptual framework for PREPARE has been previously published and is based primarily on Social Cognitive Theory,48,49 with elements from the Health Belief Model,50 the Theory of Planned Behavior,51 and Behavior Change Theory.49,52 In these theories and in behavioral studies, modeling of behaviors helps people change their behavior. Successful behavioral change interventions model skills, enhance self-efficacy, and address perceived barriers,53,54 especially literacy-appropriate interventions.8 Modeling behaviors (as in PREPARE) can also improve patients’ ability to communicate with clinicians and improve outcomes,55,56 such as increased question asking behavior and a sense of control.
during a clinical visit, an increased desire to participate in decision making, and even improved affect and functional status. PREPARE incorporates these successful teaching methods through the modeling of behaviors in videos. Video and interactive websites are more powerful mediums to teach information and change behavior than written materials, especially for those with language/literacy barriers. PREPARE includes a training and goal setting component which has been shown to be effective in changing outpatient behaviors, such as exercise.

In the design of the PREPARE website, we included essential, theory-based health education strategies, such as the use of video modeling of ACP behaviors and tailored and interactive content based on patients' values and decision preferences. To ensure PREPARE is easy to read and understand, we use clear health communication principles (e.g., targeting text to the 5th grade reading level) informed by extensive formative research and cognitive interviewing with the target population (i.e., racially and ethnically diverse older adults with limited health literacy and English proficiency) to ensure PREPARE content is acceptable to individuals from diverse cultural backgrounds. The PREPARE website leads people through a 5-step ACP process that ranges from choosing a surrogate decision maker to asking their clinicians the right questions. While going through the website, PREPARE also helps individuals answer personal values questions about their medical care, and helps them create an action plan to engage in some form of ACP. Patient-generated action plans have been shown to help patients engage in other preventative and disease management activities in the outpatient setting.

After the baseline interview, participants in the PREPARE arm review all 5 steps of the PREPARE website in Spanish in our research offices. Participants are asked to review PREPARE on their own and in its entirety. Research assistants are available to answer questions only if needed, but do not go through the website with the participants. At the end of
the program, a summary of the patient’s medical wishes and action plan are automatically
generated from the PREPARE website in written format. This information along with the
participant’s PREPARE website login information is included in a take-home folder that also
contains PREPARE information in pamphlet, booklet, and DVD format. We include PREPARE
content in non-website formats because some patients may not have access to the internet at
home. PREPARE arm participants are also given an easy-to-read advance directive in Spanish
to review and consider completing. Participants are asked to review the advance directive
form for at least 5 minutes and up to 15 minutes in research offices, and then to take the form
home to discuss with their potential surrogates and/or their clinicians. The time frame of 5-15
minutes was chosen because our goal is only to introduce the advance directive and allow
participants to ask questions. The goal is not to have patients complete the form on the day of
the study, before potential discussions with clinicians or surrogates, unless the participant would
like to do so.

AD-only arm

Participants in the control arm are only given the easy-to-read advance directive, are asked to
review it for at least 5 minutes and up to 15 minutes, and to take the form home to discuss with
their potential surrogates and clinicians.

Both arms: Reminder of primary care appointments

One to 3 days before the patient’s next scheduled primary care appointment, research staff call
the PREPARE arm participants to remind them to bring in their study materials (i.e., action plan
and advance directive) and to talk to their clinician about ACP. For the control arm, research
staff members only remind patients about their upcoming appointment and do not provide
additional encouragement about ACP.
RANDOMIZATION PROCEDURES

A statistician not involved in recruitment or data collection uses a computer-based random number generator to create a randomization scheme using block randomization by health literacy (adequate health literacy versus limited health literacy, as determined by a validated question concerning confidence with medical forms). Random block sizes of 4, 6, and 8 are used to ensure an equal number of patients with limited health literacy in each group. Randomization information is associated with a unique patient identification number and is kept separate from other patient data. Due to the need to secure interview rooms for the duration of the baseline questionnaire and intervention (i.e., approximately 2 hours for the AD-only arm and 3 hours for the PREPARE arm), randomization occurred prior to scheduling a baseline interview.

BLINING

Clinicians are blinded to patient group assignment. Although we obtain clinicians’ permission to recruit their patients, the interventions are not described, and no clinician education is provided. Participants could not be blinded to the intervention; however, they are told during consent there is a “50/50 chance” of getting one of two different ACP guides, and the non-assigned intervention is not described. Because each group obtains ACP materials, such as the easy-to-read advance directive, blinding is enhanced. The research assistant who administers the intervention cannot be blinded to the study arm, but all follow-up outcome assessments are conducted by different and blinded staff. At the start of all follow-up interviews, participants are reminded not to discuss the study materials they reviewed with assistants recording if they became unblinded. If unblinding occurs, a different blinded assistant conducts all subsequent interviews.
INTERVENTION FIDELITY

All staff members are rigorously trained and are required to read and adhere to a standardized study protocol manual, standardized study scripts, and standardized checklists for each contact and interview with participants. Several training videos have also been developed for staff. Research staff are not allowed to conduct study tasks independently until they have reviewed all written and video training materials and can demonstrate complete mastery of all scripts and checklist items. In addition, a 10% random sample of all interviews is observed by senior research staff to ensure study fidelity.

DATA COLLECTION METHODS

Live capture of research data are collected through Research Electronic Data Capture (REDCap) software. REDCap is managed by the UCSF Academic Research Systems Team and is stored behind strong-string password protected firewalls on UCSF servers, not on individual laptops or desktops. All patients are given a unique, non-identifying patient identification number that is removed from any personally identifying information (PII) or personal health information (PHI). All PII and PHI are stored in a Microsoft ACCESS database behind strong-string password protected firewalls on UCSF and ZSFG servers. To reduce missing data, REDCap has been programmed to not allow study staff to progress if data fields are left blank. We retain the use of paper surveys in the event the RedCap system is down. All paper files continue to be stored in secure, locked research offices in secure, locked file cabinets.

FOLLOW-UP AND RETENTION:

We conduct follow-up interviews one week and 3, 6, and 12-months after the primary care visit in the clinic, by phone, or in the home if needed due to patient functional limitations. We utilize
several measures to help ensure follow-up. Each follow-up interview takes between 30 to 45 minutes and participants are reimbursed $25.

**Method of contact for follow-up surveys:**
Upon enrollment, we ask participants to provide alternative phone numbers (e.g., cell or work numbers) and one to three additional phone numbers of close contacts who may know how to contact the patient in the event our study staff is unable to reach them. Many patients in safety net settings are marginally housed, have intermittent phone access, and may change locations and phone numbers during the study period. We also ask participants if they prefer a text message or an email to schedule follow-up visits and will use their preferred mode of communication. If these other modes of communication fail, we send out reminder letters. If needed, we also attempt to contact patients during scheduled clinic visits or make home visits.

**Participant Appointment Reminder Sheet**
We created an appointment reminder sheet as a reference for patient participants. This sheet shows the dates and times for upcoming appointments that the patient participant will have with us.

**Reminders for the primary care visit:**
Participants receive a brief reminder call one to 3 days before their next primary care visit. Participants in the AD-only arm are reminded to come to their scheduled appointment while participants in the PREPARE arm are reminded of their appointment and to bring the PREPARE materials to the visit.

**Reminders for study interviews:**
For all follow-up interviews, participants in both arms receive reminders of their upcoming study interview by phone or in person. To help participants follow along during the interview, the participant can receive a Participant Version of the survey via mail or email, as preferred. No survey responses or information are collected by mail or email. We use 14-point font and color-coded, standardized, large font response options to help with understanding.

Participants who miss their primary care appointment:
Participants who cancel or miss their primary care appointments and do not reschedule within 30 days of the cancelled appointment receive a courtesy phone call to remind participants to reschedule the primary care appointments in order to move on with the study schedule. For participants who cancel or miss their primary care appointments after they have been enrolled and randomized:

- If they have rescheduled and attend their primary care appointment within 6 months from when they were randomized, they receive a brief reminder call one to 3 days before their primary care appointment date. We conduct follow up assessments at 1 week, and at 3, 6, and 12 months from this primary care appointment date,

- If they do not reschedule or attend their primary care appointment within 6 months from when they were randomized, they receive a brief reminder call one to 3 days before their new primary care appointment date. We conduct follow up assessments at 6 and 12 months from the originally scheduled primary care appointment date.

Ascertaining reasons for loss of follow-up or withdrawal: For participants who want to withdraw, we ask them why in open-ended questions. If they cannot provide an answer, we prompt them from a list of reasons we obtained from prior advance care planning trials, such as the study is too long, they are too busy, the study topic is too upsetting, they are too ill, etc.
MEASURES

Aim 1 Overview:

Through cognitive interviews we obtained information about what participants liked and or didn’t like overall, and what they liked and didn’t like in terms of the wording of PREPARE, the instructions, the colors, pictures, and formatting. The full interview guide is in the protocol.

- What did you like about these materials? Why? Were there any pictures, actors, or videos that you liked? Why?
- What didn’t you like about this these materials? Why? Were there any pictures, actors, or videos that you didn’t like? Why?
- Words: Were there any words that you liked? Why? Were there any words that were hard to understand or that you think other people will have a hard time understanding? Why?
- Pictures and videos and stories: Were there any pictures/videos/stories that you liked? Why?
- Were there any pictures/videos/stories that were hard to understand or that you think other people will have a hard time understanding? Why?
- Instructions: Were there any instructions that you liked? Why? Were there any instructions that were hard to understand or that you think other people will have a hard time understanding? Why?

Probing questions:

- Tell me what you are thinking.
- What thoughts are going through your mind right now?
- That’s great. Thinking out loud like this is just what we need.

Aim 2 Overview:

Because ACP ideally is a process that occurs over time, we felt it important to measure a full range of ACP measures including ACP documentation (primary outcome) over time, and several behavior change constructs and several additional ACP actions over a 12-month period (secondary outcomes). All study measures used in this analysis, including validity and reliability information and the schedule of administration (i.e., baseline, 1-week or 3, 6, or 12-months), are included in the Outcome Measures table below. All outcomes, including secondary outcomes
Primary Outcome

The primary outcome is documentation of ACP wishes in the ZSFG/SFHN medical record (Table of Outcome Measures below). ACP documentation for the purposes of this study includes the easy-to-read advance directive or other valid advance directives or living wills, a durable power of attorney for health care document (DPOAHC), a Physicians Orders of Life Sustaining Treatment form, or other documentation of discussions concerning patients’ wishes for medical care (i.e., documentation or notes describing patients’ surrogate or goals for medical care by clinicians).

We assess baseline and 15-month ACP documentation rates and the date of documentation to determine the length of time from study enrollment to subsequent documentation. Patients in our study are enrolled, randomized, and exposed to the intervention 1 to 3 weeks prior to a primary care appointment. ACP documentation is timed to the date of intervention exposure as patients may have engaged in ACP prior to seeing their primary care provider. The patient-reported outcomes in the follow-up surveys (1 week, 3, 6, and 12-months), however, are timed to the primary care visit because those questions concern engagement in discussions with clinicians (see secondary outcomes below). This same timeframe for ACP documentation was determined from a prior PREPARE trial conducted within the VA to take into account and to standardize the expected time from intervention exposure to the primary care visit and the anticipated time to schedule and complete the final patient interview.35

Because legal forms and documented discussions can be used to direct medical care, we created a composite variable of any ACP documentation (forms and/or discussions); we also
plan to report the percentage of forms and discussions separately. All medical review data is
double coded by 2 independent, blinded research assistants. Discrepancies are adjudicated by
the principal investigator (R.L.S.).

**Secondary Outcomes**

**Main Patient-Reported Outcome**

The main patient-reported secondary outcome, the validated Advance Care Planning
Engagement Survey\(^{27,28,37}\) was chosen to measure the full process of ACP. The Advance Care
Planning Engagement Survey measures both ACP Behavior Change Processes, such as
knowledge, contemplation, self-efficacy, and readiness on a validated 57-item scale. The ACP
Behavior Change Process scale is measured on a 5-point Likert scale and average 5-point
scores will be calculated. We will also measure ACP actions on the validated 25-item Action
scale, which assesses ACP activities (yes or no) such as identifying a surrogate decision maker,
identifying values and goals for medical care, choosing the level of leeway in surrogate decision
making, discussing one’s wishes with clinicians and surrogates, and documenting one’s wishes
in an advance directive. Validity and reliability of the ACP Engagement Survey, as well as the
questionnaire’s ability to detect change in response to an ACP intervention, have been
previously described\(^{27,28,37}\).

**Patient-Advisory Board Requested Outcome**

Our Patient-Advisory Stakeholders requested we quantify the number and percentage of
patients who increased their ACP activities overtime. Our stakeholders perceive any increase in
an ACP activity over time as clinically meaningful. Thus, in addition to mean change in ACP
Engagement scores, they wanted to know the percent of patients who improved (i.e., had an
estimated slope > 0) over time for both Behavior Change scores, Actions scores, and both
combined. We therefore created this exploratory variable post-hoc.
Feasibility and Satisfaction

To evaluate whether and how PREPARE will be used in clinical practice and in the community, we also assess acceptability of the PREPARE website compared to an advance directive alone using validated scales of ease-of-use (10-point scale, “On a scale of 1 to 10, with 1 being very hard and 10 being very easy, how easy was it to use this guide?”) and satisfaction (comfort: “How comfortable were you viewing this guide?”, helpfulness: “How helpful was this guide?”, and recommendations: “How likely are you to recommend this guide to others?” assessed on a 5-point Likert scale (not-at-all to extremely) from our prior work. For the PREPARE arm only, and at the end of the 12-month interview and after unblinding, we also ask how likely patients are to recommend the PREPARE intervention to others.

Adverse Event Outcomes

In addition, to ensure that the PREPARE program does not cause undue harm, we also assess both depression and anxiety. We measure depression using the validated Patient Health Questionnaire (PHQ)-8 (scores 0-24) and anxiety Generalized Anxiety Disorder (GAD)-7 (scores 0-21) at baseline and each follow-up. Scores of 5, 10, 15, and 20 represent mild, moderate, moderately severe and severe depression or anxiety.

Potential Mediating or Moderating Variables & Participant Characteristics

Based on the previously published conceptual framework of PREPARE, we also hypothesize that PREPARE efficacy may vary across several moderator or mediator variables (e.g., health literacy using the validated Short form Test of Functional Health Literacy in Adults s-TOFHLA, scores 0-36 and dichotomized to limited = 0-22 & adequate = 23-36; clinician-patient language concordance (concordant versus discordant); and patient’s desired role in decision making both with the medical provider and with the family using the validated Decision Control Preferences
Scale (wants to make their own decision versus wants doctors/family to make decisions for them).\textsuperscript{78} We also hypothesize that PREPARE efficacy may be affected by several confounding variables (e.g., self-rated health, “How would you rate your health?” [5-point Likert]\textsuperscript{79,80} dichotomized as fair-to-poor and good-to-excellent and past experiences with ACP including prior documentation of legal forms and documented discussions. We will also assess a full range of patient-reported characteristics, as these factors may impact patient-clinician communication,\textsuperscript{20,81} such as age (“What is your date of birth?”), self-reported gender (“What gender do you consider yourself to be? male, female transgender, other”), finances (able to make ends meet versus not make ends meet), having a potential surrogate decision maker or not, education (“What is the highest educational level you have completed?” less than or equal to high school or greater than high school), internet access in the home (yes or no), and religiosity and spirituality (i.e., “How religious/spiritual do you consider yourself to be?” on 5-point Likert scale from not-at-all to extremely).

**For Aim 3:**

We will obtain input from PREPARE arm participants about how we could make PREPARE better in an open-ended question at the end of the study at the 12-month follow-up interview.

We will also conduct an in-depth focus group with our Stakeholder Advisory Board, which includes primary care clinicians and directors of the clinics in which this study was occurring. In the focus group, we will ask about workflow in the clinic, feedback about use, the impact PREPARE had on discussions, documentation, and the length of primary care visits and clinic workflow. We also asked advice about incorporating PREPARE into the clinic workflow, identifying barriers and facilitators, and obtaining logistic input about when and where patients should review the materials, who should introduce ACP.
<table>
<thead>
<tr>
<th>Construct</th>
<th>Measure</th>
<th>English Reliability/Validity</th>
<th>Spanish Reliability/Validity</th>
<th>Baseline</th>
<th>1 week</th>
<th>3 months</th>
<th>6 months</th>
<th>12 months</th>
<th>15 months</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary Outcome</strong></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>New ACP Documentation</td>
<td>Chart review: ACP documentation (i.e., legal forms and documented goals of care discussions)</td>
<td>NA</td>
<td>NA</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
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<td>X</td>
</tr>
<tr>
<td><strong>Secondary Outcomes</strong></td>
<td></td>
<td></td>
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<tr>
<td>The Full ACP Process</td>
<td>ACP Engagement Survey:  27 Behavior Change Process Measures (knowledge, contemplation, self-efficacy, readiness)</td>
<td>Behavior Change Measures: Cronbach’s α = 0.94 (0.91-0.96), ICC= 0.70 (0.54-0.82) 27</td>
<td>Action Measures: ICC*= 0.87 (0.79-0.92) 27</td>
<td>NA</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Post Hoc Secondary Outcome</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Percent increase in ACP activities</td>
<td>N (%) participants who increased their Behavior Change or Action scores from baseline (i.e., estimated slope &gt;0)</td>
<td>NA</td>
<td>NA</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Feasibility Secondary Outcomes</td>
<td>Implementation: Acceptability</td>
<td>Acceptability and Usability (a) Ease of Use and Understanding (b) Usefulness in decisions &amp; discussions (c) Attitudes about norms or expectations</td>
<td>8</td>
<td>6</td>
<td>1 factor explained 81-85% of variance/scale. Kuder-Richardson &gt;0.75&lt;sup&gt;8&lt;/sup&gt;</td>
<td>6</td>
<td>1 factor explained 81-85% of variance/scale. Kuder-Richardson &gt;0.75&lt;sup&gt;8&lt;/sup&gt;</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Adverse Event Secondary Outcomes</td>
<td>Depression</td>
<td>Patient Health Questionnaire-8</td>
<td>8</td>
<td>Scores ≥10 100% sensitive and 95% specific for major depressive disorder&lt;sup&gt;73,74&lt;/sup&gt;</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td></td>
<td>Anxiety</td>
<td>GAD-7&lt;sup&gt;75&lt;/sup&gt;</td>
<td>7</td>
<td>Cronbach’s α = 0.92&lt;sup&gt;75&lt;/sup&gt;, ICC*= 0.83</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Demographic Information</td>
<td>Demographic Information</td>
<td>Age, gender, race and ethnicity&lt;sup&gt;83&lt;/sup&gt;, marital status, and education</td>
<td>NA</td>
<td>NA</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Finances</td>
<td>“In general, how do your finances usually work out at the end of the month?”</td>
<td>1</td>
<td>Associated with functional impairment and co-morbidity&lt;sup&gt;84&lt;/sup&gt;</td>
<td>NA</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Socioeconomic Social Standing</td>
<td>Social standing ladder (i.e. place and income)</td>
<td>1</td>
<td>Associated with functional decline&lt;sup&gt;85&lt;/sup&gt;</td>
<td>NA</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Measure</td>
<td>Description</td>
<td>Cronbach’s α</td>
<td>Correlation coefficient w/ other literacy tests</td>
<td>AUROC† (CI: 90-98%)</td>
<td>AUROC† (CI: 90-98%)</td>
<td>Desired role in decision making</td>
<td></td>
<td></td>
<td></td>
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<td>----------------------------------------------</td>
<td>------------------------------------------------------------------------------</td>
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<tr>
<td><strong>Other Measures</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>Health Literacy</strong></td>
<td>s-TOFHLA, scores 0-36&lt;sup&gt;77&lt;/sup&gt; Continuous &amp; dichotomized to limited = 0-22 &amp; adequate = 23-36</td>
<td>36</td>
<td>.97</td>
<td>&gt;.95&lt;sup&gt;86&lt;/sup&gt;</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>Patient-clinician language concordance</strong></td>
<td>To clinicians: “How well do you speak Spanish?”&lt;sup&gt;87&lt;/sup&gt; Fluent, very well (concordant) vs. well, fair, or poor</td>
<td>1</td>
<td>AUROC† 94% (CI: 90-98%)&lt;sup&gt;87&lt;/sup&gt;</td>
<td>AUROC† 94% (CI: 90-98%)&lt;sup&gt;87&lt;/sup&gt;</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Desired role in decision making</strong></td>
<td>CPS with clinician&lt;sup&gt;78&lt;/sup&gt;</td>
<td>2</td>
<td>Correlation between preferred and actual role in decision making&lt;sup&gt;12,88,89&lt;/sup&gt;</td>
<td>Correlation between preferred and actual role in decision making&lt;sup&gt;90&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td><strong>Internet Access</strong></td>
<td>Do you have access to the internet in your home?</td>
<td>1</td>
<td>NA</td>
<td>NA</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
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<tr>
<td><strong>U.S. Acculturation</strong></td>
<td>Based on Acculturation scale (USAS) “How many years have you lived in the U.S.?”</td>
<td>1</td>
<td>Associated w/ desire to know prognosis&lt;sup&gt;91&lt;/sup&gt;</td>
<td>NA</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>Functional Status</strong></td>
<td>ADL (0-16 point scale) &amp; IADL measure (0-12 item scale)&lt;sup&gt;92,93&lt;/sup&gt;</td>
<td>13</td>
<td>Morbidity/mortality correlation&lt;sup&gt;126,127&lt;/sup&gt;</td>
<td>Cronbach’s alpha =0.94&lt;sup&gt;94&lt;/sup&gt;</td>
<td></td>
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<tr>
<td><strong>Self-rated health status</strong></td>
<td>How would you rate your health? (5pt Likert)&lt;sup&gt;79,80&lt;/sup&gt;</td>
<td>1</td>
<td>Morbidity/mortality correlation&lt;sup&gt;79,80&lt;/sup&gt;</td>
<td>NA</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
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<tr>
<td>Prior ACP experience</td>
<td>Prior ACP experiences (e.g., (“Ever had to make life threatening medical decisions?”)</td>
<td>5</td>
<td>NA</td>
<td>NA</td>
<td>X</td>
<td></td>
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<tr>
<td>Social support</td>
<td>Modified MOS-SS (scores 11-55)</td>
<td>11</td>
<td>Cronbach’s α = 0.88-.95</td>
<td>Cronbach’s α = 0.94</td>
<td>X</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Presence of a possible Surrogate Decision maker</td>
<td>11</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Religion/Spirituality</td>
<td>Self-reported extent of how spiritual/religious (5-pt Likert) and role play in decision making</td>
<td>4</td>
<td>Spirituality associated with quality of life. Religiosity associated with wanting all measures to extend life</td>
<td>NA</td>
<td>X</td>
<td></td>
<td></td>
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</table>

Abbreviations: NA, Not Applicable; ACP, advance care planning; ICC, Intraclass correlation; AUROC, Area under the receiver operating curve; GAD, Generalized Anxiety Disorder; s-TOFHLA, Short form Test of Functional Health Literacy in Adults; CPS, Control Preference Scale; ADL, Activities of Daily Living; IADL, Instrumental Activities of Daily Living; MOS-SS, Medical Outcomes Study Social Support; pt, point

Legend: If a validated Spanish-version of a survey was not available, we translated the English version into Spanish. Mediator variables, measured at baseline, may explain how or why a particular effect or relationship occurs, but these variables may also be affected by the intervention and are therefore also considered secondary outcome variables measured over time (i.e., knowledge, self-efficacy, and readiness, as well as barriers and attitudes).
STATISTICAL ANALYSIS PLAN

Our primary analyses will compare change in ACP documentation between study arms from baseline to 15 months. Secondary outcomes will include ACP Engagement with respect to 5 ACP Actions (yes/no and a 0-25-point scale) and Behavior Change scores (average 5-point Likert scores) from baseline to 1 week, and 3, 6, and 12 months. Variables will be assessed for distributional and outlier values using standard summary statistics. Baseline comparability will be assessed between groups using unpaired t-tests, Chi-square tests or Fisher’s exact tests. Using t-tests or Chi-squared tests, we will also compare patient’s age and self-reported gender between those who refused versus those who enrolled and differences between arms of those who withdrew versus those who did not. We will use intention-to-treat analysis using SAS version 9.4 (SAS Institute Inc.) and STATA 15.0 (College Station, TX). All p-values will be 2-tailed and set at .05 for the primary outcome and Bonferroni adjusted for secondary patient-reported outcomes. To compare outcomes between the two arms longitudinally, we will use mixed effects linear, Poisson, or negative binomial regression for continuous measures and mixed effects logistic regression for dichotomous measures. The mixed effects models will include fixed effects for the primary modeling terms of time (baseline and 15 months for ACP documentation and baseline and 1 week, 3 months, 6 months, and 12 months for ACP Engagement with time modeled using dummy variables to allow for non-linearity); arm (AD-only versus PREPARE); an interaction term of study arm and time; and a random effect for subjects. We will adjust for the randomization blocking factors limited vs. adequate literacy, and any predictor variables that differ between arms. All models also will also be adjusted for baseline ACP documentation and will include random physician intercepts to account for nesting of patients within physicians. We will use standardized, clinically meaningful effect sizes (i.e., 0.20-0.49 small, 0.50-0.79 medium, and ≥0.80 large). Per stakeholder request, we will conduct post-hoc mixed-effects regression to calculate the percentage of participants who increased
their Behavior Change score, Action scores, or both Behavior Change and Action scores from baseline (i.e., estimated slope > 0) by study arm; p-values adjusted to a significance of 0.017.

For moderator analysis, we will test for interactions by adding interaction terms to the group by time variable for health literacy (limited versus adequate) controlling for prior ACP documentation and clustering effects by clinician. All other interaction terms are adjusted for health literacy (randomization blocking variable) prior ACP documentation and clustering effects by clinician. Additional interaction terms to be added to the group by time variable include patient-clinician language (concordance vs. discordance), decision control preferences for making decisions with doctors and family (i.e., makes own decisions versus doctor/family makes decisions), age (i.e., < 65 years versus ≥65 years of age), sex/gender (i.e., self-reported man versus woman), race/ethnicity (i.e., white versus non-white), health status (i.e., good-to-excellent versus fair-to-poor), presence of a potential surrogate (i.e., yes versus no), and internet access at home (i.e., yes versus no). A p-value for interaction <0.05 is considered significant.

Other secondary outcomes variables will be assessed for distributional and outlier values using standard summary statistics. Baseline comparability will be assessed between groups using unpaired t-tests, Chi-square tests or Fisher’s exact tests. We will use intention-to-treat analysis. To compare outcomes between the two arms longitudinally, we will use mixed effects linear, Poisson, or negative binomial regression for continuous measures and mixed effects logistic regression for dichotomous measures.

Missing data for the primary outcome will be assessed. If there is 10% or more of missing data, we will use a mean imputation approach. All available data will be included in mixed-effects models. We will assess whether any research staff member became unblinded during follow-up.
assessment and conduct sensitivity analysis as needed. If 10% or more of data are missing on secondary outcomes or predictor variables of interest, we also plan to use multiple imputation techniques (i.e., chained equations imputation, Stata 12).

For qualitative analysis of cognitive interview data, after each cognitive interview or focus group, the team will debrief to review impressions. Research assistants will take detailed notes, and a report will be prepared after each interview. Data will be analyzed qualitatively using qualitative software. Through qualitative (thematic) content analysis, we will identify “theme categories” that will provide insight as to any further domains or content that should be added to PREPARE to ensure its usability. Themes will be identified through coding, in which passages of transcripts are marked according to their substantive content to facilitate retrieval, review, and consolidation into overarching themes. The preliminary coding scheme will follow the cognitive interview guide or focus group. Two independent reviewers will code the data and discrepancies of coding will be resolved by a third party.

**SAMPLE SIZE AND POWER CALCULATIONS**

We will measure a full range of ACP behaviors including discussions. However, written advance directive completion of legal forms is a primary outcome and is the most well-studied. Power from longitudinal analyses with repeated measures will be stronger, but to be conservative, we consider power for a single post-intervention time point (e.g., 15 months). A recent meta-analysis of written advance directive documentation studies demonstrated a pooled effect size of 0.50 (95% CI; 0.17 -0.83), as did an RCT of an ACP workbook that included both behavior change constructs and a social work visit, and our prior RCT of an easy-to-read AD at ZSFG which showed an increased AD completion rate from 7% to 15%. Because both the intervention and control arm will receive the easy-to-read advance directive, we assume that both arms will have an advance directive completion rate of ≤ 15%. Based on prior studies, we
assume PREPARE will result in additional benefit of advance directive completion with a minimum effect size of 0.5 (two-fold increase) above 15%. A sample of 350, (175 per arm), will afford us 92% power (2-tailed alpha of 0.05) to detect a difference of advance directive completion rates of 15% in controls vs. 30% in the PREPARE arm and 80% power to detect a difference of 15% vs. 27%. Power is also expected to be strong for the ACP behavioral change scale outcomes (preliminary data demonstrated a pre-to-post improvement of 0.5 SD). With a conservative assumption that controls will improve by 0.1 to 0.2 SD, we will have 85% to 98% power, respectively, to conclude that the improvement is better in the PREPARE arm. We expect a 15% drop out rate at 12 months based on our prior randomized, controlled trial at ZSFG, and will therefore attempt to recruit 402 patients, or 201 in each arm.

Our sample size will also allow adequate power to detect clinically important interactions based on potential moderators (literacy, control preferences, language concordance) for our outcomes. In a prior trial of an easy-to-read advance directive in the same patient population with only 200 patients, we found significant interactions for literacy. Thus, if we consider the power scenario of the control group ACP documentation rate of 15% and the PREPARE group of 28% and suppose the control group rate is the same (15%) for both levels of the moderating factor, then for a moderating factor split of 1:1, we would have 80% power to detect an interaction. If the PREPARE arm ACP documentation rate is 18% for one level of the factor and 40% for the other, this corresponds to a relative rate of ACP documentation of 2.2 times as high for one level of the factor compared to the other. A 2:1 split of the moderating factor still allows detection of a 2.4-fold increase in the relative rate of documentation.
ETHICS AND ADVISORY COMMITTEES

This study is approved by the University of California, San Francisco (UCSF) (IRB reference #13-10847). This study is guided by a Patient-Clinical Stakeholder Advisory Board that is comprised of patients and patient advocates (including native Spanish-speakers), surrogates, and ZSFG/SFHN primary care clinic staff and medical directors. It is also guided by a DSMB consisting of 4 experts in randomized trials, human subjects research and consent, vulnerable populations, palliative care, advance care planning, and biostatistics. Both advisory groups reviewed and approved all study protocols and related materials. In addition, we continue to meet with both groups every 4-6 months to review the progress of the trial, make suggestions for recruitment, review any potentially adverse events, and ensure that we are following our study protocols in a way that protects vulnerable patient populations.

HUMAN SUBJECTS PROTECTIONS

Protection of the rights and welfare of participants:

All study staff are required to take annual training regarding the rights and protections of research participants. Additionally, weekly study team meetings will ensure that all study staff are following the research protocol and that all study participants are consented according to our study protocol.

Furthermore, our consent process ensures that study participants have a clear understanding of the study and understand that they can choose to not participate in the study at any point in time, and that the care they receive will not be affected by declining to participate in our study. Our consent process involves using a consent form written below a 6th-grade reading level, reading the form to potential subjects verbatim, allowing time for questions and discussion, and then assessing comprehension using teach-to-goal. If questions are not answered correctly, repeated education and reassessment of comprehension are continued until complete
comprehension is achieved. If subjects take more than three passes through the comprehension assessment, formal assessment for cognitive impairment will be completed. If patients are found to be cognitively impaired, they are excluded from the study. If they are not cognitively impaired, we will re-do teach back once more, after which the participant will be deemed ineligible for the study if they are unable to demonstrate comprehension of the study.

Additionally, we include UCSF Clinical Research Office contact information on all consent forms as required for all non-biomedical studies.

**Steps taken to minimize risks to subjects:**

We have developed a modified research consent process that has been shown to be successful in vulnerable patient populations as described above. All study fliers, consent forms, and questionnaires are read to the subjects in their entirety by native Spanish-speaking research staff. Participants are reminded that they can opt out of the study at any time. All study materials are in an easy-to-read (5th grade reading level, large 14-point font) format. The consent materials and the study interviews are conducted in Spanish.

This study will employ research assistants who are fluent in Spanish. Only fluent research assistants will be in contact and will communicate with Spanish-speaking participants. We will also ensure that all study materials are accurately translated into Spanish by having them initially translated from English to Spanish by native Spanish-speaking subjects. We will then have them back translated into English to ensure accuracy. Finally, we will have the final translated documents reviewed for accuracy by third party native Spanish-speaking subjects. To help participants follow along during the interview, they may review a large font Participant Version of the survey at baseline and all follow-ups that can be reviewed while the research assistant is asking
research questions verbatim. We use 14-point font and color-coded, standardized, large font response options to help with understanding.

Data security:

- Data are stored securely in the encrypted, secure UCSF MyResearch environment
- Data are coded; data key is kept separately and securely
- Data are kept in a locked file cabinet
- Data are kept in a locked office or suite
- Electronic data are protected with a password
- Data are stored on a secure network
- Data are collected/stored using REDCap or REDCap Survey

Measures to ensure confidentiality and protect identifiers from improper disclosure

Risks to subjects are minimal and may include loss of confidentiality and psychological discomfort about discussing end-of-life issues. Subjects are assured that their answers to study questions will not be directly linked to their names. Instead, any identifying information is coded and separated from the data. The identifying information will only be known to the primary investigators but will not be used in data analysis. In addition, signed consent forms are kept in locked file cabinets and kept separate from the data collection instruments. Study subjects are also reminded that the information obtained will not be shared with their providers except in non-identifying aggregate form at the end of the study. We also make clear that the responses to the PREPARE guide are only for research purposes and will not be shared with their clinicians or put in their medical record.

We will store all study materials in locked offices and locked storage cabinets. We will utilize UCSF MyResearch and REDCap to enter and maintain data in a secure environment. In order
to be more environmentally-conscious, we will attempt to use the LiveCapture function of RedCap and thus reduce the use of paper resources. We will retain the use of paper surveys in case the RedCap system is down. These paper files are stored in secure, locked research offices in secure, locked file cabinets.

As some of the questions concerning end-of-life may cause psychological discomfort for some study subjects, subjects are reminded at the beginning of the interview of their right to refuse to answer any and all questions and their right to terminate the interview at any time. We will also reassure subjects that if they choose not to be in the study or choose to terminate the interview, it will not change the medical care that they normally receive from their clinic or their clinician. In addition, we will reiterate that the information shared within the research interview will not be shared with their clinicians or used in medical care. However, subjects can take home a copy of the PREPARE guide with them and bring it back to their clinicians if they wish. Subjects are given the name and number of the primary investigator and may call if they have questions or are concerned about their participation in the study.

**Required reportable information:**

As these interviews may be completed in people’s home and, in the interviews, we are asking patients to describe their experiences and opinions, it is possible that reportable events such as elder abuse, suicidal or homicidal ideation may be detected. If they are detected, they will be handled according to the American Psychological Association code of ethics. If elder abuse is suspected, the participant will be encouraged to take steps to ensure their safety. They will be offered contact information for local supportive services and informed that the concerns will be discussed with the elder abuse hotline for assistance. When there are concerns about self-harm or harm to others, severity of harm will be assessed. Participants will be offered local support services and officials will be notified as necessary.
**Patient Depression/Anxiety Protocols**

With input from the Patient-Clinician Stakeholder Advisory Board, and to err on the side of caution, we created a flow diagram with detailed instructions, including study scripts and contact names and telephone numbers for research staff to use in the event scored in the moderately severe depression or anxiety range on the PHQ-8 and GAD-7 or a participant expressed suicide ideation.

**DATA SAFETY MONITORITY PLAN**

Monitoring will focus on recruitment, baseline comparability of treatment groups, protocol adherence, completeness of data, accrual of primary endpoint data, safety, and follow-up rates. This monitoring will provide the basis for monthly review by the study investigators, review by the ZSFG Patient-Clinician Advisory Committee, and Data Safety and Monitoring Board (DSMB), and yearly reporting to our IRBs. We will implement methods of verifying entered data and of quality control. All study materials data are kept on secure, password-protected, encrypted servers. All consent materials and any identifying information are kept in locked cabinets within locked offices, on password-protected, encrypted servers, on card-key protected research floors. Dr. Sudore, will be directly responsible for identifying and immediately reporting all adverse events to the IRBs Privacy Officers, and funding agency as appropriate. The ZSFG Patient-Clinician Advisory Committee will ensure participant safety in the clinic and will meet up to 4 times per year. The formal DSMB includes 4 experts in randomized trials, human subjects research and consent, vulnerable populations, palliative care, advance care planning, and biostatistics. The DSMB will review and approve the research protocol and plans for data and safety monitoring; and assess data quality; participant recruitment, accrual and retention; baseline comparability of treatment groups, accrual of primary endpoints; and participant safety
(e.g., adverse events, protocol violations). They will also develop stopping rules for the trial. The DSMB will meet up to 4 times per year.

**CHARTER OF DATA SAFETY MONITORING BOARD**

The Data and Safety Monitoring Board (DSMB) will act in an advisory capacity to monitor participant safety, data quality and evaluate the progress of the study. The DSMB for this study includes 2 outside clinicians with expertise in RCTs and an outside biostatistician. The DSMB will review and approve the research protocol and plans for data and safety monitoring; and assess data quality; participant recruitment, accrual and retention; baseline comparability of treatment groups, accrual of primary endpoints; and participant safety (e.g., adverse events, protocol violations). They will also develop stopping rules for the trial. The DSMB will meet 2 and up to 4 times per year.

**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 and the Principal Investigator concerning continuation, termination or other modifications of the trial based on the observed beneficial or adverse effects of the treatment under study;
• if appropriate, review interim analyses in accordance with stopping rules, which are clearly defined in advance of data analysis and have the approval of the DSMB;
• 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 last participant completes the study.

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

relevant clinical expertise,
clinical trial methodology, and
biostatistics.

The DSMB members:

• In addition to the NIA program officer members include:
• Dr. David Bekelman, MD, MPH, an internist, psychiatrist, and palliative medicine physician at the University of Colorado School of Medicine and is an expert in health communication and medical decision making
• Dr. Nathan Goldstein, MD, a geriatrician and a national expert in palliative care, communication, and medical decision making at Mt. Sinai School of Medicine,
• Dr. James Wiley, PhD a statistician and Professor in the Institute for Health Policy Studies at the University of California, San Francisco. Dr. Wiley has extensive experience with RCTs and working with safety net populations. Although Dr. Wiley is at UCSF, he does not otherwise work with Dr. Sudore. Membership have no financial, scientific, or other conflict of interest with the trial.

Written documentation attesting to absence of conflict of interest has been obtained.

Dr. Nathan Goldstein, Mount Sinai School of Medicine, has been appointed by NIA to serve as the Chairperson and is responsible for overseeing the meetings, developing the agenda in consultation with the NIA Program Official and the Principal Investigator. The Chair is the contact person for the DSMB. The University of California, San Francisco shall provide the logistical management and support of the DSMB. Dr. Nathan Goldstein is also the safety officer and contact person for serious adverse event reporting. A log of all potential adverse events and protocol violations will be kept and reviewed quarterly by the DSMB. Procedures for notifying the Chair of the DSMB and the NIA Program Official will be discussed and agreed upon at the first meeting.

**Board Process**

At the first meeting the DSMB will discuss the protocol, suggest modifications, and establish guidelines to study monitoring by the Board. The DSMB Chairperson in consultation with the
Principal Investigator and the NIA Program Official will prepare the agenda to address the review of study materials, modifications to the study protocol and informed consent document, initiation of the trial, appointment of a safety officer, as needed, reporting of adverse events, statistical analysis plan including interim analysis and stopping rules, etc.

Meetings of the DSMB will be held 2-4 times per year at the call of the Chairperson and/or NIA Program Official to ensure patient safety and to review stopping rules for the trial. The NIA Program Official or designee will attend most of the meetings. An emergency meeting of the DSMB may be called at any time by the Chair or by the NIA should participant safety questions or other unanticipated problems arise.

Meetings are closed to the public because discussions may address confidential participant data. Meetings are attended by the Principal Investigator and members of his/her staff. Meetings may be convened as conference calls as well as in-person.

**Meeting Format**

Each meeting must include a recommendation to continue or to terminate the study and whether the DSMB has any concerns about participant safety made by a formal 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 his decision.

**Meeting Materials**

DSMB interim report templates will be prepared by the study staff, to be reviewed by the DSMB members at each meeting. The reports will list the study aims, the status of the study, and summarize safety data.

**Reports from the DSMB**

A formal report containing the recommendations for continuation or modifications of the study will be prepared by the DSMB Chairperson, NIA Program Official or its designee. The draft report will be sent to the DSMB members for review and approval.

**Confidentiality**

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

**PATIENT-CLINICAN STAKEHOLDER ADVISORY COMMITTEE ROLE**

This study is guided by a Patient-Clinical Stakeholder Advisory Board that is comprised of patients and patient advocates (including native Spanish-speakers), surrogates, and ZSFH primary care clinic staff and medical directors. These individuals are paid key personnel on the study and have agreed to meet up to 4 times per year to oversee all aspects of the study. Native Spanish-speaking staff will be present to translate for our Spanish-speaking patient stakeholders during advisory meetings. All study materials will be translated into Spanish. The advisory committee will be involved in providing ongoing advice about the following important study related activities:
Recruitment, including study scripts, fliers, methods

- Eligibility and exclusion
- Patient safety and research staff safety
- Clinic workflow and clinical champions
- Informed consent
- Research outcomes
- Presentation of findings
- Dissemination of results

REPRODUCIBILITY AND TRANSPARENCY OF RESEARCH

In order to support the ability of others to replicate our research findings, the research team will create a study protocol that will be made available to PCORI. Other researchers wishing to access these materials can submit a request to PCORI or directly to the study’s Principal Investigator. Requests should include a proposed plan of use of the protocol and plan to assign credit to PCORI and this study’s research team in the dissemination of the replicated study results as appropriate. If the PREPARE website is shown to be effective, the research team will work with our community and clinical partners to disseminate the website. We will create a research section on the website that will contain information concerning the study. Authorship will be based on International Committee of Medical Journal Editors standard guidelines.
REFERENCES


