

Preparing Spanish-speaking Older Adults for Advance Care Planning and Medical Decision Making

This trial is registered at ClinicalTrials.gov: NCT01990235 for English-speakers, registered on November 4th, 2013.

This document includes the following items:

1. Original protocol and statistical analysis plan (March 2013)
2. Final protocol and statistical analysis plan and summary of changes (September 2017)

12

Protocol

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Original Version

14

March 2013

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Original Protocol Table of Contents

| | |
|--|-----------|
| Funding | 5 |
| ClinicalTrials.gov Information | 5 |
| Introduction and Rationale | 5 |
| Preliminary Studies | 6 |
| Overview of the Trial Design | 8 |
| Study Setting | 10 |
| Participants and Eligibility and Exclusion Criteria | 10 |
| Recruitment Methods | 13 |
| Consent Procedures | 15 |
| Intervention and Comparison Conditions | 16 |
| Randomization Procedures | 18 |
| Blinding | 18 |
| Intervention Fidelity | 18 |
| Data Collection Methods | 19 |
| Follow-up and Retention | 19 |
| Measures | 20 |
| Statistical Analysis Plan | 24 |
| Sample Size and Power Calculations | 25 |
| Ethics and Advisory Committees | 26 |
| Human Subjects Protections | 27 |
| Data Safety Monitoring Plan | 30 |
| Charter of the Data and Safety Monitoring Board | 31 |
| Patient-Clinician Stakeholder Advisory Committee Role | 35 |
| References | 37 |

17 **FUNDING**

18 For this trial, recruitment of English-speaking older adults is funded through a National Institute
19 on Aging R01 grant (R01 AG045043).

20

21 **CLINICALTRIALS.GOV INFORMATION**

22 This trial is registered at ClinicalTrials.gov: NCT01990235 for English-speakers, registered on
23 November 4th, 2013.

24

25 **INTRODUCTION AND RATIONALE**

26 Millions of older adults will face complex medical decisions over the course of advanced illness,²
27 yet most are unprepared.^{3,4} Lack of preparation can lead to uninformed choices, receipt of care
28 inconsistent with personal goals, and lack of patient empowerment during clinical encounters,⁵⁻⁹
29 especially for individuals with limited health literacy.¹⁰ Conventional preparation, called advance
30 care planning (ACP), has typically focused on having patients pre-specify preferences for life
31 prolonging procedures, such as mechanical ventilation, and to document these choices in an
32 advance directive (AD).¹¹ Yet, ADs are hard to understand and are often not completed,
33 especially by minorities.^{12,13} And, even when ADs are completed, they often fail to affect the
34 care received at the end-of-life, decrease the stress of decision making, or result in what most
35 experts agree is the most important component of ACP – ongoing conversations between
36 patients, their loved ones (surrogates), and clinicians.^{5,14-17} To overcome these limitations, we
37 developed a new paradigm of ACP that focuses instead on preparing diverse, older adults to
38 communicate their evolving wishes over time and to make real-time, complex medical decisions
39 over the course of chronic and advanced illness.¹¹ We propose to test this new paradigm of
40 ACP using a patient-centered, interactive website in a double-blind, randomized, efficacy trial.

41

42

43

44 **PRELIMINARY STUDIES**

45 **We have experience conducting RCTs among diverse, older adults at the San Francisco**

46 **Health Network (SFHN).**¹⁸ Dr. Sudore designed and tested an AD written at a 5th grade

47 reading level among 205 chronically ill, diverse, older adults from San Francisco General

48 Hospital (SFGH) with a 6-month follow-up of 85%. The AD was preferred over a standard AD,

49 with significant interactions for limited literacy (e.g., higher preference rates in patients with

50 limited literacy). It also resulted in greater 6-month AD completion rates (15% vs. 7%, $p = .03$),

51 doubling the rates from baseline. This AD has been adopted as the official AD for SFGH and is

52 being disseminated in California. It will serve as the active control.

53 **We designed and tested an informed consent process for diverse, older adults with**

54 **limited literacy.**¹⁹ We found that many patients do not understand simplified consent

55 information and were unsure how to ask questions. But, informed decisions can be improved by

56 providing both easy-to-read materials and a teach-back method. We will use this interactive

57 consent method for this study.

58 **Multiple steps of the ACP process.**²⁰ We found that most patients go through a series of ACP

59 behavioral steps. Six months after exposure to the easy-to-read AD, 61% of older adults

60 contemplated ACP, 56% discussed ACP with family or friends and 22% with clinicians, and 13%

61 completed an AD. This work shows that measuring a full range of ACP outcomes, in addition to

62 ADs, and associated behavior change steps (contemplation to action) is important and informs

63 our study outcomes. Previously described barriers to ACP, such as not wanting to burden

64 family,²¹ are addressed in PREPARE.

65 **Evidence supporting the new ACP paradigm and content of PREPARE.**²² We completed 13

66 focus groups with 69 diverse, English- and Spanish-speaking older patients (mean age 78 +/- 8,

67 61% non- White) and surrogates (mean age 57 +/- 10, 91% non-White) from safety-net settings
68 who reported making serious medical decisions. We used semi-structured interviews to ask
69 about what best prepared them for decision making. Qualitative analysis identified 5 overarching
70 themes, beyond ADs, that prepared patients and surrogates for decision making: (1) choose
71 surrogates wisely and verify they know their role, (2) identify goals based on past experiences
72 and personal values, (3) decide whether to grant leeway in surrogate decision making, (4)
73 inform other family and friends of one's wishes to prevent conflict, and (5) ask clinicians
74 questions. These themes have been incorporated as educational domains of PREPARE.

75 **Validity and reliability of the survey to measure ACP engagement:** Surveys were designed
76 with input from Co-Is and extensive cognitive interviews to measure discrete ACP actions (i.e.,
77 main outcomes: ACP discussions, AD completion,) and ACP behavior change (e.g.,
78 contemplation, self-efficacy, readiness). We recruited 50 older adults, aged ≥ 60 years with ≥ 2
79 illnesses (32% female, 42% non-White). Internal consistency 7-day test-retest reliability, and
80 discriminant validity (scores compared to healthy young adults – 50% female, 75% non-White)
81 was high. Scores did not differ by race/ethnicity or literacy, $p > .05$. We will also use validated
82 surveys on ACP attitudes and methods to classify patients into behavior change categories.^{23,24}

83 **Preliminary evidence that PREPARE is beneficial.** In a recent pilot,²⁵ we recruited 43 diverse,
84 older adults from low-income senior centers. All subjects rated PREPARE easy to use (mean
85 9/10-point scale). Pre to post ACP behavior change scores from our validated surveys (0-124
86 points) increased from 72 ± 33 SD to 87 ± 22 , a 15-point increase and an effect size of 0.5.

87 **Vulnerable populations have unique needs.** The aforementioned pilot demonstrated that,
88 unlike our work with Veterans, patients in safety-net settings are less trustful of research and
89 require in-person recruitment. In addition, these patients are often socially isolated and require
90 tailored ACP for persons without surrogates or families. They also lack ready access to health

91 information and ancillary support such as social workers or nurses necessitating access to ACP
92 outside of the clinical environment. These findings add further evidence for the need to tailor
93 PREPARE for vulnerable populations and to test PREPARE within safety-net settings.

94

95 **OVERVIEW OF THE TRIAL DESIGN**

96 Study overview:

97 This study is a randomized, controlled trial that uses blinded outcome ascertainment to
98 determine the efficacy of the ACP PREPARE website to engage ethnically diverse English- and
99 Spanish-speaking older primary care patients in the ACP process.¹ First, we obtained a Health
100 Insurance Portability and Accountability Act waiver to identify individuals who meet our
101 inclusion/exclusion criteria and have upcoming primary care appointments. Administrative data
102 and chart review are used to determine potentially eligible patients.

103

104 Then primary care clinicians' permission is obtained to allow the study team to inform their
105 patients about the study. Patients are then recruited, screened for eligibility, and scheduled for a
106 baseline interview before an upcoming primary care appointment. To standardize the timing of
107 exposure to the intervention and primary care follow-up, study participants are scheduled for
108 baseline procedures 1-3 weeks prior to an upcoming primary care appointment.²⁶

109

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

115

116 We then conduct blinded outcome ascertainment by performing chart reviews to determine ACP
117 documentation at baseline and at the end of the study. We also conduct blinded outcome
118 ascertainment using patient surveys at 1 week, and 3, 6, and 12 months after the primary care
119 appointment. We are choosing an active control arm (i.e., an easy-to-read advance directive)
120 because we believe provision of an advance directive for chronically and seriously ill older
121 patients should be the standard of care, even if it is not often “usual” care in clinical practice.⁸ In
122 addition, the easy-to-read advance directive used in this study has been adopted by the San
123 Francisco Health Network (SFHN) and San Francisco General Hospital (SFGH) and is available
124 in the primary care clinics.

125

126 **Research Aims and Study Hypotheses:**

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

132

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

137

138 Our secondary hypotheses are that, compared to an advance directive alone, PREPARE will
139 result in more engagement in behavior change processes concerning ACP, including increased
140 self-efficacy and readiness, as well as greater engagement in a full range of ACP actions,
141 including discussions with surrogate decision makers and other trusted family and friends.

142 Secondary outcomes will be ascertained using validated surveys.^{23,27,28} We also hypothesize
143 that PREPARE will result in improved satisfaction with patient-doctor communication and
144 informed medical decision making and that PREPARE efficacy may vary across moderator
145 variables such as patient health literacy, clinician-patient language concordance, and patients'
146 desired role in decision making.

147

148

149 **STUDY SETTING**

150 Recruitment for this randomized trial is occurring in 4 separate primary care clinics associated
151 with the San Francisco Health Network (SFHN) and the San Francisco General Hospital
152 (SFGH) in San Francisco, California. These 4 clinics are housed in 3 separate physical
153 locations in San Francisco. SFGH is an urban, public hospital that, with the SFHN, serves
154 racially and ethnically diverse, low-income and indigent patients; 30% of patients are Spanish-
155 speaking.¹⁸

156

157 **PARTICIPANTS AND ELIGIBILITY AND EXCLUSION CRITERIA**

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

166

Inclusion and Exclusion Criteria

167 We are recruiting patients ≥ 55 years of age (rather than ≥ 65) because adults in safety net
168 settings experience accelerated aging, functional decline, and sequelae of chronic disease,
169 necessitating decision making and ACP at a younger age than patients with higher
170 socioeconomic status.^{29,30} The goal is to start ACP early to change the trajectory of decision
171 making and care over the course of illness. Our inclusion criteria of ≥ 2 primary care visits and \geq
172 2 additional visits in the past year ensures patients have established primary care and access
173 care frequently. This will enhance recruitment and follow-up.

174

175 Patients will be excluded if their clinician is a principal investigator, co-investigator or clinician-
176 member of the Patient-Clinician Advisory Board. They will also be excluded if they have medical
177 record documentation of being deaf, blind, having dementia, or being psychotic or are deemed
178 by their clinician to be too mentally or physically ill to participate. Through in-person or phone
179 screening by study staff, patients are also excluded if they self-report vision too poor to read a
180 newspaper, lack of a phone (needed for follow-up interviews and scheduling), or plans to be out
181 of the country for ≥ 3 months; if they screen positive for moderate-to-severe cognitive
182 impairment using the validated Short Portable Mental Status Questionnaire followed by the Mini-
183 Cog,³¹⁻³³ or self-report or are determined by study staff to be blind, deaf, intoxicated or actively
184 psychotic. Because ACP is an iterative process and people may change their preferences over
185 time,^{11,34} subjects with prior ACP experiences (e.g., an advance directive) are not excluded.

| | |
|--------------------|---|
| Inclusion Criteria | 55 years of age or older |
| | Obtains care in the primary care clinics at in the San Francisco Health Network (SFHN). |
| | Has been seen at least twice in the last year by a primary care provider (a marker of established primary care) and had at least two additional visits to SFHN in the past year (a marker of illness) |
| Exclusion Criteria | Clinician is the PI, Co-I or member of the Patient-Clinician Advisory Board |
| | Dementia by ICD-9/ICD-10 codes, clinician assessment, chart review or self-report |
| | Blindness or poor vision by ICD-9/ICD-10 codes, clinician assessment, chart review, self-report of blindness or the inability to read print on a newspaper ³⁵ |
| | Deafness by ICD-9/ICD-10 codes, clinician assessment, self-report, chart review or research staff assessment |
| | Cognitive impairment as assessed by research staff of any deficits on the validated Short Portable Mental Status Questionnaire (SPMSQ) ³⁶ and the mini-Cog ^{31,37} |
| | Delirium or psychosis as assessed by a clinician or research staff |
| | Does not report speaking English or Spanish “well” or “very well” |
| | No phone for additional study contacts and follow-up interviews |
| | Patients who report they will be out of town during their scheduled follow-up interview dates outside of a window of 3 months. |
| | Patients who cannot answer consent teach-back questions after three attempts |

187 **RECRUITMENT METHODS**

188 **Data Extraction:**

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

199

200 **Clinician Permission to Contact Patients:**

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

212

213 **Recruitment Methods and Materials:**

214 Study-related fliers written at a 5th-grade reading level in English and Spanish are posted in
215 approved areas in SFHN/SFGH-affiliated primary care clinics. Because many patients may be
216 too ill to come to frequent clinic appointments and to be interviewed or hear about the study in
217 busy clinic waiting rooms, we include several recruitment strategies. Therefore, in addition, opt-
218 out letters written at a 5th grade reading level in English and Spanish are mailed and describe
219 the research study as well as provide a telephone number to opt-out. If a clinician gives us
220 explicit permission to contact their patients, we will inform patients that their individual doctor
221 gave us permission to contact them. If the clinician merely assents by not responding to multiple
222 attempts to reach them by study staff, patients will be sent non-personalized letters from the
223 study team. Although patients can opt out at any time, those who do not call study staff to
224 decline participation within 1 week of the mailings are deemed eligible to be contacted to
225 describe the study, assess willingness to participate and assess study eligibility. To standardize
226 the timing between intervention exposure and primary care follow-up, we schedule patients for
227 the baseline interview and exposure to PREPARE or the control intervention 1 to 3 weeks prior
228 to their upcoming primary care appointment. Weekly administrative data pulls from the
229 electronic health record identify patients with upcoming primary care appointments and are used
230 to target patient recruitment efforts. Potential participants are then contacted in the clinic.

231
232 Patients who consent and enroll are paid \$25 for a screening interview and \$25 for a baseline
233 interview as well as given a \$10 taxi voucher to come back to follow-up interviews in person if
234 they desire. Participants are also reimbursed \$25 for each of the 1-week, 3, 6, and 12-month
235 interviews.

236
237 Diverse, vulnerable populations are often difficult to recruit for research studies. We employ
238 several strategies to enhance our recruitment. First, we attempt to hire individuals who have

239 experience with diverse populations and individuals who are bilingual (native Spanish-speaking)
240 and bicultural. Furthermore, we conduct extensive sensitivity training with all research staff and
241 require staff to use approved study scripts when speaking to patients. These study scripts and
242 all study materials used for recruitment are vetted, updated and approved by both our patient
243 advisory and clinical advisory boards. All materials and study scripts are written at a 5th grade
244 reading level and are provided to patients in their preferred language (i.e., English or Spanish).

245

246 **CONSENT PROCEDURES**

247 We use a modified consent process that several co-authors designed for vulnerable
248 populations.^{19,26} Consent forms written at the 5th grade reading level are provided and read to
249 participants in English or Spanish. This review is then followed by standardized “teach-to-goal”
250 questions to ensure understanding. If potential participants cannot correctly complete the teach-
251 back process after 3 attempts, the patient is deemed ineligible.

252

253 The consent form has been approved by the UCSF and SFGH Institutional Review Boards, the
254 patient/clinical advisory board, and the Data and Safety Monitoring Board (DSMB). The consent
255 form states the following for the purpose of the study: “Why is this study being done?
256 Sometimes patients and their families have to make hard medical decisions. We want to design
257 and test an easy-to-understand handout to help. This handout will help people think about their
258 values, or what is most important to them in their life. It will also help prepare patients to make
259 medical decisions.” We use the word “handout” because, in pilot testing, both groups are given
260 handout materials and written advance directives. For randomization we explain, “We will ask
261 you to look over a handout and answer some questions about your experience with making
262 medical decisions. There will be two groups that will be given different handouts. You will have a
263 50/50 chance of being in either group.”

264

265 **INTERVENTION AND COMPARISON CONDITIONS**

266 PREPARE arm

267 As previously described, PREPARE is an easy-to-use, patient-centered, interactive website that
268 is available in English or Spanish, is written at a 5th grade reading level, includes voice-overs of
269 all text for the reading-impaired and closed-captioning of all videos for the hearing impaired
270 (www.prepareforyourcare.org).^{25,26} The conceptual framework for PREPARE has been
271 previously published and is based primarily on Social Cognitive Theory,^{38,39} with
272 elements from the Health Belief Model,⁴⁰ the Theory of Planned Behavior,⁴¹ and Behavior
273 Change Theory.^{39,42} In these theories and in behavioral studies, modeling of behaviors helps
274 people change their behavior. Successful behavioral change interventions model skills, enhance
275 self-efficacy, and address perceived barriers,^{43,44} especially literacy-appropriate interventions.¹⁸
276 Modeling behaviors (as in PREPARE) can also improve patients' ability to communicate with
277 clinicians and improve outcomes,^{45,46} such as increased question asking behavior and a sense
278 of control during a clinical visit,^{46,47} an increased desire to participate in decision making, and
279 even improved affect and functional status.^{43,48-50} PREPARE incorporates these successful
280 teaching methods through the modeling of behaviors in videos. Video and interactive websites
281 are more powerful mediums to teach information and change behavior than written materials,
282 especially for those with language/literacy barriers.⁵¹⁻⁵⁷ PREPARE includes a training and goal
283 setting component which has been shown to be effective in changing outpatient behaviors, such
284 as exercise.⁵⁸

285

286 In the design of the PREPARE website, we included essential, theory-based health education
287 strategies, such as the use of video modeling of ACP behaviors and tailored and interactive
288 content based on patients' values and decision preferences. To ensure PREPARE is easy to
289 read and understand, we use clear health communication principles (e.g., targeting text to the
290 5th grade reading level) informed by extensive formative research and cognitive interviewing

291 with the target population (i.e., racially and ethnically diverse older adults with limited health
292 literacy and English proficiency) to ensure PREPARE content is acceptable to individuals from
293 diverse cultural backgrounds.²⁵ The PREPARE website leads people through a 5-step ACP
294 process that ranges from choosing a surrogate decision maker to asking their clinicians the right
295 questions. While going through the website, PREPARE also helps individuals answer personal
296 values questions about their medical care, and helps them create an action plan to engage in
297 some form of ACP. Patient-generated action plans have been shown to help patients engage in
298 other preventative and disease management activities in the outpatient setting.⁵⁹

299
300 After the baseline interview, participants in the PREPARE arm review all 5 steps of the
301 PREPARE website in English or Spanish in our research offices. Participants are asked to
302 review PREPARE on their own and in its entirety. Research assistants are available to answer
303 questions only if needed, but do not go through the website with the participants. At the end of
304 the program, a summary of the patient's medical wishes and action plan are automatically
305 generated from the PREPARE website in written format. This information along with the
306 participant's PREPARE website login information is included in a take-home folder that also
307 contains PREPARE information in pamphlet, booklet, and DVD format. We include PREPARE
308 content in non-website formats because some patients may not have access to the internet at
309 home. PREPARE arm participants are also given an easy-to-read advance directive in English
310 or Spanish to review and consider completing.^{18,60} Participants are asked to review the advance
311 directive form for at least 5 minutes and up to 15 minutes in research offices, and then to take
312 the form home to discuss with their potential surrogates and/or their clinicians. The time frame
313 of 5-15 minutes was chosen because our goal is only to introduce the advance directive and
314 allow participants to ask questions. The goal is not to have patients complete the form on the
315 day of the study, before potential discussions with clinicians or surrogates, unless the participant
316 would like to do so.

317

318 AD-only arm

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

322

323 Both arms: Reminder of primary care appointments

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

329 **RANDOMIZATION PROCEDURES**

330 A statistician not involved in recruitment or data collection uses a computer-based random
331 number generator to create a randomization scheme using block randomization by health
332 literacy (adequate health literacy versus limited health literacy, as determined by a validated
333 question concerning confidence with medical forms) and race/ethnicity (non-white versus
334 white).⁶¹ Random block sizes of 4, 6, and 8 are used to ensure an equal number of patients with
335 limited health literacy in each group. Randomization information is associated with a unique
336 patient identification number and is kept separate from other patient data. Due to the need to
337 secure interview rooms for the duration of the baseline questionnaire and intervention (i.e.,
338 approximately 2 hours for the AD-only arm and 3 hours for the PREPARE arm), randomization
339 occurred prior to scheduling a baseline interview.

340

341 **BLINDING**

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

353

354 **INTERVENTION FIDELITY**

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

362

363 **DATA COLLECTION METHODS**

364 Paper surveys are collected and entered into REDCap. REDCap is managed by the UCSF
365 Academic Research Systems Team and is stored behind strong-string password protected
366 firewalls on UCSF servers, not on individual laptops or desktops. All patients are given a unique,
367 non-identifying patient identification number that is removed from any personally identifying

368 information (PII) or personal health information (PHI). All PII and PHI are stored in a Microsoft
369 ACCESS database behind strong-string password protected firewalls on UCSF and SFGH
370 servers. All paper files are stored in secure, locked research offices in secure, locked file
371 cabinets.

372

373 **FOLLOW-UP AND RETENTION:**

374 We conduct follow-up interviews one week and 3, 6, and 12-months after the primary care visit
375 in the clinic, by phone. We utilize several measures to help ensure follow-up. Each follow-up
376 interview takes between 30 to 45 minutes and participants are reimbursed \$25.

377

378 Method of contact for follow-up surveys:

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

387

388 Reminders for the primary care visit:

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

393

394 Reminders for study interviews:

395 For all follow-up interviews, participants in both arms receive reminders of their upcoming study
396 interview by phone or in person.

397

398 **Ascertaining reasons for loss of follow-up or withdrawal:** For participants who want to
399 withdraw, we ask them why in open-ended questions. If they cannot provide an answer, we
400 prompt them from a list of reasons we obtained from prior advance care planning trials, such as
401 the study is too long, they are too busy, the study topic is too upsetting, they are too ill, etc.⁶²

402

403

404 **MEASURES**

405 **Overview**

406 Because ACP ideally is a process that occurs over time, we felt it important to measure a full
407 range of ACP measures including ACP documentation (primary outcome) over time, and
408 several behavior change constructs and several additional ACP actions over a 12-month period
409 (secondary outcomes). The main outcome measures are described in detail below.

410

411 **Primary Outcome**

412 The primary outcome is documentation of ACP wishes in the SFHN/SFGH medical record. ACP
413 documentation for the purposes of this study includes the easy-to-read advance directive or
414 other valid advance directives or living wills, a durable power of attorney for health care
415 document (DPOAHC), a Physicians Orders of Life Sustaining Treatment form, or other
416 documentation of discussions concerning patients' wishes for medical care (i.e., documentation
417 of oral directives by a physician or notes describing patients' goals for medical care by
418 clinicians).

419

420 We assess baseline and 12-month ACP documentation rates and the date of documentation to
421 determine the length of time from study enrollment to subsequent documentation. Patients in
422 our study are enrolled, randomized, and exposed to the intervention 1 to 3 weeks prior to a
423 primary care appointment. ACP documentation is timed to the date of intervention exposure as
424 patients may have engaged in ACP prior to seeing their primary care provider. The patient-
425 reported outcomes in the follow-up surveys (1 week, 3, 6, and 12-months), however, are timed
426 to the primary care visit because those questions concern engagement in discussions with
427 clinicians (see secondary outcomes below).

428

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

434

435 **Secondary Outcomes**

436 **Main Patient-Reported Outcome**

437 The main patient-reported secondary outcome, the validated Advance Care Planning
438 Engagement Survey,²⁵⁻²⁷ was chosen to measure the full process of ACP. The Advance Care
439 Planning Engagement Survey measures both ACP Behavior Change Processes, such as
440 knowledge, contemplation, self-efficacy, and readiness on a validated 57-item scale. The ACP
441 Behavior Change Process scale is measured on a 5-point Likert scale and average 5-point
442 scores will be calculated. We will also measure ACP actions on the validated 25-item Action
443 scale, which assesses ACP activities (yes or no) such as identifying a surrogate decision maker,
444 identifying values and goals for medical care, choosing the level of leeway in surrogate decision
445 making, discussing one's wishes with clinicians and surrogates, and documenting one's wishes

446 in an advance directive. Validity and reliability of the ACP Engagement Survey, as well as the
447 questionnaire's ability to detect change in response to an ACP intervention, have been
448 previously described.²⁵⁻²⁷

449

450 **Feasibility and Satisfaction**

451 To evaluate whether and how PREPARE will be used in clinical practice and in the community,
452 we also assess acceptability of the PREPARE website compared to an advance directive alone
453 using validated scales of ease-of-use (10-point scale, "On a scale of 1 to 10, with 1 being very
454 hard and 10 being very easy, how easy was it to use this guide?") and satisfaction (comfort:
455 "How comfortable were you viewing this guide?", helpfulness: "How helpful was this guide?",
456 and recommendations: "How likely are you to recommend this guide to others?" assessed on a
457 5-point Likert scale (not-at-all to extremely) from our prior work.¹⁸ For the PREPARE arm only,
458 and at the end of the 12-month interview and after unblinding, we also ask how likely patients
459 are to recommend the PREPARE intervention to others.⁶³

460

461 **Adverse Event Outcomes**

462 In addition, to ensure that the PREPARE program does not cause undue harm, we also assess
463 both depression^{64,65} and anxiety.^{66,67} We administer the Patient Health Questionnaire (PHQ)-4
464 at baseline and at each follow-up interview.⁶⁸ The PHQ-4 includes the PHQ-2 for depression
465 and the Generalized Anxiety Disorder (GAD)-2 anxiety screening tool. A score of 3 or greater on
466 a 0 to 6 scale suggests possible depression or anxiety.

467

468 **Potential Mediating or Moderating Variables & Participant Characteristics**

469 Based on the previously published conceptual framework of PREPARE,²⁵ we also hypothesize
470 that PREPARE efficacy may vary across several moderator or mediator variables (e.g., health
471 literacy using the validated Short form Test of Functional Health Literacy in Adults s-TOFHLA,

472 scores 0-36⁶⁹ and dichotomized to limited = 0-22 & adequate = 23-36, and patient’s desired role
473 in decision making with the medical provider using the validated Decision Control Preferences
474 Scale (i.e., wants to make their own decision versus wants doctors/family to make decisions for
475 them).⁷⁰ We also hypothesize that PREPARE efficacy may be affected by several confounding
476 variables (e.g., self-rated health, “How would you rate your health?” (5-point Likert)^{71,72}
477 dichotomized as fair-to-poor and good-to-excellent and past experiences with ACP including
478 prior documentation of legal forms and documented discussions. We will also assess a full
479 range of patient-reported characteristics, as these factors may impact patient-clinician
480 communication,^{73,74} such as age (“What is your date of birth?”), self-reported gender (“What
481 gender do you consider yourself to be? male, female transgender, other”), finances (able to
482 make ends meet versus not make ends meet), having a potential surrogate decision maker or
483 not, education (“What is the highest educational level you have completed?” less than or equal
484 to high school or greater than high school), internet access in the home (yes or no), and
485 religiosity and spirituality (i.e., “How religious/spiritual do you consider yourself to be?” on 5-
486 point Likert scale from not-at-all to extremely).

487

488 **STATISTICAL ANALYSIS PLAN**

489 Our primary analyses will compare change in ACP documentation between study arms from
490 baseline to 12 months. Secondary outcomes will include ACP Engagement with respect to 5
491 ACP Actions (yes/no and a 0-25-point scale) and Behavior Change Process scores (average 5-
492 point Likert scores) from baseline to 1 week, and 3, 6, and 12 months. Variables will be
493 assessed for distributional and outlier values using standard summary statistics. Baseline
494 comparability will be assessed between groups using unpaired t-tests, Chi-square tests or
495 Fisher’s exact tests. We will use intention-to-treat analysis using SAS version 9.4 (SAS Institute
496 Inc.) and STATA 15.0 (College Station, TX). All p-values will be 2-tailed and set at .05 for the
497 primary outcome. To compare outcomes between the two arms longitudinally, we will use mixed

498 effects linear, Poisson, or negative binomial regression for continuous measures and mixed
499 effects logistic regression for dichotomous measures. The mixed effects models will include
500 fixed effects for the primary modeling terms of time (baseline and 12 months for ACP
501 documentation and baseline and 1 week, 3 months, 6 months, and 12 months for ACP
502 Engagement with time modeled using dummy variables to allow for non-linearity); arm (AD-only
503 versus PREPARE); an interaction term of study arm and time; and a random effect for subjects.
504 We will adjust for the randomization blocking factors limited vs. adequate literacy,⁷⁵ and any
505 predictor variables that differ between arms. All models also will include random physician
506 intercepts to account for nesting of patients within physicians.

507
508 For moderator analysis, we will test for interactions by adding interaction terms to the group by
509 time variable for health literacy (limited versus adequate) controlling for prior ACP
510 documentation and clustering effects by clinician. All other interaction terms are adjusted for
511 health literacy (randomization blocking variable) prior ACP documentation and clustering effects
512 by clinician. Additional interaction terms to be added to the group by time variable include
513 decision control preferences for making decisions (i.e., makes own decisions versus doctor
514 makes decisions), age (i.e., < 65 years versus ≥65 years of age), sex/gender (i.e., self-reported
515 man versus woman), race/ethnicity (i.e., white versus non-white), health status (i.e., good-to-
516 excellent versus fair-to-poor), presence of a potential surrogate (i.e., yes versus no), and
517 internet access at home (i.e., yes versus no). For Spanish-speakers, we will also assess patient-
518 clinician language (concordance vs. discordance). A p-value for interaction <0.05 is considered
519 significant.

520
521 Missing data for the primary outcome will be assessed. If there is 10% or more of missing data,
522 we will use a mean imputation approach and all available data will be included in mixed-effects

523 models. We will assess whether any research staff member became unblinded during follow-up
524 assessment and conduct sensitivity analysis as needed.

525

526 **SAMPLE SIZE AND POWER CALCULATIONS**

527 We will measure a full range of ACP behaviors including discussions. However, written advance
528 directive completion of legal forms is a primary outcome and is the most well-studied.⁷⁶ Power
529 from longitudinal analyses with repeated measures will be stronger, but to be conservative, we
530 consider power for a single post-intervention time point (e.g., 12 months). A recent meta-
531 analysis of written advance directive documentation studies demonstrated a pooled effect size
532 of 0.50 (95% CI; 0.17 -0.83),⁷⁶ as did an RCT of an ACP workbook that included both behavior
533 change constructs and a social work visit,⁷⁷ and our prior RCT of an easy-to-read AD at SFGH
534 which showed an increased AD completion rate from 7% to 15%.¹⁸ Because both the
535 intervention and control arm will receive the easy-to-read advance directive, we assume that
536 both arms will have an advance directive completion rate of $\leq 15\%$. Based on prior studies, we
537 assume PREPARE will result in additional benefit of advance directive completion with a
538 minimum effect size of 0.5 (two-fold increase) above 15%. A sample of 350, (175 per arm), will
539 afford us 92% power (2-tailed alpha of 0.05) to detect a difference of advance directive
540 completion rates of 15% in controls vs. 30% in the PREPARE arm and 80% power to detect a
541 difference of 15% vs. 27%. Power is also expected to be strong for the ACP behavioral change
542 scale outcomes (preliminary data demonstrated a pre-to-post improvement of 0.5 SD).²⁵ With a
543 conservative assumption that controls will improve by 0.1 to 0.2 SD, we will have 85% to 98%
544 power, respectively, to conclude that the improvement is better in the PREPARE arm. We
545 expect a 15% drop out rate at 12 months based on our prior randomized, controlled trial at
546 SFGH,¹⁸ and will therefore attempt to recruit 402 patients, or 201 in each arm for each language
547 (English and Spanish) for a total recruitment of 804 patients.

548

549 Our sample size will also allow adequate power to detect clinically important interactions based
550 on potential moderators (literacy, control preferences, language concordance) for our outcomes.
551 In a prior trial of an easy-to-read advance directive in the same patient population with only 200
552 patients, we found significant interactions for literacy.⁸ Thus, if we consider the power scenario
553 of the control group ACP documentation rate of 15% and the PREPARE group of 28%, and
554 suppose the control group rate is the same (15%) for both levels of the moderating factor, then
555 for a moderating factor split of 1:1, we would have 80% power to detect an interaction. If the
556 PREPARE arm ACP documentation rate is 18% for one level of the factor and 40% for the
557 other, this corresponds to a relative rate of ACP documentation of 2.2 times as high for one
558 level of the factor compared to the other. A 2:1 split of the moderating factor still allows
559 detection of a 2.4-fold increase in the relative rate of documentation. Power to detect
560 interactions will likely be stronger for continuous outcomes (e.g. engagement/behavioral scales).

561

562 **ETHICS AND ADVISORY COMMITTEES**

563 This study is approved by the University of California, San Francisco (UCSF) (IRB reference
564 #13-10847). This study is guided by a Patient-Clinical Stakeholder Advisory Board that is
565 comprised of patients and patient advocates (including native Spanish-speakers), surrogates,
566 and SFHN/SFGH primary care clinic staff and medical directors. It is also guided by a DSMB
567 consisting of 4 experts in randomized trials, human subjects research and consent, vulnerable
568 populations, palliative care, advance care planning, and biostatistics. Both advisory groups will
569 review and approve all study protocols and related materials. In addition, we continue to meet
570 with both groups every 4-6 months to review the progress of the trial, make suggestions for
571 recruitment, review any potentially adverse events, and ensure that we are following our study
572 protocols in a way that protects vulnerable patient populations.

573

574 **HUMAN SUBJECTS PROTECTIONS**

575 **Protection of the rights and welfare of participants:**

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

580
581 Furthermore, our consent process ensures that study participants have a clear understanding of
582 the study and understand that they can choose to not participate in the study at any point in
583 time, and that the care they receive will not be affected by declining to participate in our study.
584 Our consent process involves using a consent form written below a 6th-grade reading level,
585 reading the form to potential subjects verbatim, allowing time for questions and discussion, and
586 then assessing comprehension using teach-to-goal. If questions are not answered correctly,
587 repeated education and reassessment of comprehension are continued until complete
588 comprehension is achieved. If subjects take more than three passes through the
589 comprehension assessment, formal assessment for cognitive impairment will be completed. If
590 patients are found to be cognitively impaired, they are excluded from the study. If they are not
591 cognitively impaired, we will re-do teach back once more, after which the participant will be
592 deemed ineligible for the study if they are unable to demonstrate comprehension of the study.

593
594 Additionally, we include UCSF Clinical Research Office contact information on all consent forms
595 as required for all non-biomedical studies.

596
597 **Steps taken to minimize risks to subjects:**
598 We have developed a modified research consent process that has been shown to be successful
599 in vulnerable patient populations as described above.¹⁹ All study fliers, consent forms, and
600 questionnaires are read to the subjects in their entirety by native English- and Spanish-speaking

601 research staff. Participants are reminded that they can opt out of the study at any time. All study
602 materials are in an easy-to-read (5th grade reading level, large 14-point font) format. The
603 consent materials and the study interviews are conducted in the language the participant is
604 most comfortable speaking (English or Spanish).

605

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

616

617 **Data security:**

618 - Data are stored securely in the encrypted, secure UCSF MyResearch environment

619 - Data are coded; data key is kept separately and securely

620 - Data are kept in a locked file cabinet

621 - Data are kept in a locked office or suite

622 - Electronic data are protected with a password

623 - Data are stored on a secure network

624 - Data are collected/stored using REDCap or REDCap Survey

625

626 **Measures to ensure confidentiality and protect identifiers from improper disclosure**

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

637

638 We will store all study materials in locked offices and locked storage cabinets. We will utilize
639 UCSF MyResearch and REDCap to enter and maintain data in a secure environment. The
640 paper files are stored in secure, locked research offices in secure, locked file cabinets.

641

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

652

653 **Required reportable information:**

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

663

664 **DATA SAFETY MONITORITY PLAN**

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

679 safety monitoring; and assess data quality; participant recruitment, accrual and retention;
680 baseline comparability of treatment groups, accrual of primary endpoints; and participant safety
681 (e.g., adverse events, protocol violations). They will also develop stopping rules for the trial. The
682 DSMB will meet up to 4 times per year.

683

684 **CHARTER OF DATA SAFETY MONITORING BOARD**

685 The Data and Safety Monitoring Board (DSMB) will act in an advisory capacity to the National
686 Institute of Aging (NIA) and PCORI to monitor participant safety, data quality and evaluate the
687 progress of the study. Dr. Sudore, University of California, San Francisco is conducting a
688 comparative trial of two advance care planning interventions among English- and Spanish-
689 speakers. The DSMB for this study includes 2 outside clinicians with expertise in randomized
690 control trials(RCTs) and an outside biostatistician. The DSMB will review and approve the
691 research protocol and plans for data and safety monitoring; and assess data quality; participant
692 recruitment, accrual and retention; baseline comparability of treatment groups, accrual of
693 primary endpoints; and participant safety (e.g., adverse events, protocol violations). They will
694 also develop stopping rules for the trial. The DSMB will meet 2 and up to 4 times per year.

695

696 **DSMB Responsibilities**

697 The DSMB responsibilities are to:

- 698 • review the research protocol, informed consent documents and plans for data safety and
699 monitoring;
- 700 • advise the NIA on the readiness of the study staff to initiate recruitment;
- 701 • evaluate the progress of the trial, including periodic assessments of data quality and
702 timeliness, recruitment, accrual and retention, participant risk versus benefit, performance of
703 the trial sites, and other factors that can affect study outcome;

- 704 • consider factors external to the study when relevant information becomes available, such as
705 scientific or therapeutic developments that may have an impact on the safety of the
706 participants or the ethics of the trial;
- 707 • review study performance, make recommendations and assist in the resolution of problems
708 reported by the Principal Investigator;
- 709 • protect the safety of the study participants;
- 710 • report to NIA on the safety and progress of the trial;
- 711 • make recommendations to the NIA and the Principal Investigator concerning continuation,
712 termination or other modifications of the trial based on the observed beneficial or adverse
713 effects of the treatment under study;
- 714 • if appropriate, review interim analyses in accordance with stopping rules, which are clearly
715 defined in advance of data analysis and have the approval of the DSMB;
- 716 • ensure the confidentiality of the study data and the results of monitoring; and,
- 717 • assist the NIA by commenting on any problems with study conduct, enrollment, sample size
718 and/or data collection.

719

720 The DSMB will discharge itself from its duties when the last participant completes the study.

721

722 **Membership**

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

724 relevant clinical expertise,

725 clinical trial methodology, and

726 biostatistics.

727

728 The DSMB members:

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

740

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

742

743 Dr. Nathan Goldstein, Mount Sinai School of Medicine, has been appointed by NIA to serve as

744 the Chairperson and is responsible for overseeing the meetings, developing the agenda in

745 consultation with the NIA Program Official and the Principal Investigator. The Chair is the

746 contact person for the DSMB. The University of California, San Francisco shall provide the

747 logistical management and support of the DSMB. Dr. Nathan Goldstein is also the safety officer

748 and contact person for serious adverse event reporting. A log of all potential adverse events and

749 protocol violations will be kept and reviewed quarterly by the DSMB. Procedures for notifying

750 the Chair of the DSMB and the NIA Program Official will be discussed and agreed upon at the

751 first meeting.

752

753 **Board Process**

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

760

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

766

767 Meetings are closed to the public because discussions may address confidential participant
768 data. Meetings are attended by the Principal Investigator and members of his/her staff.

769 Meetings may be convened as conference calls as well as in-person.

770

771 **Meeting Format**

772 Each meeting must include a recommendation to continue or to terminate the study and
773 whether the DSMB has any concerns about participant safety made by a formal DSMB majority
774 or unanimous vote. Should the DSMB decide to issue a termination recommendation, the full
775 vote of the DSMB is required. In the event of a split vote, majority vote will rule and a minority
776 report should be appended. The DSMB Chair provides the tiebreaking vote in the event of a 50-
777 50 split vote.

778

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

784

785 **Meeting Materials**

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

789

790 **Reports from the DSMB**

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

794

795 **Confidentiality**

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

798

799 **PATIENT-CLINICAN STAKEHOLDER ADVISORY COMMITTEE ROLE**

800 This study is guided by a Patient-Clinical Stakeholder Advisory Board that is comprised of
801 patients and patient advocates (including native Spanish-speakers), surrogates, and
802 SFHN/SFGH primary care clinic staff and medical directors. These individuals are paid key
803 personnel on the study and have agreed to meet up to 4 times per year to oversee all aspects of

804 the study. Native Spanish-speaking staff will be present to translate for our Spanish-speaking
805 patient stakeholders during advisory meetings. All study materials will be translated into
806 Spanish. The advisory committee will be involved in providing ongoing advice about the
807 following important study related activities:

- 808 • Recruitment, including study scripts, fliers, methods
- 809 • Eligibility and exclusion
- 810 • Patient safety and research staff safety
- 811 • Clinic workflow and clinical champions
- 812 • Informed consent
- 813 • Research outcomes
- 814 • Presentation of findings
- 815 • Dissemination of results

816

817

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Protocol

Final Version

September 2017

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|--|-----------|
| Funding | 45 |
| ClinicalTrials.gov Information | 45 |
| Introduction and Rationale | 45 |
| Preliminary Studies | 47 |
| Overview of the Trial Design | 49 |
| Study Setting | 53 |
| Participants and Eligibility and Exclusion Criteria | 53 |
| Recruitment Methods | 56 |
| Consent Procedures | 58 |
| Intervention and Comparison Conditions | 59 |
| Randomization Procedures | 61 |
| Blinding | 62 |
| Intervention Fidelity | 62 |
| Data Collection Methods | 63 |
| Follow-up and Retention | 63 |
| Measures | 65 |
| Statistical Analysis Plan | 74 |
| Sample Size and Power Calculations | 75 |
| Ethics and Advisory Committees | 77 |
| Human Subjects Protections | 77 |
| Data Safety Monitoring Plan | 81 |
| Charter of the Data and Safety Monitoring Board | 82 |
| Patient-Clinician Stakeholder Advisory Committee Role | 86 |
| Summary of Protocol Changes Table | 88 |

Summary of Statistical Analysis Plan Changes

92

References

93

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1045 Sudore is also funded in part by a National Institute on Aging K24 (K24AG054415).

1046

1047 **CLINICALTRIALS.GOV INFORMATION**

1048 This trial is registered at ClinicalTrials.gov: NCT01990235 for English-speakers, registered on
1049 November 4th, 2013 and NCT02072941 for Spanish-speakers, registered on February 4th, 2014.

1050

1051 **INTRODUCTION AND RATIONALE**

1052 **Background**

1053 The population is aging,^{1,2} and the prevalence of chronic disease is increasing, especially
1054 among underserved and vulnerable populations (i.e., economically disadvantaged, racial and
1055 ethnic minorities, the uninsured, etc.).³ A critical aspect of chronic and serious disease
1056 management is advance care planning (ACP), a process whereby patients plan for their future
1057 medical care. Traditionally, advance directives have been the main focus of ACP, but
1058 unfortunately, most are written with complex, legal language.⁴ This lack of attention to limited
1059 health literacy and limited English proficiency may explain why advance directives are often not
1060 completed and may explain, in part, why less than 20% of racially and ethnically diverse, older
1061 adults engage in advance care planning (ACP) by the end-of-life.⁵⁻⁸

1062

1063 Furthermore, for ethnic minorities, a population rapidly increasing in the U.S., medical decisions
1064 are often complicated by a lack of trust and perceived racism.⁹⁻¹¹ Ethnic minorities are also more
1065 likely to prefer aggressive treatment, mistrust advance directives, and have non-autonomous
1066 views on decision making (i.e., prefer that family and doctors make medical decisions for

1067 them).^{9,12-16} Hispanics/Latinos account for 15% of the U.S. population, a proportion projected to
1068 grow to 30% by 2050.^{1,2} Spanish-speaking patients face significant communication barriers, and
1069 literacy- and language-appropriate ACP tools that address unique aspects of Latino culture
1070 (e.g., *familismo* or a strong commitment and orientation to the family) are lacking.¹⁰ In addition,
1071 the mean reading level in the U.S. is only at the 8th grade level, and for adults over 65 years of
1072 age it is only at the 5th grade level.^{17,18} Patients with limited literacy often lack self-efficacy to
1073 communicate their wishes or ask questions,¹⁹ and the combination of limited literacy and limited
1074 English-proficiency results in low satisfaction with doctor-patient communication and decision
1075 making.²⁰⁻²² However, studies show that patients can be motivated to take action in response to
1076 culturally- and linguistically-appropriate information they trust and can understand.^{8,23}

1077

1078 To address these gaps in advance care planning and shortcomings of advance directives, we
1079 developed a novel, comprehensive paradigm of ACP focused on preparing patients to identify
1080 their wishes, communicate with surrogate decision makers and clinicians, and make complex,
1081 decisions over the course of chronic and serious illness.²⁴ This approach recognizes patients'
1082 wishes change based on changing clinical contexts and that advance directives are but one tool
1083 to be used to inform in-the-moment decision making.^{25,26} To address the gaps in advance care
1084 planning for racially and ethnically diverse older adults, and based on the new comprehensive
1085 ACP paradigm, we created the interactive, patient-centered PREPARE website
1086 (prepareforyourcare.org) in English and Spanish that is culturally, linguistically, and literacy-
1087 appropriate. PREPARE has been shown in pilot studies among English-speakers to help older
1088 adults engage in the ACP process, but it has yet to be tested in a randomized trial with both
1089 English- and Spanish-speaking older adults.²⁷ Both the new ACP paradigm and the PREPARE
1090 intervention have been described in detail elsewhere.^{27,28} In addition, a description of a related
1091 trial of the efficacy of PREPARE among U.S. Veterans describes the theoretical framework
1092 underlying the PREPARE website.²⁸

1093 **PRELIMINARY STUDIES**

1094 **We have experience conducting RCTs among diverse, older adults at the San Francisco**

1095 **Health Network (SFHN) primary care clinics.**⁸ Dr. Sudore designed and tested an AD written

1096 at a 5th grade reading level among 205 chronically ill, diverse, older adults from Zuckerberg San

1097 Francisco General Hospital (ZSFG) with a 6-month follow-up of 85%. The AD was preferred

1098 over a standard AD, with significant interactions for limited literacy (e.g., higher preference rates

1099 in patients with limited literacy). It also resulted in greater 6-month AD completion rates (15% vs.

1100 7%, $p = .03$), doubling the rates from baseline. This AD has been adopted as the official AD for

1101 ZSFG and is being disseminated in California. It will serve as the active control.

1102 **We designed and tested an informed consent process for diverse, older adults with**

1103 **limited literacy.**²⁹ We found that many patients do not understand simplified consent

1104 information and were unsure how to ask questions. But, informed decisions can be improved by

1105 providing both easy-to-read materials and a teach-back method. We will use this interactive

1106 consent method for this study.

1107 **Multiple steps of the ACP process.**³⁰ We found that most patients go through a series of ACP

1108 behavioral steps. Six months after exposure to the easy-to-read AD, 61% of older adults

1109 contemplated ACP, 56% discussed ACP with family or friends and 22% with clinicians, and 13%

1110 completed an AD. This work shows that measuring a full range of ACP outcomes, in addition to

1111 ADs, and associated behavior change steps (contemplation to action) is important and informs

1112 our study outcomes. Previously described barriers to ACP, such as not wanting to burden

1113 family,³¹ are addressed in PREPARE.

1114 **Evidence supporting the new ACP paradigm and content of PREPARE.**³² We completed 13

1115 focus groups with 69 diverse, English- and Spanish-speaking older patients (mean age 78 +/- 8,

1116 61% non- White) and surrogates (mean age 57 +/- 10, 91% non-White) from safety-net settings

1117 who reported making serious medical decisions. We used semi-structured interviews to ask
1118 about what best prepared them for decision making. Qualitative analysis identified 5 overarching
1119 themes, beyond ADs, that prepared patients and surrogates for decision making: (1) choose
1120 surrogates wisely and verify they know their role, (2) identify goals based on past experiences
1121 and personal values, (3) decide whether to grant leeway in surrogate decision making, (4)
1122 inform other family and friends of one's wishes to prevent conflict, and (5) ask clinicians
1123 questions. These themes have been incorporated as educational domains of PREPARE.

1124 **Validity and reliability of the survey to measure ACP engagement:** Surveys were designed
1125 with input from Co-Is and extensive cognitive interviews to measure discrete ACP actions (i.e.,
1126 main outcomes: ACP discussions, AD completion,) and ACP behavior change (e.g.,
1127 contemplation, self-efficacy, readiness). We recruited 50 older adults, aged ≥ 60 years with ≥ 2
1128 illnesses (32% female, 42% non-White). Internal consistency 7-day test-retest reliability, and
1129 discriminant validity (scores compared to healthy young adults – 50% female, 75% non-White)
1130 was high. Scores did not differ by race/ethnicity or literacy, $p > .05$. We will also use validated
1131 surveys on ACP attitudes and methods to classify patients into behavior change categories.^{33,34}

1132 **Preliminary evidence that PREPARE is beneficial.** In a recent pilot,²⁷ we recruited 43 diverse,
1133 older adults from low-income senior centers. All subjects rated PREPARE easy to use (mean
1134 9/10-point scale). Pre to post ACP behavior change scores from our validated surveys (0-124
1135 points) increased from 72 ± 33 SD to 87 ± 22 , a 15-point increase and an effect size of 0.5.

1136 **Vulnerable populations have unique needs.** The aforementioned pilot demonstrated that,
1137 unlike our work with Veterans, patients in safety-net settings are less trustful of research and
1138 require in-person recruitment. In addition, these patients are often socially isolated and require
1139 tailored ACP for persons without surrogates or families. They also lack ready access to health
1140 information and ancillary support such as social workers or nurses necessitating access to ACP

1141 outside of the clinical environment. These findings add further evidence for the need to tailor
1142 PREPARE for vulnerable populations and to test PREPARE within safety-net settings.

1143 **PREPARE has been shown to increase ACP Documentation and Engagement among**
1144 **Veterans.** A prior trial of PREPARE was conducted among 414 Veterans.³⁵ The mean age of
1145 the cohort was 71.1 (7.8) years, 91% were men, 57% were white, 20% had limited literacy, 29%
1146 reported fair-to-poor health status, and 51% had evidence of prior ACP documentation. The
1147 follow-up time point was 6 months and there was a 90% retention rate. There were no
1148 differences in demographic characteristics between study arms. In this VA population, advance
1149 care planning documentation 6 months after enrollment was higher in the PREPARE arm vs the
1150 AD-alone arm (adjusted 35%vs 25%; odds ratio, 1.61 [95%CI, 1.03-2.51]; P = .04). PREPARE
1151 also resulted in higher self-reported ACP engagement at each follow-up, including higher
1152 process and action scores; P <.001 at each follow-up). These findings add further evidence of
1153 the validity of PREPARE. However, PREPARE has never been tested among diverse, English-
1154 and Spanish-speaking older adults in a safety-net setting.

1155

1156 **OVERVIEW OF THE TRIAL DESIGN**

1157 Study overview:

1158 This study is a randomized, controlled trial that uses blinded outcome ascertainment to
1159 determine the efficacy of the ACP PREPARE website to engage ethnically diverse English- and
1160 Spanish-speaking older primary care patients in the ACP process.³⁶ First, we obtained a Health
1161 Insurance Portability and Accountability Act waiver to identify individuals who meet our
1162 inclusion/exclusion criteria and have upcoming primary care appointments. Administrative data
1163 and chart review are used to determine potentially eligible patients (Figure, Study Flow Chart).

1164

1165 Then primary care clinicians' permission is obtained to allow the study team to inform their
1166 patients about the study. Patients are then recruited, screened for eligibility and scheduled for a
1167 baseline interview before an upcoming primary care appointment. To standardize the timing of
1168 exposure to the intervention and primary care follow-up, study participants are scheduled for
1169 baseline procedures 1-3 weeks prior to an upcoming primary care appointment.²⁸

1170
1171 Next, informed consent is obtained, and those patients who provide consent are randomized to
1172 the PREPARE intervention arm (i.e., the PREPARE website with action plan exercises plus an
1173 easy-to-read advance directive plus PREPARE materials to take home, which include a website
1174 login, and a PREPARE pamphlet, booklet, and DVD) or the control arm (i.e., an easy-to-read
1175 advance directive alone). See Study Flow Figure and a full description of the intervention below.

1176
1177 We then conduct blinded outcome ascertainment by performing chart reviews to determine ACP
1178 documentation at baseline and at the end of the study. We also conduct blinded outcome
1179 ascertainment using patient surveys at 1 week, and 3, 6, and 12 months after the primary care
1180 appointment. We are choosing an active control arm (i.e., an easy-to-read advance directive)
1181 because we believe provision of an advance directive for chronically and seriously ill older
1182 patients should be the standard of care, even if it is not often "usual" care in clinical practice.⁸ In
1183 addition, the easy-to-read advance directive used in this study has been adopted by the San
1184 Francisco Health Network (SFHN) and Zuckerberg San Francisco General Hospital (ZSFG) and
1185 is available in the primary care clinics.

1186

1187 **Research Aims and Study Hypotheses:**

1188 The aims of this study are to (1) To determine the efficacy of PREPARE to engage diverse,
1189 English- and Spanish-speaking older adults with chronic illness in advance care planning (ACP)
1190 compared to controls (AD only) and (2) To determine whether PREPARE efficacy varies by

1191 race/ethnicity, literacy, clinician-patient language concordance, and patient's desired role in
1192 decision making.³⁶

1193

1194 Our primary hypothesis is that the PREPARE program plus an easy-to-read advance directive
1195 will result in greater documentation of ACP wishes, including advance directives and
1196 documentation of ACP discussions in the medical record, than an easy-to-read advance
1197 directive alone in elderly populations with chronic illness.

1198

1199 Our secondary hypotheses are that, compared to an advance directive alone, PREPARE will
1200 result in more engagement in behavior change processes concerning ACP, including increased
1201 self-efficacy and readiness, as well as greater engagement in a full range of ACP actions,
1202 including discussions with surrogate decision makers and other trusted family and friends.

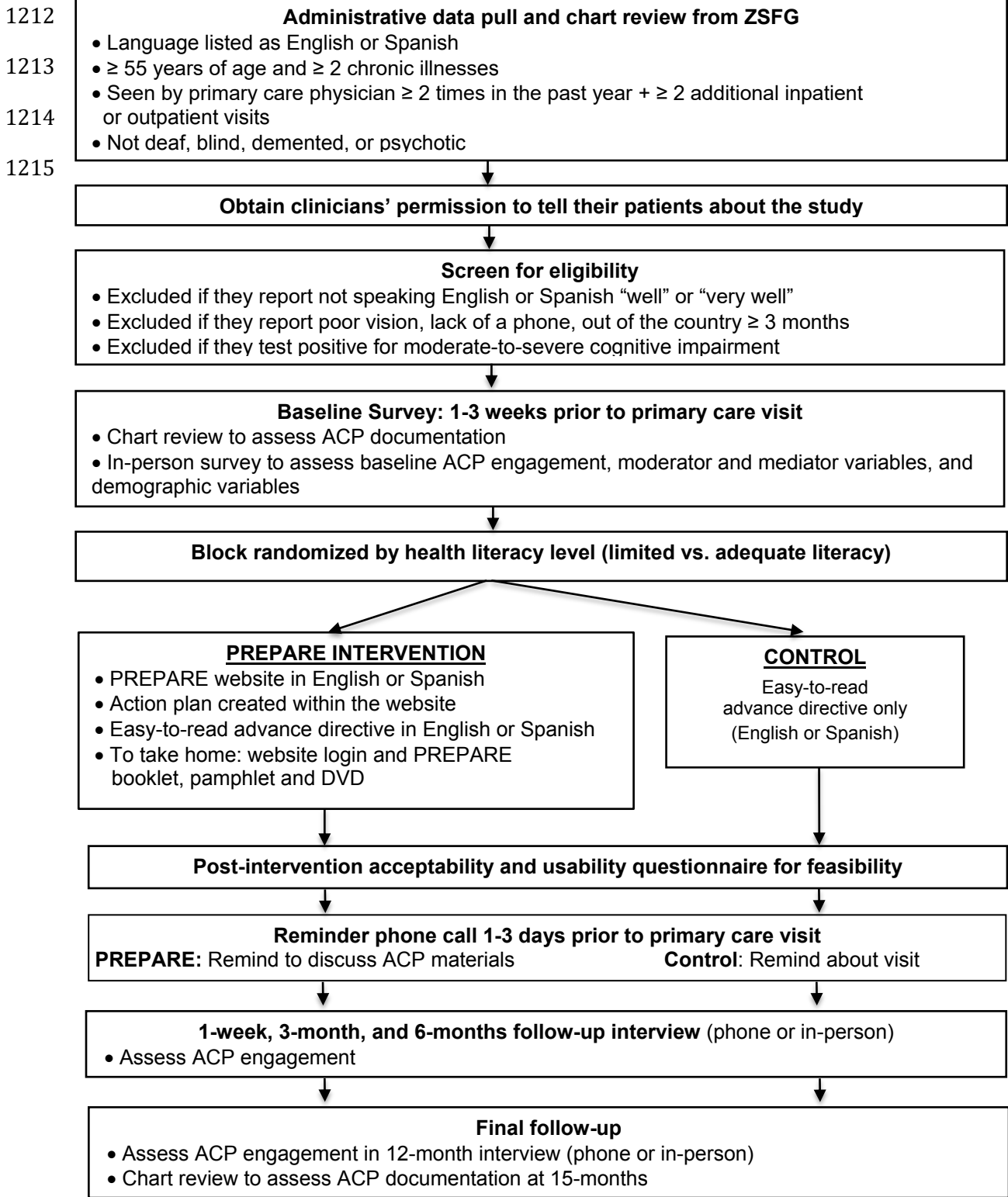
1203 Secondary outcomes will be ascertained using validated surveys.^{33,37,38} We also hypothesize
1204 that PREPARE will result in improved satisfaction with patient-doctor communication and
1205 informed medical decision making and that PREPARE efficacy may vary across moderator
1206 variables such as patient health literacy, clinician-patient language concordance, and patients'
1207 desired role in decision making.

1208

1209

1210

1211 **Figure 1: PREPARE Study Flow Diagram**



1216 **STUDY SETTING**

1217 Recruitment for this randomized trial is occurring in 4 separate primary care clinics associated
1218 with the San Francisco Health Network (SFHN) and the Zuckerberg San Francisco General
1219 Hospital (ZSFG) in San Francisco, California. These 4 clinics are housed in 3 separate physical
1220 locations in San Francisco. ZSFG is an urban, public hospital that, with the SFHN, serves
1221 racially and ethnically diverse, low-income and indigent patients; 30% of patients are Spanish-
1222 speaking.⁸

1223

1224 **PARTICIPANTS AND ELIGIBILITY AND EXCLUSION CRITERIA**

1225 There are no inclusion or exclusion criteria based on gender, race or ethnicity. We assess
1226 eligibility in person or over the phone. Older adults are included in this study if they self-report
1227 speaking English or Spanish “well” or “very well”; are 55 years of age or older; have ≥ 2 chronic
1228 illnesses determined by chart review; have seen a primary care clinician (physician, nurse
1229 practitioner, or physician assistant) at ZSFG/SFHN-affiliated primary care clinics ≥ 2 times in the
1230 past year (an indication of established primary care); and have had ≥ 2 additional outpatient or
1231 inpatient visits in the past year (an indication of severity of illness). Their primary care clinician
1232 must also give us permission to contact them to tell them about the study.

1233

1234 We are recruiting patients ≥ 55 years of age (rather than ≥ 65) because adults in safety net
1235 settings experience accelerated aging, functional decline, and sequelae of chronic disease,
1236 necessitating decision making and ACP at a younger age than patients with higher
1237 socioeconomic status.^{39,40} The goal is to start ACP early to change the trajectory of decision
1238 making and care over the course of illness. Our inclusion criteria of ≥ 2 primary care visits and \geq
1239 2 additional visits in the past year ensures patients have established primary care and access
1240 care frequently. This will enhance recruitment and follow-up.

1241 Patients will be excluded if their clinician is a principal investigator, co-investigator or clinician-
1242 member of the Patient-Clinician Advisory Board or they had been enrolled in a previous pilot
1243 study of the PREPARE website or been exposed to the PREPARE study materials. They will
1244 also be excluded if they have medical record documentation of being deaf, blind, having
1245 dementia, or being psychotic or are deemed by their clinician to be too mentally or physically ill
1246 to participate. Participants will also be excluded if they have evidence of active drug or alcohol
1247 abuse within the past 3 months determined by clinician assessment, self-report, chart review or
1248 research staff assessment. Through in-person or phone screening by study staff, patients are
1249 also excluded if they self-report vision too poor to read a newspaper, lack of a phone (needed
1250 for follow-up interviews and scheduling), or plans to be out of the country for ≥ 3 months; if they
1251 screen positive for moderate-to-severe cognitive impairment using the validated Short Portable
1252 Mental Status Questionnaire followed by the Mini-Cog,⁴¹⁻⁴³ or self-report or are determined by
1253 study staff to be blind, deaf, intoxicated or actively psychotic. Because ACP is an iterative
1254 process and people may change their preferences over time,^{24,44} subjects with prior ACP
1255 experiences (e.g., an advance directive) are not excluded.

1256

1257 To minimize the risk of unblinding by fellow research participants, any spouse/partner of a
1258 currently enrolled patient who is also a patient at SFHN/ZSFG, meets the eligibility criteria, and
1259 therefore, is also a potential patient participant, will be excluded from being a patient participant.

1260 This will avoid a situation where 2 closely related people living in the same home could be
1261 randomized to different study arms and result in unblinding. In addition, an individual who is
1262 named as an enrolled patient's potential surrogate decision maker (regardless of cohabitation or
1263 spousal status), who is also a patient at SFHN/ZSFG, meets the eligibility criteria, and therefore,
1264 is also a potential patient participant, will only be eligible to be a surrogate participant in our
1265 study and will be excluded from being a patient participant. In addition, we are excluding any

1266 patient who has been enrolled in a previous PREPARE-related study or is known to have
 1267 previously been exposed to PREPARE (e.g. note in medical record).
 1268
 1269 To save research staff considerable time and effort, potential participants who miss an interview
 1270 (i.e. no show) more than 2 times (for the same baseline interview appointment) without prior
 1271 notification and rescheduling with study staff will be considered ineligible, unless there are
 1272 extenuating circumstances.

Inclusion and Exclusion Criteria

| | |
|--------------------|---|
| Inclusion Criteria | 55 years of age or older |
| | Obtains care in the primary care clinics at in the San Francisco Health Network (SFHN). |
| | Has been seen at least twice in the last year by a primary care provider (a marker of established primary care) and had at least two additional visits to SFHN in the past year (a marker of illness) |
| Exclusion Criteria | Clinician is the PI, Co-I or member of the Patient-Clinician Advisory Board |
| | In a prior PREPARE-related study, such as a focus group or pilot study |
| | Dementia by ICD-9/ICD-10 codes, clinician assessment, chart review or self-report |
| | Blindness or poor vision by ICD-9/ICD-10 codes, clinician assessment, chart review, self-report of blindness or the inability to read print on a newspaper ⁴⁵ |
| | Deafness by ICD-9/ICD-10 codes, clinician assessment, self-report, chart review or research staff assessment |
| | Cognitive impairment as assessed by research staff of any deficits on the validated Short Portable Mental Status Questionnaire (SPMSQ) ⁴⁶ and the mini-Cog ^{41,47} |
| | Delirium or psychosis as assessed by a clinician or research staff |
| | Does not report speaking English or Spanish “well” or “very well” |
| | No phone for additional study contacts and follow-up interviews |
| | Active drug or alcohol abuse within the past 3 months determined by clinician assessment, self-report, chart review or research staff assessment. |
| | Patients who report they will be out of town during their scheduled follow-up interview dates outside of a window of 3 months. |
| | Report being a spouse or surrogate of another enrolled participant |
| | Patients who cannot answer consent teach-back questions after three attempts |
| | 2 or more no-show baseline interview appointments without rescheduling |

1273
 1274
 1275
 1276

1277 **RECRUITMENT METHODS**

1278 **Data Extraction:**

1279 To facilitate recruitment, we obtained a Health Insurance Portability and Accountability Act
1280 waiver to access patients' names, age, primary language, phone numbers, addresses, medical
1281 record numbers, as well as dates of outpatient primary care clinic appointments in the past year
1282 and up to 3 months in the future, other appointments and hospitalizations and emergency room
1283 visits in the past year, and the name of patients' outpatient primary care providers. From these
1284 data, we obtain a list of potentially eligible patient participants and send a secure email to their
1285 primary care providers asking for permission for our study team to tell their patients about the
1286 study through a recruitment opt-out study letter, followed by phone or in-person recruitment.
1287 Weekly administrative data pulls from the electronic health record identify patients with
1288 upcoming primary care appointments and are used to target patient recruitment efforts.

1289

1290 **Clinician Permission to Contact Patients:**

1291 Upon completion of the administrative data pulls, providers from all recruitment sites are sent a
1292 letter/e-mail informing them about the research study and asking them to review a list of their
1293 patients, to refer patient(s) on their patient list who would be appropriate for the study, and to
1294 obtain permission to contact their patients to tell them more about the study. Clinicians are also
1295 informed that if the study team receives their approval, their eligible participants will receive a
1296 letter describing the research study and offering them the opportunity to decline to be contacted
1297 by research personnel and/or will be contacted in clinic. Additionally, clinicians are informed that
1298 if they do not respond one week after the 3rd attempt to contact them by the study team
1299 (including by email, phone, and/or in-person), we will assume assent to contact their patients
1300 and a letter describing the study will be sent to patients on behalf of the study team. We obtain
1301 permission from all of the Service Chiefs before their clinicians are contacted.

1302

1303 **Recruitment Methods and Materials:**

1304 Study-related fliers written at a 5th-grade reading level in English and Spanish are posted in
1305 approved areas in SFHN/ZSFG-affiliated primary care clinics. Because many patients may be
1306 too ill to come to frequent clinic appointments and to be interviewed or hear about the study in
1307 busy clinic waiting rooms, we include several recruitment strategies. Therefore, in addition,
1308 recruitment letters and postcards written at a 5th grade reading level in English and Spanish are
1309 mailed and describe the research study as well as provide a telephone number to either opt-out
1310 or to hear more about the study. Although patients can opt out at any time, those who do not
1311 call study staff to decline participation within 1 week of the mailings are deemed eligible to be
1312 contacted to describe the study, assess willingness to participate and assess study eligibility. To
1313 standardize the timing between intervention exposure and primary care follow-up, we schedule
1314 patients for the baseline interview and exposure to PREPARE or the control intervention 1 to 3
1315 weeks prior to their upcoming primary care appointment. Weekly administrative data pulls from
1316 the electronic health record identify patients with upcoming primary care appointments and are
1317 used to target patient recruitment efforts. Potential participants are then contacted by phone or
1318 in the clinic.

1319

1320 Patients who consent and enroll are paid \$50 for the baseline interview and given \$10 in MUNI
1321 (municipal transportation vouchers) to help participants come back to follow-up interviews in
1322 person if they desire. Participants are also reimbursed \$25 for each of the 1-week, 3, 6, and 12-
1323 month interviews.

1324

1325 Diverse, vulnerable populations are often difficult to recruit for research studies. We employ
1326 several strategies to enhance our recruitment. First, we attempt to hire individuals who have
1327 experience with diverse populations and individuals who are bilingual (native Spanish-speaking)
1328 and bicultural. Furthermore, we conduct extensive sensitivity training with all research staff and

1329 require staff to use approved study scripts when speaking to patients. These study scripts and
1330 all study materials used for recruitment are vetted, updated and approved by both our patient
1331 advisory and clinical advisory boards. All materials and study scripts are written at a 5th grade
1332 reading level and are provided to patients in their preferred language (i.e., English or Spanish).

1333

1334 **CONSENT PROCEDURES**

1335 We use a modified consent process that several co-authors designed for vulnerable
1336 populations.^{28,29} Consent forms written at the 5th grade reading level are provided and read to
1337 participants in English or Spanish. This review is then followed by standardized “teach-to-goal”
1338 questions to ensure understanding. If potential participants cannot correctly complete the teach-
1339 back process after 3 attempts, the patient is deemed ineligible.

1340

1341 The consent form is approved by the UCSF and ZSFG Institutional Review Boards, the
1342 patient/clinical advisory board, and the Data and Safety Monitoring Board (DSMB). The consent
1343 form states the following for the purpose of the study: “Why is this study being done?
1344 Sometimes patients and their families have to make hard medical decisions. We want to design
1345 and test an easy-to-understand handout to help. This handout will help people think about their
1346 values, or what is most important to them in their life. It will also help prepare patients to make
1347 medical decisions.” We use the word “handout” because, in pilot testing, both groups are given
1348 handout materials and written advance directives. For randomization we explain, “We will ask
1349 you to look over a handout and answer some questions about your experience with making
1350 medical decisions. There will be two groups that will be given different handouts. You will have a
1351 50/50 chance of being in either group.”

1352

1353 Due to exclusions based on several missed baseline appointments and for staff safety and the
1354 need to exclude or withdraw participants who were intoxicated, psychotic, or threatening, the

1355 consent also explains, “We also may ask you to stop taking part in this study if we feel it is in
1356 your best interest or if you do not follow the study rules.”

1357

1358 It was determined with our Patient-Clinician Advisory Board that clinicians of patients should be
1359 contacted in the event that the patient reports severe depression or anxiety. Our DSMB agreed
1360 and our consent forms explain:

1361 “We would need to contact your regular doctor or a medical provider for the following reasons:

- 1362 • You report or we observe that you are having a medical emergency,
- 1363 • Such as a serious medical illness
- 1364 • Or, a serious mental illness, such as major depression
- 1365 • You report that you may harm yourself, you may harm someone else, or someone is
1366 harming you.”

1367

1368 **INTERVENTION AND COMPARISON CONDITIONS**

1369 PREPARE arm

1370 As previously described, PREPARE is an easy-to-use, patient-centered, interactive website that
1371 is available in English or Spanish, is written at a 5th grade reading level, includes voice-overs of
1372 all text for the reading-impaired and closed-captioning of all videos for the hearing impaired
1373 (www.prepareforyourcare.org).^{27,28} The conceptual framework for PREPARE has been
1374 previously published and is based primarily on Social Cognitive Theory,^{48,49} with elements from
1375 the Health Belief Model,⁵⁰ the Theory of Planned Behavior,⁵¹ and Behavior Change Theory.^{49,52}
1376 In these theories and in behavioral studies, modeling of behaviors helps people change their
1377 behavior. Successful behavioral change interventions model skills, enhance self-efficacy, and
1378 address perceived barriers,^{53,54} especially literacy-appropriate interventions.⁸ Modeling
1379 behaviors (as in PREPARE) can also improve patients’ ability to communicate with clinicians
1380 and improve outcomes,^{55,56} such as increased question asking behavior and a sense of control
1381 during a clinical visit,^{56,57} an increased desire to participate in decision making, and even

1382 improved affect and functional status.^{53,58-60} PREPARE incorporates these successful teaching
1383 methods through the modeling of behaviors in videos. Video and interactive websites are more
1384 powerful mediums to teach information and change behavior than written materials, especially
1385 for those with language/literacy barriers.⁶¹⁻⁶⁷ PREPARE includes a training and goal setting
1386 component which has been shown to be effective in changing outpatient behaviors, such as
1387 exercise.⁶⁸

1388

1389 In the design of the PREPARE website, we included essential, theory-based health education
1390 strategies, such as the use of video modeling of ACP behaviors and tailored and interactive
1391 content based on patients' values and decision preferences. To ensure PREPARE is easy to
1392 read and understand, we use clear health communication principles (e.g., targeting text to the
1393 5th grade reading level) informed by extensive formative research and cognitive interviewing
1394 with the target population (i.e., racially and ethnically diverse older adults with limited health
1395 literacy and English proficiency) to ensure PREPARE content is acceptable to individuals from
1396 diverse cultural backgrounds.²⁷ The PREPARE website leads people through a 5-step ACP
1397 process that ranges from choosing a surrogate decision maker to asking their clinicians the right
1398 questions. While going through the website, PREPARE also helps individuals answer personal
1399 values questions about their medical care, and helps them create an action plan to engage in
1400 some form of ACP. Patient-generated action plans have been shown to help patients engage in
1401 other preventative and disease management activities in the outpatient setting.⁶⁹

1402

1403 After the baseline interview, participants in the PREPARE arm review all 5 steps of the
1404 PREPARE website in English or Spanish in our research offices. Participants are asked to
1405 review PREPARE on their own and in its entirety. Research assistants are available to answer
1406 questions only if needed, but do not go through the website with the participants. At the end of
1407 the program, a summary of the patient's medical wishes and action plan are automatically

1408 generated from the PREPARE website in written format. This information along with the
1409 participant's PREPARE website login information is included in a take-home folder that also
1410 contains PREPARE information in pamphlet, booklet, and DVD format. We include PREPARE
1411 content in non-website formats because some patients may not have access to the internet at
1412 home. PREPARE arm participants are also given an easy-to-read advance directive in English
1413 or Spanish to review and consider completing.^{8,70} Participants are asked to review the advance
1414 directive form for at least 5 minutes and up to 15 minutes in research offices, and then to take
1415 the form home to discuss with their potential surrogates and/or their clinicians. The time frame
1416 of 5-15 minutes was chosen because our goal is only to introduce the advance directive and
1417 allow participants to ask questions. The goal is not to have patients complete the form on the
1418 day of the study, before potential discussions with clinicians or surrogates, unless the participant
1419 would like to do so.

1420

1421 AD-only arm

1422 Participants in the control arm are only given the easy-to-read advance directive, are asked to
1423 review it for at least 5 minutes and up to 15 minutes, and to take the form home to discuss with
1424 their potential surrogates and clinicians.

1425

1426 Both arms: Reminder of primary care appointments

1427 One to 3 days before the patient's next scheduled primary care appointment, research staff call
1428 the PREPARE arm participants to remind them to bring in their study materials (i.e., action plan
1429 and advance directive) and to talk to their clinician about ACP. For the control arm, research
1430 staff members only remind patients about their upcoming appointment and do not provide
1431 additional encouragement about ACP.

1432

1433 **RANDOMIZATION PROCEDURES**

1434 A statistician not involved in recruitment or data collection uses a computer-based random
1435 number generator to create a randomization scheme using block randomization by health
1436 literacy (adequate health literacy versus limited health literacy, as determined by a validated
1437 question concerning confidence with medical forms).⁷¹ Random block sizes of 4, 6, and 8 are
1438 used to ensure an equal number of patients with limited health literacy in each group.
1439 Randomization information is associated with a unique patient identification number and is kept
1440 separate from other patient data. Due to the need to secure interview rooms for the duration of
1441 the baseline questionnaire and intervention (i.e., approximately 2 hours for the AD-only arm and
1442 3 hours for the PREPARE arm), randomization occurred prior to scheduling a baseline
1443 interview.

1444

1445

1446 **BLINDING**

1447 Clinicians are blinded to patient group assignment. Although we obtain clinicians' permission to
1448 recruit their patients, the interventions are not described, and no clinician education is provided.
1449 Participants could not be blinded to the intervention; however, they are told during consent there
1450 is a "50/50 chance" of getting one of two different ACP guides, and the non-assigned
1451 intervention is not described. Because each group obtains ACP materials, such as the easy-to-
1452 read advance directive, blinding is enhanced. The research assistant who administers the
1453 intervention cannot be blinded to the study arm, but all follow-up outcome assessments are
1454 conducted by different and blinded staff. At the start of all follow-up interviews, participants are
1455 reminded not to discuss the study materials they reviewed with assistants recording if they
1456 became unblinded. If unblinding occurs, a different blinded assistant conducts all subsequent
1457 interviews.

1458

1459 **INTERVENTION FIDELITY**

1460 All staff members are rigorously trained and are required to read and adhere to a standardized
1461 study protocol manual, standardized study scripts, and standardized checklists for each contact
1462 and interview with participants. Several training videos have also been developed for staff.
1463 Research staff are not allowed to conduct study tasks independently until they have reviewed all
1464 written and video training materials and can demonstrate complete mastery of all scripts and
1465 checklist items. In addition, a 10% random sample of all interviews is observed by senior
1466 research staff to ensure study fidelity.

1467

1468 **DATA COLLECTION METHODS**

1469 Live capture of research data are collected through Research Electronic Data Capture
1470 (REDCap) software. REDCap is managed by the UCSF Academic Research Systems Team
1471 and is stored behind strong-string password protected firewalls on UCSF servers, not on
1472 individual laptops or desktops. All patients are given a unique, non-identifying patient
1473 identification number that is removed from any personally identifying information (PII) or
1474 personal health information (PHI). All PII and PHI are stored in a Microsoft ACCESS database
1475 behind strong-string password protected firewalls on UCSF and ZSFG servers. To reduce
1476 missing data, REDCap has been programmed to not allow study staff to progress if data fields
1477 are left blank. We retain the use of paper surveys in the event the RedCap system is down. All
1478 paper files continue to be stored in secure, locked research offices in secure, locked file
1479 cabinets.

1480

1481 **FOLLOW-UP AND RETENTION:**

1482 We conduct follow-up interviews one week and 3, 6, and 12-months after the primary care visit
1483 in the clinic, by phone, or in the home if needed due to patient functional limitations. We utilize
1484 several measures to help ensure follow-up. Each follow-up interview takes between 30 to 45
1485 minutes and participants are reimbursed \$25.

1486

1487 Method of contact for follow-up surveys:

1488 Upon enrollment, we ask participants to provide alternative phone numbers (e.g., cell or work
1489 numbers) and one to three additional phone numbers of close contacts who may know how to
1490 contact the patient in the event our study staff is unable to reach them. Many patients in safety
1491 net settings are marginally housed, have intermittent phone access, and may change locations
1492 and phone numbers during the study period. We also ask participants if they prefer a text
1493 message or an email to schedule follow-up visits and will use their preferred mode of
1494 communication. If these other modes of communication fail, we send out reminder letters. If
1495 needed, we also attempt to contact patients during scheduled clinic visits or make home visits.

1496

1497 Participant Appointment Reminder Sheet

1498 We created an appointment reminder sheet as a reference for patient participants. This sheet
1499 shows the dates and times for upcoming appointments that the patient participant will have with
1500 us.

1501

1502 Reminders for the primary care visit:

1503 Participants receive a brief reminder call one to 3 days before their next primary care visit.
1504 Participants in the AD-only arm are reminded to come to their scheduled appointment while
1505 participants in the PREPARE arm are reminded of their appointment and to bring the PREPARE
1506 materials to the visit.

1507

1508 Reminders for study interviews:

1509 For all follow-up interviews, participants in both arms receive reminders of their upcoming study
1510 interview by phone or in person. To help participants follow along during the interview, the
1511 participant can receive a Participant Version of the survey via mail or email, as

1512 preferred. No survey responses or information are collected by mail or email. We use 14-point
1513 font and color-coded, standardized, large font response options to help with understanding.

1514

1515 Participants who miss their primary care appointment:

1516 Participants who cancel or miss their primary care appointments and do not reschedule within

1517 30 days of the cancelled appointment receive a courtesy phone call to remind participants to

1518 reschedule the primary care appointments in order to move on with the study schedule. For

1519 participants who cancel or miss their primary care appointments after they have been enrolled

1520 and randomized:

1521 • If they have rescheduled and attend their primary care appointment within 6 months from
1522 when they were randomized, they receive a brief reminder call one to 3 days before their
1523 primary care appointment date. We conduct follow up assessments at 1 week, and at 3, 6,
1524 and 12 months from this primary care appointment date,

1525 • If they do not reschedule or attend their primary care appointment within 6 months from
1526 when they were randomized, they receive a brief reminder call one to 3 days before their
1527 new primary care appointment date. We conduct follow up assessments at 6 and 12 months
1528 from the originally scheduled primary care appointment date.

1529

1530 **Ascertaining reasons for loss of follow-up or withdrawal:** For participants who want to
1531 withdraw, we ask them why in open-ended questions. If they cannot provide an answer, we
1532 prompt them from a list of reasons we obtained from prior advance care planning trials, such as
1533 the study is too long, they are too busy, the study topic is too upsetting, they are too ill, etc.³⁵

1534

1535 **MEASURES**

1536 **Overview**

1537 Because ACP ideally is a process that occurs over time, we felt it important to measure a full
1538 range of ACP measures including ACP documentation (primary outcome) over time, and
1539 several behavior change constructs and several additional ACP actions over a 12-month period
1540 (secondary outcomes). All study measures used in this analysis, including validity and reliability
1541 information in English and Spanish and the schedule of administration (i.e., baseline, 1-week or
1542 3, 6, or 12-months), are included in the Outcome Measures table below. All outcomes, including
1543 secondary outcomes not used in our main analysis, are included in our published protocol.³⁶
1544 The main outcome measures are described in detail below.

1545

1546 **Primary Outcome**

1547 The primary outcome is new documentation of ACP wishes in the ZSFG/SFHN medical record
1548 (Table of Outcome Measures below). ACP documentation for the purposes of this study
1549 includes the easy-to-read advance directive or other valid advance directives or living wills, a
1550 durable power of attorney for health care document (DPOAHC), a Physicians Orders of Life
1551 Sustaining Treatment form, or other documentation of discussions concerning patients' wishes
1552 for medical care (i.e., documentation of oral directives by a physician or notes describing
1553 patients' goals for medical care by clinicians).

1554

1555 We assess baseline and 15-month new ACP documentation rates and the date of
1556 documentation to determine the length of time from study enrollment to subsequent
1557 documentation. Patients in our study are enrolled, randomized, and exposed to the intervention
1558 1 to 3 weeks prior to a primary care appointment. ACP documentation is timed to the date of
1559 intervention exposure as patients may have engaged in ACP prior to seeing their primary care
1560 provider. The patient-reported outcomes in the follow-up surveys (1 week, 3, 6, and 12-months),
1561 however, are timed to the primary care visit because those questions concern engagement in
1562 discussions with clinicians (see secondary outcomes below). This same timeframe for ACP

1563 documentation was determined from a prior PREPARE trial conducted within the VA to take into
1564 account and to standardize the expected time from intervention exposure to the primary care
1565 visit and the anticipated time to schedule and complete the final patient interview.³⁵

1566

1567 Because legal forms and documented discussions can be used to direct medical care, we
1568 created a composite variable of any ACP documentation (forms and/or discussions); we also
1569 plan to report the percentage of forms and discussions separately. All medical review data is
1570 double coded by 2 independent, blinded research assistants. Discrepancies are adjudicated by
1571 the principal investigator (R.L.S.).

1572

1573 **Secondary Outcomes**

1574 **Main Patient-Reported Outcome**

1575 The main patient-reported secondary outcome, the validated Advance Care Planning
1576 Engagement Survey,^{27,28,37} was chosen to measure the full process of ACP. The Advance Care
1577 Planning Engagement Survey measures both ACP Behavior Change Processes, such as
1578 knowledge, contemplation, self-efficacy, and readiness on a validated 57-item scale. The ACP
1579 Behavior Change Process scale is measured on a 5-point Likert scale and average 5-point
1580 scores will be calculated. We will also measure ACP actions on the validated 25-item Action
1581 scale, which assesses ACP activities (yes or no) such as identifying a surrogate decision maker,
1582 identifying values and goals for medical care, choosing the level of leeway in surrogate decision
1583 making, discussing one's wishes with clinicians and surrogates, and documenting one's wishes
1584 in an advance directive. Validity and reliability of the ACP Engagement Survey, as well as the
1585 questionnaire's ability to detect change in response to an ACP intervention, have been
1586 previously described.^{27,28,37}

1587

1588 **Feasibility and Satisfaction**

1589 To evaluate whether and how PREPARE will be used in clinical practice and in the community,
1590 we also assess acceptability of the PREPARE website compared to an advance directive alone
1591 using validated scales of ease-of-use (10-point scale, “On a scale of 1 to 10, with 1 being very
1592 hard and 10 being very easy, how easy was it to use this guide?”) and satisfaction (comfort:
1593 “How comfortable were you viewing this guide?”, helpfulness: “How helpful was this guide?”,
1594 and recommendations: “How likely are you to recommend this guide to others?” assessed on a
1595 5-point Likert scale (not-at-all to extremely) from our prior work.⁸ For the PREPARE arm only,
1596 and at the end of the 12-month interview and after unblinding, we also ask how likely patients
1597 are to recommend the PREPARE intervention to others.⁷²

1598

1599 **Clinical and Patient-Advisory Board Requested Outcome**

1600 Our Patient-Advisory Stakeholders requested we quantify the number and percentage of
1601 patients who increased their ACP activities overtime. Our stakeholders perceive any increase in
1602 an ACP activity over time as clinically meaningful. Thus, in addition to mean change in ACP
1603 Engagement scores, they wanted to know the percent of patients who improved (i.e., had an
1604 estimated slope > 0) over time for both Behavior Change scores, Actions scores, and both
1605 combined. We therefore created this exploratory variable post-hoc.

1606

1607 **Adverse Event Outcomes**

1608 In addition, to ensure that the PREPARE program does not cause undue harm, we also assess
1609 both depression^{73,74} and anxiety.^{75,76} We measure depression using the validated Patient Health
1610 Questionnaire (PHQ)-8 (scores 0-24) and anxiety Generalized Anxiety Disorder (GAD)-7
1611 (scores 0-21) at baseline and each follow-up.^{74,75} Scores of 5, 10, 15, and 20 represent mild,
1612 moderate, moderately severe and severe depression or anxiety.

1613

1614 **Potential Mediating or Moderating Variables & Participant Characteristics**

1615 Based on the previously published conceptual framework of PREPARE,²⁷ we also hypothesize
1616 that PREPARE efficacy may vary across several moderator or mediator variables (e.g., health
1617 literacy using the validated Short form Test of Functional Health Literacy in Adults s-TOFHLA,
1618 scores 0-36⁷⁷ and dichotomized to limited = 0-22 & adequate = 23-36; clinician-patient language
1619 concordance (concordant versus discordant); and patient’s desired role in decision making with
1620 the medical provider using the validated Decision Control Preferences Scale(wants to make
1621 their own decision versus wants doctors/family to make decisions for them).⁷⁸ We also
1622 hypothesize that PREPARE efficacy may be affected by several confounding variables (e.g.,
1623 self-rated health, “How would you rate your health?” [5-point Likert]^{79,80} dichotomized as fair-to-
1624 poor and good-to-excellent and past experiences with ACP including prior documentation of
1625 legal forms and documented discussions. We will also assess a full range of patient-reported
1626 characteristics, as these factors may impact patient-clinician communication,^{20,81} such as age
1627 (“What is your date of birth?”), self-reported gender (“What gender do you consider yourself to
1628 be? male, female transgender, other”), finances (able to make ends meet versus not make ends
1629 meet), having a potential surrogate decision maker or not, education (“What is the highest
1630 educational level you have completed?” less than or equal to high school or greater than high
1631 school), internet access in the home (yes or no), and religiosity and spirituality (i.e., “How
1632 religious/spiritual do you consider yourself to be?” on 5-point Likert scale from not-at-all to
1633 extremely).

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1637

Outcome Measures Table

| Construct | Measure | # items | English Reliability/Validity | Spanish Reliability/Validity | Baseline | 1 week | 3 months | 6 months | 12 months | 15 months |
|-------------------------------|---|--------------|--|--|----------|--------|----------|----------|-----------|-----------|
| | Primary Outcome | | | | | | | | | |
| New ACP Documentation | Chart review: ACP documentation (i.e., legal forms and documented goals of care discussions) ^{35,36} | | | | X | | | | | X |
| | Secondary Outcomes | | | | | | | | | |
| The Full ACP Process | ACP Engagement Survey: ²⁷ Behavior Change Process Measures (knowledge, contemplation, self-efficacy, readiness) Action Measures: values identification and discussions | 57 25 | Behavior Change Measures: Cronbach's $\alpha = 0.94$ (0.91-0.96), ICC= 0.70 (0.54-0.82) ²⁷ Action Measures: ICC*= 0.87 (0.79-0.92) ²⁷ | - | X | X | X | X | X | |
| Implementation: Acceptability | Acceptability and Usability (a) Ease of Use and Understanding (b) Usefulness in decisions & discussions (c) Attitudes about norms or expectations | 8 6 6 | 1 factor explained 81-85% of variance/scale. Kuder-Richardson >0.75 ⁸ | 1 factor explained 81-85% of variance/scale. Kuder-Richardson >0.75 ⁸ | X | | | | | |
| | Adverse Event Outcomes | | | | | | | | | |
| Depression | Patient Health Questionnaire-8 | 8 | Scores ≥ 10 100% sensitive and 95% specific for major depressive disorder. ^{73,74} | Scores ≥ 10 77% sensitive and 100% specific for major | X | X | X | X | X | |

| Construct | Measure | # items | English Reliability/Validity | Spanish Reliability/Validity | Baseline | 1 week | 3 months | 6 months | 12 months | 15 months |
|------------------------------------|--|---------|---|---|----------|--------|----------|----------|-----------|-----------|
| | | | | depressive disorder ⁸² | | | | | | |
| Anxiety | GAD-7 ⁷⁵ | 7 | Cronbach's $\alpha = 0.92$ ⁷⁵ ICC* = 0.83 | Cronbach's $\alpha = 0.88$ ⁷⁶ ICC* = 0.64 | X | X | X | X | X | |
| | Exploratory Outcome | | | | | | | | | |
| Percent increase in ACP activities | N (%) participants who increased their Behavior Change or Action scores from baseline (i.e., estimated slope > 0) | | - | - | X | X | X | X | X | |
| | Demographic Information | | | | | | | | | |
| Demographic Information | Age, gender, race/ethnicity ⁸³ , marital status, and education | | | | X | | | | | |
| Finances | "In general, how do your finances usually work out at the end of the month?" | 1 | Associated with functional impairment and co-morbidity ⁸⁴ | - | X | | | | | |
| Socioeconomic Social Standing | Social standing ladder (i.e. place an "x" where you think you stand relative to other people in society) | 1 | Associated with functional decline ⁸⁵ | - | X | | | | | |
| | Other Measures | | | | | | | | | |
| Health Literacy | Short form Test of Functional Health Literacy in Adults s-TOFHLA, scores 0-36) ⁷⁷ Continuous & dichotomized to limited = 0-22 & adequate | 36 | Cronbach's $\alpha = .97$ Correlation coefficient w/ other literacy tests > 0.80 ⁷⁷ | Cronbach's $\alpha > .95$ ⁸⁶ | X | | | | | |

| Construct | Measure | # items | English Reliability/Validity | Spanish Reliability/Validity | Baseline | 1 week | 3 months | 6 months | 12 months | 15 months |
|--|---|---------|---|--|----------|--------|----------|----------|-----------|-----------|
| | = 23-36 | | | | | | | | | |
| Patient-clinician language concordance | To clinicians: "How well do you speak Spanish?" ⁸⁷ Fluent, very well (concordant) vs. well, fair, or poor" | 1 | AUROC [†] 94% (CI: 90-98%) ⁸⁷ | AUROC [†] 94% (CI: 90-98%) ⁸⁷ | X | | | | | |
| Desired role in decision making | Control Preference Scale (CPS) with clinician ⁷⁸ | 2 | Correlation between preferred and actual role in decision making. ^{12,88,89} | Correlation between preferred and actual role in decision making ⁹⁰ | X | | | | X | |
| Internet Access | Do you have access to the internet in your home? | 1 | - | - | X | | | | | |
| U.S. Acculturation | Based on Acculturation scale (USAS) "How many years have you lived in the U.S.?" | 1 | Cronbach's α = .98 Associated w/ desire to know prognosis ⁹¹ | - | X | | | | | |
| Functional Status | Activities of Daily Living (ADL) (0-16 point scale)& Instrumental (IADL) measure (0-12 item scale) ^{92,93} | 13 | Morbidity/mortality correlation. ^{126,127} | Cronbach's alpha =0.94 ⁹⁴ | X | | | | | |
| Self-rated health status | How would you rate your health? (5pt Likert) ^{79,80} | 1 | Cronbach α = .80 ⁸⁰ | - | X | | | | | |
| Prior ACP experience | Prior ACP experiences (e.g., "Ever had to make life threatening medical decisions?") ⁸ | 5 | | - | X | | | | | |
| Social support | Modified Medical Outcomes Study Social Support (scores 11-55) ⁹⁵ | 11 | Cronbach's α = 0.88-.93 ⁹⁵ | Cronbach's α = 0.94 ⁹⁶ | X | | | | | |
| | Presence of a possible | 11 | | | | | | | | |

| Construct | Measure | # items | English Reliability/Validity | Spanish Reliability/Validity | Baseline | 1 week | 3 months | 6 months | 12 months | 15 months |
|-----------------------|---|---------|--|------------------------------|----------|--------|----------|----------|-----------|-----------|
| | Surrogate Decision maker | | | | | | | | | |
| Religion/Spirituality | Self-reported extent of how spiritual/religious (5-pt Likert) and role play in decision making. ⁹⁷ | 4 | Spirituality associated with quality of life. Religiosity associated with wanting all measures to extend life. ⁹⁷ | - | X | | | | | |
| | | | | | | | | | | |

1639 Only the variables included in the current analysis are listed in the table. All measures including other secondary and exploratory outcomes not
1640 included in this analysis are listed in the published protocol.³⁶

1641 If a validated Spanish-version of a survey was not available, we translated the English version into Spanish.

1642 *ICC = Intraclass correlation

1643 † Area under the receiver operating curve (AUROC)

1644 ‡ While mediator variables, measured at baseline, may explain how or why a particular effect or relationship occurs, these variables may also be
1645 affected by the intervention and are therefore also considered secondary outcome variables measured over time (i.e., knowledge, self-efficacy,
1646 and readiness, as well as barriers and attitudes).

1647

1648 **STATISTICAL ANALYSIS PLAN**

1649 Our primary analyses will compare change in ACP documentation between study arms from
1650 baseline to 15 months. Secondary outcomes will include ACP Engagement with respect to 5
1651 ACP Actions (yes/no and a 0-25-point scale) and behavior change scores (average 5-point
1652 Likert scores) from baseline to 1 week, and 3, 6, and 12 months. Variables will be assessed for
1653 distributional and outlier values using standard summary statistics. Baseline comparability will
1654 be assessed between groups using unpaired t-tests, Chi-square tests or Fisher's exact tests.
1655 Using t-tests or Chi-squared tests, we will also compare patient's age and self-reported gender
1656 between those who refused versus those who enrolled and differences between arms of those
1657 who withdrew versus those who did not. We will use intention-to-treat analysis using SAS
1658 version 9.4 (SAS Institute Inc.) and STATA 15.0 (College Station, TX). All p-values will be 2-
1659 tailed and set at .05 for the primary outcome and Bonferroni adjusted for secondary patient-
1660 reported outcomes. In addition, because of differences in ACP engagement among English and
1661 Spanish speakers,⁸ and based on preferences of our stakeholders and granting agencies, we
1662 decided, *a priori*, to analyze our results overall and stratified by English and Spanish language.
1663 To compare outcomes between the two arms longitudinally, we will use mixed effects linear,
1664 Poisson, or negative binomial regression for continuous measures and mixed effects logistic
1665 regression for dichotomous measures. The mixed effects models will include fixed effects for the
1666 primary modeling terms of time (baseline and 15 months for ACP documentation and baseline
1667 and 1 week, 3 months, 6 months, and 12 months for ACP Engagement with time modeled using
1668 dummy variables to allow for non-linearity); arm (AD-only versus PREPARE); an interaction
1669 term of study arm and time; and a random effect for subjects. We will adjust for the
1670 randomization blocking factors limited vs. adequate literacy,⁹⁸ and any predictor variables that
1671 differ between arms. All models also will also be adjusted for baseline ACP documentation and
1672 will include random physician intercepts to account for nesting of patients within physicians. We
1673 will use standardized, clinically meaningful effect sizes (i.e., 0.20-0.49 small, 0.50-0.79 medium,

1674 and ≥ 0.80 large).⁹⁹ Per stakeholder request, we will conduct post-hoc mixed-effects regression
1675 to calculate the percentage of participants who increased their Behavior Change score, Action
1676 scores, or both Behavior Change and Action scores from baseline (i.e., estimated slope > 0) by
1677 study arm; p-values adjusted to a significance of 0.017.

1678

1679 For moderator analysis, we will test for interactions by adding interaction terms to the group by
1680 time variable for health literacy (limited versus adequate) controlling for prior ACP
1681 documentation and clustering effects by clinician. All other interaction terms are adjusted for
1682 health literacy (randomization blocking variable) prior ACP documentation and clustering effects
1683 by clinician. Additional interaction terms to be added to the group by time variable include
1684 language (i.e., English versus Spanish), control preferences for decision making (i.e., makes
1685 own decisions versus doctor makes decisions), age (i.e., < 65 years versus ≥ 65 years of age),
1686 sex/gender (i.e., self-reported man versus woman), race/ethnicity (i.e., white versus non-white),
1687 health status (i.e., good-to-excellent versus fair-to-poor), presence of a potential surrogate (i.e.,
1688 yes versus no), internet access at home (i.e., yes versus no), and, for Spanish-speakers,
1689 patient-clinician language (concordance vs. discordance). A p-value for interaction < 0.05 is
1690 considered significant.

1691

1692 Missing data for the primary outcome will be assessed. If there is 10% or more of missing data,
1693 we will use a mean imputation approach. All available data will be included in mixed-effects
1694 models. We will assess whether any research staff member became unblinded during follow-up
1695 assessment and conduct sensitivity analysis as needed.

1696

1697 **SAMPLE SIZE AND POWER CALCULATIONS**

1698 We will measure a full range of ACP behaviors including discussions. However, written advance
1699 directive completion of legal forms is a primary outcome and is the most well-studied.¹⁰⁰ Power

1700 from longitudinal analyses with repeated measures will be stronger, but to be conservative, we
1701 consider power for a single post-intervention time point (e.g., 15 months). A recent meta-
1702 analysis of written advance directive documentation studies demonstrated a pooled effect size
1703 of 0.50 (95% CI; 0.17 -0.83),¹⁰⁰ as did an RCT of an ACP workbook that included both behavior
1704 change constructs and a social work visit,¹⁰¹ and our prior RCT of an easy-to-read AD at ZSFG
1705 which showed an increased AD completion rate from 7% to 15%.⁸ Because both the
1706 intervention and control arm will receive the easy-to-read advance directive, we assume that
1707 both arms will have an advance directive completion rate of $\leq 15\%$. Based on prior studies, we
1708 assume PREPARE will result in additional benefit of advance directive completion with a
1709 minimum effect size of 0.5 (two-fold increase) above 15%. A sample of 350, (175 per arm), will
1710 afford us 92% power (2-tailed alpha of 0.05) to detect a difference of advance directive
1711 completion rates of 15% in controls vs. 30% in the PREPARE arm and 80% power to detect a
1712 difference of 15% vs. 27%. Power is also expected to be strong for the ACP behavioral change
1713 scale outcomes (preliminary data demonstrated a pre-to-post improvement of 0.5 SD).²⁷ With a
1714 conservative assumption that controls will improve by 0.1 to 0.2 SD, we will have 85% to 98%
1715 power, respectively, to conclude that the improvement is better in the PREPARE arm. We
1716 expect a 15% drop out rate at 12 months based on our prior randomized, controlled trial at
1717 ZSFG,⁸ and will therefore attempt to recruit 402 patients, or 201 in each arm for each language
1718 (English and Spanish) for a total recruitment of 804 patients.

1719
1720 Our sample size will also allow adequate power to detect clinically important interactions based
1721 on potential moderators (literacy, control preferences, language concordance) for our outcomes.
1722 In a prior trial of an easy-to-read advance directive in the same patient population with only 200
1723 patients, we found significant interactions for literacy.⁸ Thus, if we consider the power scenario
1724 of the control group ACP documentation rate of 15% and the PREPARE group of 28%, and
1725 suppose the control group rate is the same (15%) for both levels of the moderating factor, then

1726 for a moderating factor split of 1:1, we would have 80% power to detect an interaction. If the
1727 PREPARE arm ACP documentation rate is 18% for one level of the factor and 40% for the
1728 other, this corresponds to a relative rate of ACP documentation of 2.2 times as high for one
1729 level of the factor compared to the other. A 2:1 split of the moderating factor still allows
1730 detection of a 2.4-fold increase in the relative rate of documentation. Power to detect
1731 interactions will likely be stronger for continuous outcomes (e.g. engagement/behavioral scales).

1732

1733 **ETHICS AND ADVISORY COMMITTEES**

1734 This study is approved by the University of California, San Francisco (UCSF) (IRB reference
1735 #13-10847). This study is guided by a Patient-Clinical Stakeholder Advisory Board that is
1736 comprised of patients and patient advocates (including native Spanish-speakers), surrogates,
1737 and ZSFG/SFHN primary care clinic staff and medical directors. It is also guided by a DSMB
1738 consisting of 4 experts in randomized trials, human subjects research and consent, vulnerable
1739 populations, palliative care, advance care planning, and biostatistics. Both advisory groups
1740 reviewed and approved all study protocols and related materials. In addition, we continue to
1741 meet with both groups every 4-6 months to review the progress of the trial, make suggestions
1742 for recruitment, review any potentially adverse events, and ensure that we are following our
1743 study protocols in a way that protects vulnerable patient populations.

1744

1745 **HUMAN SUBJECTS PROTECTIONS**

1746 **Protection of the rights and welfare of participants:**

1747 All study staff are required to take annual training regarding the rights and protections of
1748 research participants. Additionally, weekly study team meetings will ensure that all study staff
1749 are following the research protocol and that all study participants are consented according to
1750 our study protocol.

1751

1752 Furthermore, our consent process ensures that study participants have a clear understanding of
1753 the study and understand that they can choose to not participate in the study at any point in
1754 time, and that the care they receive will not be affected by declining to participate in our study.
1755 Our consent process involves using a consent form written below a 6th-grade reading level,
1756 reading the form to potential subjects verbatim, allowing time for questions and discussion, and
1757 then assessing comprehension using teach-to-goal. If questions are not answered correctly,
1758 repeated education and reassessment of comprehension are continued until complete
1759 comprehension is achieved. If subjects take more than three passes through the
1760 comprehension assessment, formal assessment for cognitive impairment will be completed. If
1761 patients are found to be cognitively impaired, they are excluded from the study. If they are not
1762 cognitively impaired, we will re-do teach back once more, after which the participant will be
1763 deemed ineligible for the study if they are unable to demonstrate comprehension of the study.

1764

1765 Additionally, we include UCSF Clinical Research Office contact information on all consent forms
1766 as required for all non-biomedical studies.

1767

1768 **Steps taken to minimize risks to subjects:**

1769 We have developed a modified research consent process that has been shown to be successful
1770 in vulnerable patient populations as described above.²⁹ All study fliers, consent forms, and
1771 questionnaires are read to the subjects in their entirety by native English- and Spanish-speaking
1772 research staff. Participants are reminded that they can opt out of the study at any time. All study
1773 materials are in an easy-to-read (5th grade reading level, large 14-point font) format. The
1774 consent materials and the study interviews are conducted in the language the participant is
1775 most comfortable speaking (English or Spanish).

1776

1777 This study will employ research assistants who are fluent in English or Spanish. Only fluent
1778 research assistants will be in contact and will communicate with Spanish-speaking participants.
1779 We will also ensure that all study materials are accurately translated into Spanish by having
1780 them initially translated from English to Spanish by native Spanish- speakers. We will then have
1781 them back translated into English to ensure accuracy. Finally, we will have the final translated
1782 documents reviewed for accuracy by third party native Spanish- speakers. To help participants
1783 follow along during the interview, they may review a large font Participant Version of the survey
1784 at baseline and all follow-ups that can be reviewed while the research assistant is asking
1785 research questions verbatim. We use 14-point font and color-coded, standardized, large font
1786 response options to help with understanding.

1787

1788 **Data security:**

1789 - Data are stored securely in the encrypted, secure UCSF MyResearch environment

1790 - Data are coded; data key is kept separately and securely

1791 - Data are kept in a locked file cabinet

1792 - Data are kept in a locked office or suite

1793 - Electronic data are protected with a password

1794 - Data are stored on a secure network

1795 - Data are collected/stored using REDCap or REDCap Survey

1796

1797 **Measures to ensure confidentiality and protect identifiers from improper disclosure**

1798 Risks to subjects are minimal and may include loss of confidentiality and psychological

1799 discomfort about discussing end-of-life issues. Subjects are assured that their answers to study

1800 questions will not be directly linked to their names. Instead, any identifying information is coded

1801 and separated from the data. The identifying information will only be known to the primary

1802 investigators but will not be used in data analysis. In addition, signed consent forms are kept in

1803 locked file cabinets and kept separate from the data collection instruments. Study subjects are
1804 also reminded that the information obtained will not be shared with their providers except in non-
1805 identifying aggregate form at the end of the study. We also make clear that the responses to the
1806 PREPARE guide are only for research purposes and will not be shared with their clinicians or
1807 put in their medical record.

1808

1809 We will store all study materials in locked offices and locked storage cabinets. We will utilize
1810 UCSF MyResearch and REDCap to enter and maintain data in a secure environment. In order
1811 to be more environmentally-conscious, we will attempt to use the LiveCapture function of
1812 RedCap and thus reduce the use of paper resources. We will retain the use of paper surveys in
1813 case the RedCap system is down. These paper files are stored in secure, locked research
1814 offices in secure, locked file cabinets.

1815

1816 As some of the questions concerning end-of-life may cause psychological discomfort for some
1817 study subjects, subjects are reminded at the beginning of the interview of their right to refuse to
1818 answer any and all questions and their right to terminate the interview at any time. We will also
1819 reassure subjects that if they choose not to be in the study or choose to terminate the interview,
1820 it will not change the medical care that they normally receive from their clinic or their clinician. In
1821 addition, we will reiterate that the information shared within the research interview will not be
1822 shared with their clinicians or used in medical care. However, subjects can take home a copy of
1823 the PREPARE guide with them and bring it back to their clinicians if they wish. Subjects are
1824 given the name and number of the primary investigator and may call if they have questions or
1825 are concerned about their participation in the study.

1826

1827 **Required reportable information:**

1828 As these interviews may be completed in people's home and, in the interviews, we are asking
1829 patients to describe their experiences and opinions, it is possible that reportable events such as
1830 elder abuse, suicidal or homicidal ideation may be detected. If they are detected, they will be
1831 handled according to the American Psychological Association code of ethics. If elder abuse is
1832 suspected, the participant will be encouraged to take steps to ensure their safety. They will be
1833 offered contact information for local supportive services and informed that the concerns will be
1834 discussed with the elder abuse hotline for assistance. When there are concerns about self-harm
1835 or harm to others, severity of harm will be assessed. Participants will be offered local support
1836 services and officials will be notified as necessary.

1837

1838 Patient Depression/Anxiety Protocols

1839 With input from the Patient-Clinician Stakeholder Advisory Board, and to err on the side of
1840 caution, we created a flow diagram with detailed instructions, including study scripts and contact
1841 names and telephone numbers for research staff to use in the event scored in the moderately
1842 severe depression or anxiety range on the PHQ-8 and GAD-7 or a participant expressed suicide
1843 ideation.

1844

1845 **DATA SAFETY MONITORITY PLAN**

1846 Monitoring will focus on recruitment, baseline comparability of treatment groups, protocol
1847 adherence, completeness of data, accrual of primary endpoint data, safety, and follow-up rates.
1848 This monitoring will provide the basis for monthly review by the study investigators, review by
1849 the ZSFG Patient-Clinician Advisory Committee, and Data Safety and Monitoring Board
1850 (DSMB), and yearly reporting to our IRBs. We will implement methods of verifying entered data
1851 and of quality control. All study materials data are kept on secure, password-protected,
1852 encrypted servers. All consent materials and any identifying information are kept in locked
1853 cabinets within locked offices, on password-protected, encrypted servers, on card-key protected

1854 research floors. Dr. Sudore, will be directly responsible for identifying and immediately reporting
1855 all adverse events to the IRBs Privacy Officers, and funding agency as appropriate. The ZSFG
1856 Patient-Clinician Advisory Committee will ensure participant safety in the clinic and will meet up
1857 to 4 times per year. The formal DSMB includes 4 experts in randomized trials, human subjects
1858 research and consent, vulnerable populations, palliative care, advance care planning, and
1859 biostatistics. The DSMB will review and approve the research protocol and plans for data and
1860 safety monitoring; and assess data quality; participant recruitment, accrual and retention;
1861 baseline comparability of treatment groups, accrual of primary endpoints; and participant safety
1862 (e.g., adverse events, protocol violations). They will also develop stopping rules for the trial. The
1863 DSMB will meet up to 4 times per year.

1864

1865 **CHARTER OF DATA SAFETY MONITORING BOARD**

1866 The Data and Safety Monitoring Board (DSMB) will act in an advisory capacity to the National
1867 Institute of Aging (NIA) Director to monitor participant safety, data quality and evaluate the
1868 progress of the study. Dr. Sudore, University of California, San Francisco is conducting the
1869 "*Improving Advance Care Planning by Preparing Diverse Seniors for Decision Making*" study
1870 under a R01 funded by the National Institute of Aging. The DSMB for this study includes 2
1871 outside clinicians with expertise in RCTs and an outside biostatistician. The NIA program officer
1872 is also included. The DSMB will review and approve the research protocol and plans for data
1873 and safety monitoring; and assess data quality; participant recruitment, accrual and retention;
1874 baseline comparability of treatment groups, accrual of primary endpoints; and participant safety
1875 (e.g., adverse events, protocol violations). They will also develop stopping rules for the trial. The
1876 DSMB will meet 2 and up to 4 times per year.

1877

1878 **DSMB Responsibilities**

1879 The DSMB responsibilities are to:

- 1880 • review the research protocol, informed consent documents and plans for data safety and
1881 monitoring;
- 1882 • advise the NIA on the readiness of the study staff to initiate recruitment;
- 1883 • evaluate the progress of the trial, including periodic assessments of data quality and
1884 timeliness, recruitment, accrual and retention, participant risk versus benefit, performance of
1885 the trial sites, and other factors that can affect study outcome;
- 1886 • consider factors external to the study when relevant information becomes available, such as
1887 scientific or therapeutic developments that may have an impact on the safety of the
1888 participants or the ethics of the trial;
- 1889 • review study performance, make recommendations and assist in the resolution of problems
1890 reported by the Principal Investigator;
- 1891 • protect the safety of the study participants;
- 1892 • report to NIA on the safety and progress of the trial;
- 1893 • make recommendations to the NIA and the Principal Investigator concerning continuation,
1894 termination or other modifications of the trial based on the observed beneficial or adverse
1895 effects of the treatment under study;
- 1896 • if appropriate, review interim analyses in accordance with stopping rules, which are clearly
1897 defined in advance of data analysis and have the approval of the DSMB;
- 1898 • ensure the confidentiality of the study data and the results of monitoring; and,
- 1899 • assist the NIA by commenting on any problems with study conduct, enrollment, sample size
1900 and/or data collection.

1901

1902 The DSMB will discharge itself from its duties when the last participant completes the study.

1903

1904 **Membership**

1905 The DSMB includes experts in or representatives of the fields of:

1906 relevant clinical expertise,

1907 clinical trial methodology, and

1908 biostatistics.

1909

1910 The DSMB members:

1911 • In addition to the NIA program officer members include:

1912 • Dr. David Bekelman, MD, MPH, an internist, psychiatrist, and palliative medicine

1913 physician at the University of Colorado School of Medicine and is an expert in health

1914 communication and medical decision making

1915 • Dr. Nathan Goldstein, MD, a geriatrician and a national expert in palliative care,

1916 communication, and medical decision making at Mt. Sinai School of Medicine,

1917 • Dr. James Wiley, PhD a statistician and Professor in the Institute for Health Policy

1918 Studies at the University of California, San Francisco. Dr. Wiley has extensive

1919 experience with RCTs and working with safety net populations. Although Dr. Wiley is at

1920 UCSF, he does not otherwise work with Dr. Sudore. Membership have no financial,

1921 scientific, or other conflict of interest with the trial.

1922

1923 Written documentation attesting to absence of conflict of interest has been obtained.

1924

1925 Dr. Nathan Goldstein, Mount Sinai School of Medicine, has been appointed by NIA to serve as

1926 the Chairperson and is responsible for overseeing the meetings, developing the agenda in

1927 consultation with the NIA Program Official and the Principal Investigator. The Chair is the

1928 contact person for the DSMB. The University of California, San Francisco shall provide the
1929 logistical management and support of the DSMB. Dr. Nathan Goldstein is also the safety officer
1930 and contact person for serious adverse event reporting. A log of all potential adverse events and
1931 protocol violations will be kept and reviewed quarterly by the DSMB. Procedures for notifying
1932 the Chair of the DSMB and the NIA Program Official will be discussed and agreed upon at the
1933 first meeting.

1934

1935 **Board Process**

1936 At the first meeting the DSMB will discuss the protocol, suggest modifications, and establish
1937 guidelines to study monitoring by the Board. The DSMB Chairperson in consultation with the
1938 Principal Investigator and the NIA Program Official will prepare the agenda to address the
1939 review of study materials, modifications to the study protocol and informed consent document,
1940 initiation of the trial, appointment of a safety officer, as needed, reporting of adverse events,
1941 statistical analysis plan including interim analysis and stopping rules, etc.

1942

1943 Meetings of the DSMB will be held 2-4 times per year at the call of the Chairperson and / or NIA
1944 Program Official to ensure patient safety and to review stopping rules for the trial. The NIA
1945 Program Official or designee will attend most of the meetings. An emergency meeting of the
1946 DSMB may be called at any time by the Chair or by the NIA should participant safety questions
1947 or other unanticipated problems arise.

1948

1949 Meetings are closed to the public because discussions may address confidential participant
1950 data. Meetings are attended by the Principal Investigator and members of his/her staff.

1951 Meetings may be convened as conference calls as well as in-person.

1952

1953 **Meeting Format**

1954 Each meeting must include a recommendation to continue or to terminate the study and
1955 whether the DSMB has any concerns about participant safety made by a formal DSMB majority
1956 or unanimous vote. Should the DSMB decide to issue a termination recommendation, the full
1957 vote of the DSMB is required. In the event of a split vote, majority vote will rule and a minority
1958 report should be appended. The DSMB Chair provides the tiebreaking vote in the event of a 50-
1959 50 split vote.

1960
1961 A recommendation to terminate the study may be made by the DSMB at any time by majority
1962 vote. The Chair should provide such a recommendation to the NIA immediately by telephone
1963 and email. After the NIA Director makes a decision about whether to accept or decline the
1964 DSMB recommendation to terminate the study, the PI is immediately informed about his
1965 decision.

1966

1967 **Meeting Materials**

1968 DSMB interim report templates will be prepared by the study staff, to be reviewed by the DSMB
1969 members at each meeting. The reports will list the study aims, the status of the study, and
1970 summarize safety data.

1971

1972 **Reports from the DSMB**

1973 A formal report containing the recommendations for continuation or modifications of the study
1974 will be prepared by the DSMB Chairperson, NIA Program Official or its designee. The draft
1975 report will be sent to the DSMB members for review and approval.

1976

1977 **Confidentiality**

1978 All materials, discussions and proceedings of the DSMB are completely confidential. Members
1979 and other participants in DSMB meetings are expected to maintain confidentiality.

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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 ZSFG/SFHN 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

1999 **Summary of Changes to the Protocol:** The listed topics follow the outline and headers of the protocol

| Topic | Date | Summary of Changes |
|---------------------------------|--------------|--|
| Funding | Feb 3, 2014 | We obtained funding from the National Institute on Aging (R01AG045043) to start recruitment of English-speakers. We then also obtained Patient-Centered Outcomes Research Institute (PCORI) funding (R-1306-01500) to add Spanish-speakers to our established trial infrastructure and protocol. |
| Funding | Mar 8, 2017 | Dr. Sudore became funded, in part, by a NIA K24 (K24AG054415). |
| ClinicalTrials.gov registration | Feb 27, 2014 | When PCORI funding was obtained, PCORI required a separate Clinical.Trial.gov number. Thus, it was added in February 2014. Although English- and Spanish-speaking recruitment was supported by two funders, this was one trial with the same staff, locations, procedures, IRB, and protocol. ³⁶ |
| Background | Apr, 2016 | We updated the background to included updated references. |
| Preliminary Studies | May, 2017 | We updated the preliminary studies to include the findings from our published VA trial. The name of hospital was changed on May 3 rd , 2015 from SFGH to Zuckerberg San Francisco General Hospital (ZSFG). This change was made throughout the protocol. |
| Overview of Trial | Jan 4, 2016 | We updated the protocol to include our study flow diagram for our records. |
| Eligibility screening | Jan 16, 2014 | Eligibility screening in busy, loud, outpatient clinics was often difficult. With our patient-clinicians stakeholders, we decided to include the ability to recruit and screen by phone. See below under recruitment. |
| Exclusion criteria | Jul 15, 2014 | To minimize potential contamination, we excluded participants who may have been exposed to the PREPARE website from other sources such as being in a PREPARE-related focus group or pilot study. |
| Exclusion criteria | Oct 3, 2014 | 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, chart review or research staff assessment. |
| Exclusion criteria | Jan 16, 2014 | To minimize the risk of unblinding by fellow research participants, any spouse/partner of a currently enrolled patient or 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/ZFG 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. |

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| Exclusion criteria | Jan 27, 2014 | To save research staff considerable time and effort, potential participants who initially scheduled but then missed the baseline interview (i.e. no show) more than 2 times without prior notification and rescheduling with study staff will be considered ineligible, unless there were significant extenuating circumstances. |
| Spanish Translation | Nov 13, 2014 | All translated and back-translated study materials were approved by the UCSF IRB. |
| Recruitment methods | Nov 13, 2013 | 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 bills from the hospital. With input from our Patient-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. |
| Recruitment methods | Jan 16, 2014 | It was determined by our patient-clinician stakeholders that it would be acceptable to recruit patients by phone in addition to in clinic recruitment. In addition, because we were attempting to enroll patients 1-3 weeks prior to a primary care visit, it was proving difficult to approach patients in clinic ahead of their primary care appointments. In addition, our primary care stakeholders felt it would be better for their clinic workflow to not have research staff always in the clinic. Therefore, we expanded our recruitment options, after receiving permission from the clinician and sending recruitment letters, to both approach potential participants in clinic as well as recruit by phone. |
| Recruitment-reimbursement | Jan 16, 2014 | We initially reimbursed \$25 separately for the screening interview and \$25 for the baseline interview that included intervention exposure. We realized that the screening interview was brief and often occurred over the phone because it was difficult to conduct in busy clinic settings. We also realized, in collaboration with our patient-clinician advisory board, that it made more sense to reimburse participants for \$50 for the baseline interview since these interviews were longer and in our study offices. We also changed from taxi vouchers to municipal transportation tokens because of the increased surcharge associated with taxi vouchers and participant preference. |
| Consent forms | Jan 27, 2014 | 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." |
| Consent forms | Jan 27, 2014 | Clinicians needed to be contacted if their patient reported severe depression or anxiety. We updated our consent forms to fully explain this to participants: |

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| | | <p>“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:</p> <ul style="list-style-type: none"> • 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 |
| Randomization | Jan 16, 2014 | The initial IRB application was a Just-in-time submission for an NIH proposal. We initially planned to block randomize, as we did for a recent VA trial, ³⁵ by both health literacy and race/ethnicity. However, given the diversity of patients at SFHN/ZSFG (over 50% non-white), in comparison to the VA, we decided to only block randomize by health literacy. |
| Data Collection Methods | Jan 16, 2014 | To be more environmentally-conscious, we switched from paper surveys to use the LiveCapture function of RedCap. We retained the use of paper surveys in the event the RedCap system was down. All paper files continued to be stored in secure, locked research offices in secure, locked file cabinets. |
| Follow-up & Retention | May 28, 2014 | We created an appointment reminder sheet to show the dates and times for upcoming primary care appointments as well as upcoming study appointments to help with retention. |
| Follow-up & Retention | Jan 16, 2014 | 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 as many of our patients had functional limitations. |
| Follow-up & Retention | Jul 15, 2014 | For all participants who missed their primary care appointment and did not reschedule, we provided a courtesy phone call to remind participants to reschedule the primary care appointment. |
| Follow-up & Retention | Jul 15, 2014 | Patients were enrolled based on upcoming primary care appointments. All follow-up interviews were timed to this primary care appointment. Some primary care appointments were subsequently missed or cancelled. In consultation with our stakeholder advisory committee and the DSMB, we decided that for participants who reschedule and attend their primary care appointment within 6 months, we would still conduct interviews at 1 week, and at 3, 6, and 12 months from the primary care appointment date. If participants do not reschedule within 6 months, we will conduct follow up assessments at 6 and 12 months from the primary care appointment date. |

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| Follow-up and Retention | Jan 16, 2014 | All data capture was 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 out a Participant Version of the survey to be used during the phone call if desired. No data were collected by mail. |
| Measures & Data Collection | Jan 4, 2016 | We created a table displaying all study outcome measures, including validity and reliability information in both English and Spanish, number of survey items, references and the schedule of administration for our records and protocol. |
| Measures & Data Collection | Mar 12, 2013 | Correction: <i>A priori</i> , 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. ³⁵ We fixed this typo in our final protocol. From the prior VA trial, ³⁵ it was 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 prior published trial. ³⁵ |
| Measures & Data Collection | Jan 16, 2014 | We initially proposed to screen for depression and anxiety using the -Patient Health Questionnaire-2 item (PHQ-2) and the Generalized Anxiety Disorder-2 item (GAD-2). Our DSMB felt more precise versions of this survey should be used. Therefore, we updated our methods to reflect assessment of depression and anxiety using the Patient Health Questionnaire-8 item (PHQ-8) and Generalized Anxiety Disorder-7 item (GAD-7). |
| Measures & Data Collection | Sept 20, 2017 | 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 over time for Behavior Change scores, Actions scores, and both combined. We defined improvement as an estimated overall slope > 0. Therefore, we created this exploratory variable post-hoc and used Bonferroni corrections to set the p-value of significance at 0.017. |
| Human Subjects Protections | May 28, 2014 | Because we were assessing depression and anxiety as part of the trial, to err on the side of caution, the Patient-Clinician Stakeholder Advisory Board helped us create a flow diagram with detailed instructions, scripts, and telephone numbers for how staff could refer participants who report severe depression/anxiety if that were to occur. As above, this potential disclosure of participant information was provided on the informed consent form. |

2000 **Summary of Changes to the Statistical Analysis Plan**

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| Topic | Date | Summary of Changes |
|-----------------------------------|--------------|--|
| Refusals & withdrawal comparisons | Sep 30, 2016 | We added a description of our planned analysis to compare participants who refused based on age and self-reported gender. We also added a description of our planned analysis to compare reasons for withdrawal between study arms. |
| Bonferroni corrections | Sep 30, 2017 | We added Bonferroni adjusted p-values for all secondary and exploratory outcomes. |
| Stratifying results by language | Mar 1, 2014 | Our PCORI grant was funded on Mar 1 st , 2014 and allowed us to add Spanish-speaking participants to the trial. <i>A priori</i> and based on prior literature and the preferences of our stakeholders and grant funders, we added information about stratifying our analysis based on English and Spanish-speaking participants. |
| Models | Sep 30, 2016 | We explain more fully the modeling terms in the mixed effects models. |
| Variable added to adjusted models | Sep 30, 2016 | In addition to health literacy and clustering by clinician, we also adjusted all mixed effects models for baseline ACP documentation because, in consultation with our stakeholders, it was felt that these patients may be different from ACP naïve participants. This also mirrors the analysis in the prior VA PREPARE trial. ³⁵ |
| Effect Size Definitions | Sep 30, 2016 | We added information and references concerning clinically meaningful effect sizes. |
| Exploratory Outcome | Sep 30, 2016 | Based on stakeholder request, we included a description of an added exploratory 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. |
| Interactions | Sep 30, 2016 | We more clearly defined the variables used to test for interactions and how these variables were dichotomized for analysis. |

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