

## Protocol Supplement

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3 This trial protocol has been provided by the authors to give readers additional information about  
4 their work for this manuscript. The original trial protocol has been previously published.<sup>1</sup>

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8 This supplement includes the following items:

- 9 1. Original protocol and statistical analysis plan (March 2013)
  - 10 2. Final protocol and statistical analysis plan and summary of changes (September 2017)
- 11

12

**Protocol**

13

**Original Version**

14

**March 2013**

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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 4<sup>th</sup>, 2013.

24

25 **INTRODUCTION AND RATIONALE**

26 Millions of older adults will face complex medical decisions over the course of advanced illness,<sup>2</sup>  
27 yet most are unprepared.<sup>3,4</sup> Lack of preparation can lead to uninformed choices, receipt of care  
28 inconsistent with personal goals, and lack of patient empowerment during clinical encounters,<sup>5-9</sup>  
29 especially for individuals with limited health literacy.<sup>10</sup> 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).<sup>11</sup> Yet, ADs are hard to understand and are often not completed,  
33 especially by minorities.<sup>12,13</sup> 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.<sup>5,14-17</sup> 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.<sup>11</sup> 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).**<sup>18</sup> 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.**<sup>19</sup> 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:**<sup>20</sup> 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,<sup>21</sup> are addressed in PREPARE.

65 **Evidence supporting the new ACP paradigm and content of PREPARE:**<sup>22</sup> 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  $\geq 60$  years with  $\geq 2$   
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.<sup>23,24</sup>

83 **Preliminary evidence that PREPARE is beneficial.** In a recent pilot,<sup>25</sup> 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  $72 \pm 33$  SD to  $87 \pm 22$ , 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.<sup>1</sup> 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.<sup>26</sup>

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.<sup>8</sup> 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.<sup>1</sup>

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.<sup>23,27,28</sup> 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.<sup>18</sup>

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  $\geq 2$  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  $\geq 2$  times in the past year (an indication  
163 of established primary care); and have had  $\geq 2$  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  $\geq 55$  years of age (rather than  $\geq 65$ ) 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.<sup>29,30</sup> 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  $\geq 2$  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  $\geq 3$  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,<sup>31-33</sup> 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,<sup>11,34</sup> 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 <sup>35</sup>                              |
|                    | 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) <sup>36</sup> and the mini-Cog <sup>31,37</sup>                |
|                    | 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 5<sup>th</sup>-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 5<sup>th</sup> 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 5<sup>th</sup> 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.<sup>19,26</sup> Consent forms written at the 5<sup>th</sup> 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 5<sup>th</sup> 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](http://www.prepareforyourcare.org)).<sup>25,26</sup> The conceptual framework for PREPARE has been  
271 previously published and is based primarily on Social Cognitive Theory,<sup>38,39</sup> with  
272 elements from the Health Belief Model,<sup>40</sup> the Theory of Planned Behavior,<sup>41</sup> and Behavior  
273 Change Theory.<sup>39,42</sup> 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,<sup>43,44</sup> especially literacy-appropriate interventions.<sup>18</sup>  
276 Modeling behaviors (as in PREPARE) can also improve patients' ability to communicate with  
277 clinicians and improve outcomes,<sup>45,46</sup> such as increased question asking behavior and a sense  
278 of control during a clinical visit,<sup>46,47</sup> an increased desire to participate in decision making, and  
279 even improved affect and functional status.<sup>43,48-50</sup> 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.<sup>51-57</sup> PREPARE includes a training and goal  
283 setting component which has been shown to be effective in changing outpatient behaviors, such  
284 as exercise.<sup>58</sup>

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 5<sup>th</sup> 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.<sup>25</sup> 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.<sup>59</sup>

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.<sup>18,60</sup> 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).<sup>61</sup> 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.<sup>62</sup>

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,<sup>25-27</sup> 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.<sup>25-27</sup>

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.<sup>18</sup> 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.<sup>63</sup>

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<sup>64,65</sup> and anxiety.<sup>66,67</sup> We administer the Patient Health Questionnaire (PHQ)-4  
464 at baseline and at each follow-up interview.<sup>68</sup> 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,<sup>25</sup> 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 0-36<sup>69</sup> 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).<sup>70</sup> 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)<sup>71,72</sup>  
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,<sup>73,74</sup> 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,<sup>75</sup> 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.<sup>76</sup> 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),<sup>76</sup> as did an RCT of an ACP workbook that included both behavior  
533 change constructs and a social work visit,<sup>77</sup> and our prior RCT of an easy-to-read AD at SFGH  
534 which showed an increased AD completion rate from 7% to 15%.<sup>18</sup> 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).<sup>25</sup> 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,<sup>18</sup> 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.<sup>8</sup> 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.<sup>19</sup> 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 (5<sup>th</sup> 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

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818 **ORIGINAL PROTOCOL REFERENCES:**

- 819 1. Sudore RL, Barnes DE, Le GM, et al. Improving advance care planning for English-  
820 speaking and Spanish-speaking older adults: study protocol for the PREPARE  
821 randomised controlled trial. *BMJ open*. 2016;6(7):e011705.
- 822 2. Zhao J, Barclay S, Farquhar M, Kinmonth AL, Brayne C, Fleming J. The oldest old in the  
823 last year of life: population-based findings from Cambridge city over-75s cohort study  
824 participants aged 85 and older at death. *Journal of the American Geriatrics Society*.  
825 2010;58(1):1-11.
- 826 3. Emanuel LL, Barry MJ, Stoeckle JD, Ettelson LM, Emanuel EJ. Advance directives for  
827 medical care--a case for greater use. *N Engl J Med*. 1991;324(13):889-895.
- 828 4. Hofmann JC, Wenger NS, Davis RB, et al. Patient preferences for communication with  
829 physicians about end-of-life decisions. SUPPORT Investigators. Study to Understand  
830 Prognoses and Preference for Outcomes and Risks of Treatment. *Ann Intern Med*.  
831 1997;127(1):1-12.
- 832 5. Perkins HS. Controlling death: the false promise of advance directives. *Ann Intern Med*.  
833 2007;147(1):51-57.
- 834 6. Fried TR, O'Leary JR. Using the experiences of bereaved caregivers to inform patient-  
835 and caregiver-centered advance care planning. *J Gen Intern Med*. 2008;23(10):1602-  
836 1607.
- 837 7. Anderson WG, Arnold RM, Angus DC, Bryce CL. Posttraumatic stress and complicated  
838 grief in family members of patients in the intensive care unit. *J Gen Intern Med*.  
839 2008;23(11):1871-1876.
- 840 8. Vig EK, Starks H, Taylor JS, Hopley EK, Fryer-Edwards K. Surviving surrogate decision-  
841 making: what helps and hampers the experience of making medical decisions for others.  
842 *J Gen Intern Med*. 2007;22(9):1274-1279.
- 843 9. Wright AA, Zhang B, Ray A, et al. Associations between end-of-life discussions, patient  
844 mental health, medical care near death, and caregiver bereavement adjustment. *JAMA*.  
845 2008;300(14):1665-1673.
- 846 10. Kutner M, Greenberg E, Baer J. A first look at the literacy of America's adults in the 21st  
847 century. National Center for Education Statistics, U.S. Department of Education. 2005.
- 848 11. Sudore RL, Fried TR. Redefining the "planning" in advance care planning: preparing for  
849 end-of-life decision making. *Ann Intern Med*. 2010;153(4):256-261.

- 850 12. Krakauer EL, Crenner C, Fox K. Barriers to optimum end-of-life care for minority  
851 patients. *Journal of the American Geriatrics Society*. 2002;50(1):182-190.
- 852 13. Kwak J, Haley WE. Current research findings on end-of-life decision making among  
853 racially or ethnically diverse groups. *Gerontologist*. 2005;45(5):634-641.
- 854 14. A controlled trial to improve care for seriously ill hospitalized patients. The study to  
855 understand prognoses and preferences for outcomes and risks of treatments  
856 (SUPPORT). The SUPPORT Principal Investigators. *JAMA*. 1995;274(20):1591-1598.
- 857 15. Teno JM, Licks S, Lynn J, et al. Do advance directives provide instructions that direct  
858 care? SUPPORT Investigators. Study to Understand Prognoses and Preferences for  
859 Outcomes and Risks of Treatment. *Journal of the American Geriatrics Society*.  
860 1997;45(4):508-512.
- 861 16. Fagerlin A, Schneider CE. Enough. The failure of the living will. *Hastings Cent Rep*.  
862 2004;34(2):30-42.
- 863 17. Meier DE, Morrison RS. Autonomy reconsidered. *N Engl J Med*. 2002;346(14):1087-  
864 1089.
- 865 18. Sudore RL, Landefeld CS, Barnes DE, et al. An advance directive redesigned to meet  
866 the literacy level of most adults: a randomized trial. *Patient Educ Couns*. 2007;69(1-  
867 3):165-195.
- 868 19. Sudore RL, Landefeld CS, Williams BA, Barnes DE, Lindquist K, Schillinger D. Use of a  
869 modified informed consent process among vulnerable patients: a descriptive study. *J*  
870 *Gen Intern Med*. 2006;21(8):867-873.
- 871 20. Sudore RL, Schickedanz AD, Landefeld CS, et al. Engagement in multiple steps of the  
872 advance care planning process: a descriptive study of diverse older adults. *Journal of*  
873 *the American Geriatrics Society*. 2008;56(6):1006-1013.
- 874 21. Schickedanz AD, Schillinger D, Landefeld CS, Knight SJ, Williams BA, Sudore RL. A  
875 clinical framework for improving the advance care planning process: start with patients'  
876 self-identified barriers. *Journal of the American Geriatrics Society*. 2009;57(1):31-39.
- 877 22. McMahan RD, Knight SJ, Fried TR, Sudore RL. Advance care planning beyond advance  
878 directives: perspectives from patients and surrogates. *J Pain Symptom Manage*.  
879 2013;46(3):355-365.
- 880 23. Fried TR, Redding CA, Robbins ML, Paiva A, O'Leary JR, Iannone L. Stages of change  
881 for the component behaviors of advance care planning. *Journal of the American*  
882 *Geriatrics Society*. 2010;58(12):2329-2336.

- 883 24. Fried TR, Bullock K, Iannone L, O'Leary JR. Understanding Advance Care Planning as a  
884 Process of Health Behavior Change. *Journal of the American Geriatrics Society*.  
885 2009;57(9):1547-1555.
- 886 25. Sudore RL, Knight SJ, McMahan RD, et al. A novel website to prepare diverse older  
887 adults for decision making and advance care planning: a pilot study. *J Pain Symptom*  
888 *Manage*. 2014;47(4):674-686.
- 889 26. Sudore RL, Le GM, McMahan RD, Feuz M, Katen M, Barnes DE. The advance care  
890 planning PREPARE study among older Veterans with serious and chronic illness: study  
891 protocol for a randomized controlled trial. *Trials*. 2015;Dec(16):570.
- 892 27. Sudore RL, Stewart AL, Knight SJ, et al. Development and validation of a questionnaire  
893 to detect behavior change in multiple advance care planning behaviors. *PloS one*.  
894 2013;8(9):e72465.
- 895 28. Fried TR, Redding CA, Robbins ML, Paiva A, O'Leary JR, Iannone L. Promoting  
896 advance care planning as health behavior change: development of scales to assess  
897 Decisional Balance, Medical and Religious Beliefs, and Processes of Change. *Patient*  
898 *Educ Couns*. 2012;86(1):25-32.
- 899 29. Gruenewald TL, Karlamangla AS, Hu P, et al. History of socioeconomic disadvantage  
900 and allostatic load in later life. *Soc Sci Med*. 2012;74(1):75-83.
- 901 30. Karlamangla AS, Singer BH, McEwen BS, Rowe JW, Seeman TE. Allostatic load as a  
902 predictor of functional decline. *MacArthur studies of successful aging. Journal of clinical*  
903 *epidemiology*. 2002;55(7):696-710.
- 904 31. Borson S, Scanlan JM, Chen P, Ganguli M. The Mini-Cog as a screen for dementia:  
905 validation in a population-based sample. *Journal of the American Geriatrics Society*.  
906 2003;51(10):1451-1454.
- 907 32. Milne A, Culverwell A, Guss R, Tuppen J, Whelton R. Screening for dementia in primary  
908 care: a review of the use, efficacy and quality of measures. *Int Psychogeriatr*.  
909 2008;20(5):911-926.
- 910 33. Pfeiffer E. A short portable mental status questionnaire for the assessment of organic  
911 brain deficit in elderly patients. *J Am Geriatr Soc*. 1975;23(10):433-441.
- 912 34. Sudore RL, Lum HD, You JJ, et al. Defining Advance Care Planning for Adults: A  
913 Consensus Definition From a Multidisciplinary Delphi Panel. *J Pain Symptom Manage*.  
914 2017;53(5):821-832.e821.



- 915 35. Bergman B, Sjostrand J. A longitudinal study of visual acuity and visual rehabilitation  
916 needs in an urban Swedish population followed from the ages of 70 to 97 years of age.  
917 *Acta ophthalmologica Scandinavica*. 2002;80(6):598-607.
- 918 36. Erkinjuntti T, Sulkava R, Wikstrom J, Autio L. Short Portable Mental Status  
919 Questionnaire as a screening test for dementia and delirium among the elderly. *Journal*  
920 *of the American Geriatrics Society*. 1987;35(5):412-416.
- 921 37. Borson S, Scanlan J, Brush M, Vitaliano P, Dokmak A. The mini-cog: a cognitive 'vital  
922 signs' measure for dementia screening in multi-lingual elderly. *Int J Geriatr Psychiatry*.  
923 2000;15(11):1021-1027.
- 924 38. Bandura A. Self-efficacy: toward a unifying theory of behavioral change. *Psychol Rev*.  
925 1977;84(2):191-215.
- 926 39. Street RL, Jr. Interpersonal Communication Skills in Health Care Contexts. In: Greene  
927 JO, Bureson BR, editors. *Handbook of Communication and Social Interaction Skills*. p.  
928 909-33. Mahwah, New Jersey: Lawrence Erlbaum Associates; 2003.
- 929 40. Champion VL, Skinner CS. The health belief model. In: Glanz K, Rimer BK, Viswanath K,  
930 editors. *Health behavior and health education: Theory, research, and practice*. 4th ed.  
931 San Francisco, CA: Jossey-Bass; 2008. p. 45-65.
- 932 41. Montano DE, Kasprzyk D. Theory of reasoned Action, Theory of Planned Behavior, and  
933 the Integrated Behavioral Model. In: Glanz K, Rimer BK, Viswanath K, editors. *Health*  
934 *behavior and health education: Theory, research, and practice*. 4th ed. San Francisco,  
935 CA: Jossey-Bass; 2008. p. 67-96.
- 936 42. *Theory at a Glance: A Guide for Health Promotion Practice*. National Cancer Institute.  
937 U.S. Department of Health and Human Services of the National Institutes of Health. 2nd  
938 Edition. 2005. <http://www.cancer.gov/cancertopics/cancerlibrary/theory.pdf>. Accessed  
939 July 24th, 2013.
- 940 43. Street RL, Jr., Slee C, Kalauokalani DK, Dean DE, Tancredi DJ, Kravitz RL. Improving  
941 physician-patient communication about cancer pain with a tailored education-coaching  
942 intervention. *Patient Educ Couns*. 2010;80(1):42-47.
- 943 44. Kravitz RL, Tancredi DJ, Street RL, Jr., et al. Cancer Health Empowerment for Living  
944 without Pain (Ca-HELP): study design and rationale for a tailored education and  
945 coaching intervention to enhance care of cancer-related pain. *BMC Cancer*. 2009;9:319.
- 946 45. Rao JK, Anderson LA, Inui TS, Frankel RM. Communication interventions make a  
947 difference in conversations between physicians and patients: a systematic review of the  
948 evidence. *Med Care*. 2007;45(4):340-349.

- 949 46. Post DM, Cegala DJ, Miser WF. The other half of the whole: teaching patients to  
950 communicate with physicians. *Fam Med*. 2002;34(5):344-352.
- 951 47. Harrington J, Noble LM, Newman SP. Improving patients' communication with doctors: a  
952 systematic review of intervention studies. *Patient Educ Couns*. 2004;52(1):7-16.
- 953 48. Greenfield S, Kaplan S, Ware JE, Jr. Expanding patient involvement in care. Effects on  
954 patient outcomes. *Ann Intern Med*. 1985;102(4):520-528.
- 955 49. Roter DL. Patient question asking in physician-patient interaction. *Health Psychol*.  
956 1984;3(5):395-409.
- 957 50. Sepucha KR, Belkora JK, Mutchnick S, Esserman LJ. Consultation planning to help  
958 breast cancer patients prepare for medical consultations: effect on communication and  
959 satisfaction for patients and physicians. *J Clin Oncol*. 2002;20(11):2695-2700.
- 960 51. Volandes AE, Paasche-Orlow MK, Barry MJ, et al. Video decision support tool for  
961 advance care planning in dementia: randomised controlled trial. *BMJ*. 2009;338:b2159.
- 962 52. Volandes AE, Lehmann LS, Cook EF, Shaykevich S, Abbo ED, Gillick MR. Using video  
963 images of dementia in advance care planning. *Arch Intern Med*. 2007;167(8):828-833.
- 964 53. Davis TC, Berkel HJ, Arnold CL, Nandy I, Jackson RH, Murphy PW. Intervention to  
965 increase mammography utilization in a public hospital. *J Gen Intern Med*.  
966 1998;13(4):230-233.
- 967 54. Volandes AE, Brandeis GH, Davis AD, et al. A randomized controlled trial of a goals-of-  
968 care video for elderly patients admitted to skilled nursing facilities. *J Palliat Med*.  
969 2012;15(7):805-811.
- 970 55. Bickmore TW, Pfeifer LM, Byron D, et al. Usability of conversational agents by patients  
971 with inadequate health literacy: evidence from two clinical trials. *Journal of health*  
972 *communication*. 2010;15 Suppl 2:197-210.
- 973 56. Volandes AE, Barry MJ, Chang Y, Paasche-Orlow MK. Improving Decision Making at  
974 the End of Life with Video Images. *Med Decis Making*. 2010;30 (1)(1):29-34.
- 975 57. Wang JH, Schwartz MD, Luta G, Maxwell AE, Mandelblatt JS. Intervention tailoring for  
976 Chinese American women: comparing the effects of two videos on knowledge, attitudes  
977 and intentions to obtain a mammogram. *Health Educ Res*. 2012;27(3):523-536.
- 978 58. MacGregor K, Handley M, Wong S, et al. Behavior-change action plans in primary care:  
979 a feasibility study of clinicians. *Journal of the American Board of Family Medicine* :  
980 *JABFM*. 2006;19(3):215-223.

- 981 59. Handley M, MacGregor K, Schillinger D, Sharifi C, Wong S, Bodenheimer T. Using  
982 action plans to help primary care patients adopt healthy behaviors: a descriptive study.  
983 *Journal of the American Board of Family Medicine : JABFM*. 2006;19(3):224-231.
- 984 60. The Institute for Healthcare Advancement: [http://www.iha4health.org/our-](http://www.iha4health.org/our-services/advance-directive/)  
985 [services/advance-directive/](http://www.iha4health.org/our-services/advance-directive/). Accessed 7/25/15.
- 986 61. Chew LD, Griffin JM, Partin MR, et al. Validation of screening questions for limited health  
987 literacy in a large VA outpatient population. *J Gen Intern Med*. 2008;23(5):561-566.
- 988 62. Sudore RL, Boscardin J, Feuz MA, McMahan RD, Katen MT, Barnes DE. Effect of the  
989 PREPARE Website vs an Easy-to-Read Advance Directive on Advance Care Planning  
990 Documentation and Engagement Among Veterans: A Randomized Clinical Trial. *JAMA*  
991 *Intern Med*. 2017;177(8):1102-1109.
- 992 63. Volandes AE, Levin TT, Slovin S, et al. Augmenting advance care planning in poor  
993 prognosis cancer with a video decision aid: a preintervention-postintervention study.  
994 *Cancer*. 2012;118(17):4331-4338.
- 995 64. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity  
996 measure. *J Gen Intern Med*. 2001;16(9):606-613.
- 997 65. Kroenke K, Strine TW, Spitzer RL, Williams JB, Berry JT, Mokdad AH. The PHQ-8 as a  
998 measure of current depression in the general population. *J Affect Disord*. 2009;114(1-  
999 3):163-173.
- 1000 66. Spitzer RL, Kroenke K, Williams JB, Lowe B. A brief measure for assessing generalized  
1001 anxiety disorder: the GAD-7. *Arch Intern Med*. 2006;166(10):1092-1097.
- 1002 67. García-Campayo J, Zamorano E, Ruiz MA, Pérez-Páramo M, Vanessa L-G, Rejas J.  
1003 The assessment of generalized anxiety disorder: psychometric validation of the Spanish  
1004 version of the self-administered GAD-2 scale in daily medical practice. *Health and*  
1005 *quality of life outcomes*. 2012;10(114):10.
- 1006 68. Lowe B, Wahl I, Rose M, et al. A 4-item measure of depression and anxiety: validation  
1007 and standardization of the Patient Health Questionnaire-4 (PHQ-4) in the general  
1008 population. *J Affect Disord*. 2010;122(1-2):86-95.
- 1009 69. Baker DW, Williams MV, Parker RM, Gazmararian JA, Nurss J. Development of a brief  
1010 test to measure functional health literacy. *Patient Educ Couns*. 1999;38(1):33-42.
- 1011 70. Degner LF, Sloan JA, Venkatesh P. The Control Preferences Scale. *Can J Nurs Res*.  
1012 1997;29(3):21-43.
- 1013 71. Shadbolt B, Barresi J, Craft P. Self-rated health as a predictor of survival among patients  
1014 with advanced cancer. *J Clin Oncol*. 2002;20(10):2514-2519.

- 1015 72. Lucas-Carrasco R. The WHO quality of life (WHOQOL) questionnaire: Spanish  
1016 development and validation studies. *Qual Life Res.* 2012;21(1):161-165.
- 1017 73. Gordon HS, Street RL, Jr., Sharf BF, Soucek J. Racial differences in doctors'  
1018 information-giving and patients' participation. *Cancer.* 2006;107(6):1313-1320.
- 1019 74. Sudore RL, Landefeld CS, Perez-Stable EJ, Bibbins-Domingo K, Williams BA,  
1020 Schillinger D. Unraveling the relationship between literacy, language proficiency, and  
1021 patient-physician communication. *Patient Educ Couns.* 2009;75(3):398-402.
- 1022 75. Pocock SJ, Assmann SE, Enos LE, Kasten LE. Subgroup analysis, covariate adjustment  
1023 and baseline comparisons in clinical trial reporting: current practice and problems. *Stat*  
1024 *Med.* 2002;21(19):2917-2930.
- 1025 76. Ramsaroop SD, Reid MC, Adelman RD. Completing an advance directive in the primary  
1026 care setting: what do we need for success? *Journal of the American Geriatrics Society.*  
1027 2007;55(2):277-283.
- 1028 77. Pearlman RA, Starks H, Cain KC, Cole WG. Improvements in advance care planning in  
1029 the Veterans Affairs System: results of a multifaceted intervention. *Arch Intern Med.*  
1030 2005;165(6):667-674.
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**Protocol**

**Final Version**

**September 2017**

|  |           |
|--|-----------|
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**Summary of Statistical Analysis Plan Changes**

**92**

**References**

**93**

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1042 For this trial, recruitment of English-speaking older adults is funded through a National Institute  
1043 on Aging R01 grant (R01 AG045043) and recruitment of Spanish-speaking older adults is  
1044 funded through the Patient-Centered Outcomes Research Institute (CDR-1306-01500). Dr.  
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 4<sup>th</sup>, 2013 and NCT02072941 for Spanish-speakers, registered on February 4<sup>th</sup>, 2014.

1050

1051 **INTRODUCTION AND RATIONALE**

1052 **Background**

1053 The population is aging,<sup>1,2</sup> 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.).<sup>3</sup> 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.<sup>4</sup> 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.<sup>5-8</sup>

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.<sup>9-11</sup> 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).<sup>9,12-16</sup> Hispanics/Latinos account for 15% of the U.S. population, a proportion projected to  
1068 grow to 30% by 2050.<sup>1,2</sup> 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.<sup>10</sup> In addition,  
1071 the mean reading level in the U.S. is only at the 8<sup>th</sup> grade level, and for adults over 65 years of  
1072 age it is only at the 5<sup>th</sup> grade level.<sup>17,18</sup> Patients with limited literacy often lack self-efficacy to  
1073 communicate their wishes or ask questions,<sup>19</sup> and the combination of limited literacy and limited  
1074 English-proficiency results in low satisfaction with doctor-patient communication and decision  
1075 making.<sup>20-22</sup> 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.<sup>8,23</sup>

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.<sup>24</sup> 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.<sup>25,26</sup> 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](http://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.<sup>27</sup> Both the new ACP paradigm and the PREPARE  
1090 intervention have been described in detail elsewhere.<sup>27,28</sup> 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.<sup>28</sup>

1093 **PRELIMINARY STUDIES**

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

1095 **Health Network (SFHN) primary care clinics.**<sup>8</sup> 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.**<sup>29</sup> 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.**<sup>30</sup> 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,<sup>31</sup> are addressed in PREPARE.

1114 **Evidence supporting the new ACP paradigm and content of PREPARE.**<sup>32</sup> 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  $\geq 60$  years with  $\geq 2$   
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.<sup>33,34</sup>

1132 **Preliminary evidence that PREPARE is beneficial.** In a recent pilot,<sup>27</sup> 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  $72 \pm 33$  SD to  $87 \pm 22$ , 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.<sup>35</sup> 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.<sup>36</sup> 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.<sup>28</sup>

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.<sup>8</sup> 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.<sup>36</sup>

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.

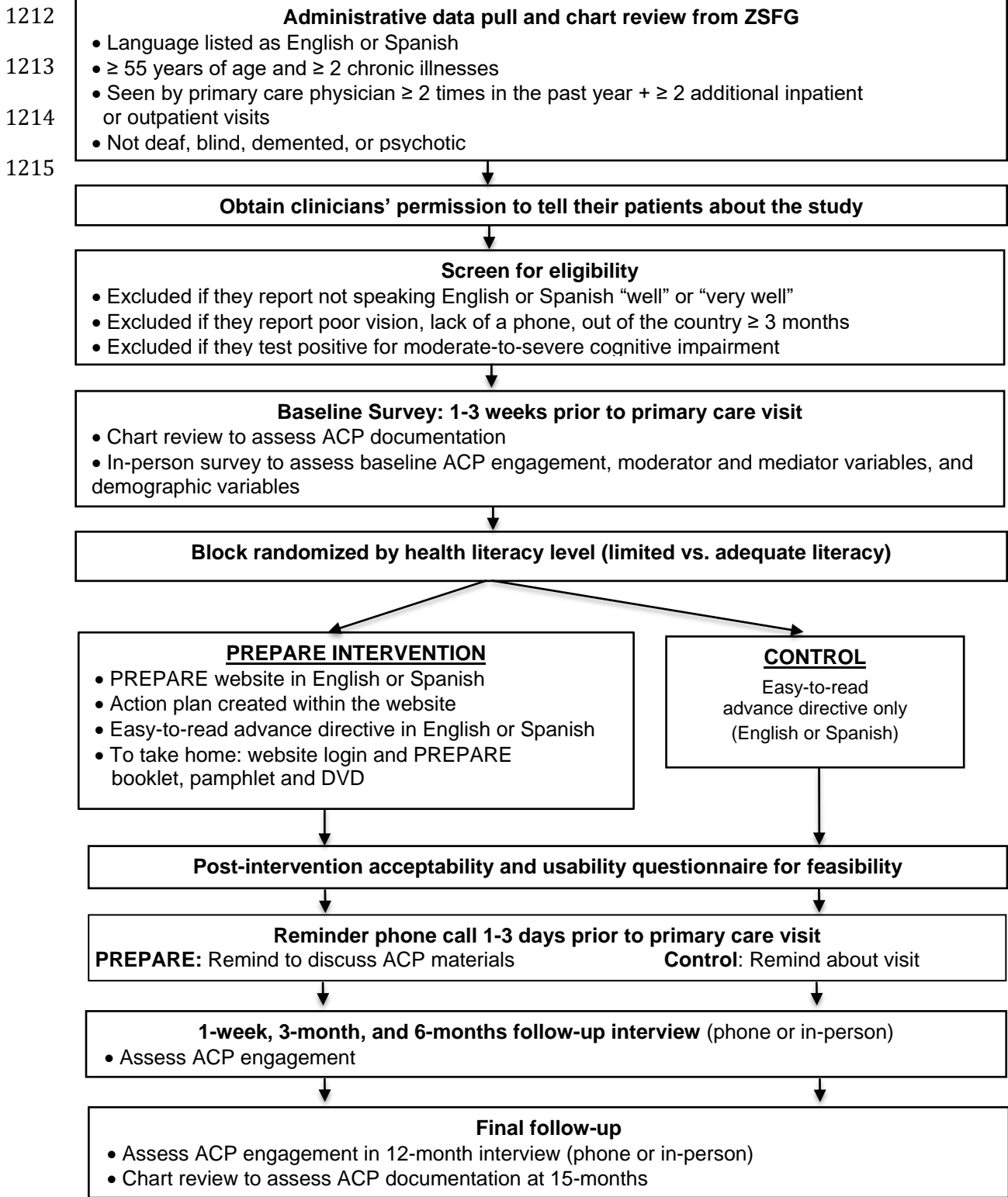
1203 Secondary outcomes will be ascertained using validated surveys.<sup>33,37,38</sup> We also hypothesize  
1204 that PREPARE will result in improved satisfaction with patient-doctor communication and  
1205 informed medical decision making and that PREPARE efficacy may vary across moderator  
1206 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.<sup>8</sup>

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  $\geq 2$  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  $\geq 2$  times in the  
1230 past year (an indication of established primary care); and have had  $\geq 2$  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  $\geq 55$  years of age (rather than  $\geq 65$ ) 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.<sup>39,40</sup> 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  $\geq 2$  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  $\geq 3$  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,<sup>41-43</sup> 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,<sup>24,44</sup> 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 <sup>45</sup>                              |
|                    | 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) <sup>46</sup> and the mini-Cog <sup>41,47</sup>                |
|                    | 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 5<sup>th</sup>-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 5<sup>th</sup> 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 5<sup>th</sup> 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.<sup>28,29</sup> Consent forms written at the 5<sup>th</sup> 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 5<sup>th</sup> 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](http://www.prepareforyourcare.org)).<sup>27,28</sup> The conceptual framework for PREPARE has been  
1374 previously published and is based primarily on Social Cognitive Theory,<sup>48,49</sup> with elements from  
1375 the Health Belief Model,<sup>50</sup> the Theory of Planned Behavior,<sup>51</sup> and Behavior Change Theory.<sup>49,52</sup>  
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,<sup>53,54</sup> especially literacy-appropriate interventions.<sup>8</sup> Modeling  
1379 behaviors (as in PREPARE) can also improve patients’ ability to communicate with clinicians  
1380 and improve outcomes,<sup>55,56</sup> such as increased question asking behavior and a sense of control  
1381 during a clinical visit,<sup>56,57</sup> an increased desire to participate in decision making, and even

1382 improved affect and functional status.<sup>53,58-60</sup> 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.<sup>61-67</sup> PREPARE includes a training and goal setting  
1386 component which has been shown to be effective in changing outpatient behaviors, such as  
1387 exercise.<sup>68</sup>

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 5<sup>th</sup> 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.<sup>27</sup> 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.<sup>69</sup>

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.<sup>8,70</sup> 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).<sup>71</sup> 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.<sup>35</sup>

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.<sup>36</sup>  
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.<sup>35</sup>

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,<sup>27,28,37</sup> 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.<sup>27,28,37</sup>

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.<sup>8</sup> 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.<sup>72</sup>

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<sup>73,74</sup> and anxiety.<sup>75,76</sup> 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.<sup>74,75</sup> 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,<sup>27</sup> 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 0-36<sup>77</sup> 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).<sup>78</sup> 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]<sup>79,80</sup> 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,<sup>20,81</sup> 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).

1634

1635

1636

1637



**Outcome Measures Table**

| Construct                     | Measure   | # items      | English Reliability/Validity  | Spanish Reliability/Validity   | Baseline | 1 week | 3 months | 6 months | 12 months | 15 months |
|-------------------------------|---|--------------|---|--|----------|--------|----------|----------|-----------|-----------|
|                               | <b>Primary Outcome</b>  |              |   |  |          |        |          |          |           |           |
| New ACP Documentation         | Chart review: ACP documentation (i.e., legal forms and documented goals of care discussions) <sup>35,36</sup>   |              |   |  | X        |        |          |          |           | X         |
|                               | <b>Secondary Outcomes</b>   |              |   |  |          |        |          |          |           |           |
| The Full ACP Process          | ACP Engagement Survey: <sup>27</sup><br>Behavior Change Process Measures (knowledge, contemplation, self-efficacy, readiness)<br><br>Action Measures: values identification and discussions | 57<br><br>25 | Behavior Change Measures:<br>Cronbach's $\alpha = 0.94$ (0.91-0.96), ICC= 0.70 (0.54-0.82) <sup>27</sup><br><br>Action Measures:<br>ICC* = 0.87 (0.79-0.92) <sup>27</sup> | -  | X        | X      | X        | X        | X         |           |
| Implementation: Acceptability | Acceptability and Usability<br>(a) Ease of Use and Understanding<br>(b) Usefulness in decisions & discussions<br>(c) Attitudes about norms or expectations                                  | 8<br>6<br>6  | 1 factor explained 81-85% of variance/scale. Kuder-Richardson >0.75 <sup>8</sup>  | 1 factor explained 81-85% of variance/scale. Kuder-Richardson >0.75 <sup>8</sup> | X        |        |          |          |           |           |
|                               | <b>Adverse Event Outcomes</b>   |              |   |  |          |        |          |          |           |           |
| Depression                    | Patient Health Questionnaire-8  | 8            | Scores $\geq 10$ 100% sensitive and 95% specific for major depressive disorder. <sup>73,74</sup>  | Scores $\geq 10$ 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 <sup>82</sup>                       |          |        |          |          |           |           |
| Anxiety                            | GAD-7 <sup>75</sup>  | 7       | Cronbach's $\alpha = 0.92$ <sup>75</sup><br>ICC* = 0.83   | Cronbach's $\alpha = 0.88$ <sup>76</sup><br>ICC* = 0.64 | X        | X      | X        | X        | X         |           |
|                                    | <b>Exploratory Outcome</b>   |         |   |   |          |        |          |          |           |           |
| 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         |           |
|                                    | <b>Demographic Information</b>   |         |   |   |          |        |          |          |           |           |
| Demographic Information            | Age, gender, race/ethnicity <sup>83</sup> , 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 <sup>84</sup>                                    | -   | 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 <sup>85</sup>  | -   | X        |        |          |          |           |           |
|                                    | <b>Other Measures</b>  |         |   |   |          |        |          |          |           |           |
| Health Literacy                    | Short form Test of Functional Health Literacy in Adults s-TOFHLA, scores 0-36) <sup>77</sup><br>Continuous & dichotomized to limited = 0-22 & adequate | 36      | Cronbach's $\alpha = .97$<br>Correlation coefficient w/<br>other literacy tests ><br>0.80 <sup>77</sup> | Cronbach's $\alpha > .95$ <sup>86</sup>                 | 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?" <sup>87</sup> Fluent, very well (concordant) vs. well, fair, or poor" | 1       | AUROC <sup>†</sup> 94% (CI: 90-98%) <sup>87</sup>                                     | AUROC <sup>†</sup> 94% (CI: 90-98%) <sup>87</sup>                              | X        |        |          |          |           |           |
| Desired role in decision making        | Control Preference Scale (CPS) with clinician <sup>78</sup>   | 2       | Correlation between preferred and actual role in decision making. <sup>12,88,89</sup> | Correlation between preferred and actual role in decision making <sup>90</sup> | 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 $\alpha$ = .98 Associated w/ desire to know prognosis <sup>91</sup>        | -  | X        |        |          |          |           |           |
| Functional Status                      | Activities of Daily Living (ADL) (0-16 point scale)& Instrumental (IADL) measure (0-12 item scale) <sup>92,93</sup>   | 13      | Morbidity/mortality correlation. <sup>126,127</sup>                                   | Cronbach's alpha =0.94 <sup>94</sup>   | X        |        |          |          |           |           |
| Self-rated health status               | How would you rate your health? (5pt Likert) <sup>79,80</sup>   | 1       | Cronbach $\alpha$ = .80 <sup>80</sup>   | -  | X        |        |          |          |           |           |
| Prior ACP experience                   | Prior ACP experiences (e.g., "Ever had to make life threatening medical decisions?") <sup>8</sup>                     | 5       |   | -  | X        |        |          |          |           |           |
| Social support                         | Modified Medical Outcomes Study Social Support (scores 11-55) <sup>95</sup>   | 11      | Cronbach's $\alpha$ = 0.88-.93 <sup>95</sup>  | Cronbach's $\alpha$ = 0.94 <sup>96</sup>                                       | 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. <sup>97</sup> | 4       | Spirituality associated with quality of life. Religiosity associated with wanting all measures to extend life. <sup>97</sup> | -                            | 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.<sup>36</sup>

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,<sup>8</sup> 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,<sup>98</sup> 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  $\geq 0.80$  large).<sup>99</sup> 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  $\geq 65$  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.<sup>100</sup> 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),<sup>100</sup> as did an RCT of an ACP workbook that included both behavior  
1704 change constructs and a social work visit,<sup>101</sup> and our prior RCT of an easy-to-read AD at ZSFG  
1705 which showed an increased AD completion rate from 7% to 15%.<sup>8</sup> 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).<sup>27</sup> 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,<sup>8</sup> 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.<sup>8</sup> 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.<sup>29</sup> 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 (5<sup>th</sup> 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

| <b>Topic</b>                    | <b>Date</b>  | <b>Summary of Changes</b>  |
|---------------------------------|--------------|--|
| 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. <sup>36</sup>  |
| 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 <sup>rd</sup> , 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. |

|                           |              |  |
|---------------------------|--------------|--|
| 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:  |

|                         |              |  |
|-------------------------|--------------|--|
|                         |              | <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"> <li>• A medical emergency such as a serious medical illness</li> <li>• Or, a serious mental illness, such as major depression</li> <li>• You report that you may harm yourself, you may harm someone else, or someone is harming you</li> </ul>  |
| 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, <sup>35</sup> 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. |

|                            |               |  |
|----------------------------|---------------|--|
| 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. <sup>35</sup> We fixed this typo in our final protocol. From the prior VA trial, <sup>35</sup> 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. <sup>35</sup> |
| 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**

2001

| 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 <sup>st</sup> , 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. <sup>35</sup> |
| 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.  |

2002

2003 **FINAL PROTOCOL REFERENCES**

- 2004 1. The United Nations Department of Economic and Social Affairs Population Division.  
2005 World Population Aging: 1950-2050.  
2006 <http://www.un.org/esa/population/publications/worldageing19502050/>. Accessed March  
2007 29th, 2012.
- 2008 2. 2010 United States Census. Overview of Race and Hispanic Origin: 2010.  
2009 <http://www.census.gov/prod/cen2010/briefs/c2010br-02.pdf>. Accessed 7-1-13.
- 2010 3. Wilper AP, Woolhandler S, Lasser KE, McCormick D, Bor DH, Himmelstein DU. A  
2011 national study of chronic disease prevalence and access to care in uninsured U.S.  
2012 adults. *Ann Intern Med.* 2008;149(3):170-176.
- 2013 4. Castillo LS, Williams BA, Hooper SM, Sabatino CP, Weithorn LA, Sudore RL. Lost in  
2014 translation: the unintended consequences of advance directive law on clinical care. *Ann*  
2015 *Intern Med.* 2011;154(2):121-128.
- 2016 5. Wu P, Lorenz KA, Chodosh J. Advance care planning among the oldest old. *J Palliat*  
2017 *Med.* 2008;11(2):152-157.
- 2018 6. Krakauer EL, Crenner C, Fox K. Barriers to optimum end-of-life care for minority  
2019 patients. *Journal of the American Geriatrics Society.* 2002;50(1):182-190.
- 2020 7. Crawley LM. Palliative care in African American communities. *J Palliat Med.*  
2021 2002;5(5):775-779.
- 2022 8. Sudore RL, Landefeld CS, Barnes DE, et al. An advance directive redesigned to meet  
2023 the literacy level of most adults: a randomized trial. *Patient Educ Couns.* 2007;69(1-  
2024 3):165-195.
- 2025 9. Crawley L, Payne R, Bolden J, Payne T, Washington P, Williams S. Palliative and end-  
2026 of-life care in the African American community. *Jama.* 2000;284(19):2518-2521.
- 2027 10. Smith AK, Sudore RL, Perez-Stable EJ. Palliative care for Latino patients and their  
2028 families: whenever we prayed, she wept. *JAMA.* 2009;301(10):1047-1057, E1041.
- 2029 11. Moody-Ayers SY, Stewart AL, Covinsky KE, Inouye SK. Prevalence and correlates of  
2030 perceived societal racism in older african-american adults with type 2 diabetes mellitus.  
2031 *Journal of the American Geriatrics Society.* 2005;53(12):2202-2208.
- 2032 12. Singh JA, Sloan JA, Atherton PJ, et al. Preferred roles in treatment decision making  
2033 among patients with cancer: a pooled analysis of studies using the Control Preferences  
2034 Scale. *Am J Manag Care.* 2010;16(9):688-696.



- 2035 13. Welch LC, Teno JM, Mor V. End-of-life care in black and white: race matters for medical  
2036 care of dying patients and their families. *Journal of the American Geriatrics Society*.  
2037 2005;53(7):1145-1153.
- 2038 14. Kwak J, Haley WE. Current research findings on end-of-life decision making among  
2039 racially or ethnically diverse groups. *Gerontologist*. 2005;45(5):634-641.
- 2040 15. Kreling B, Selsky C, Perret-Gentil M, Huerta EE, Mandelblatt JS. 'The worst thing about  
2041 hospice is that they talk about death': contrasting hospice decisions and experience  
2042 among immigrant Central and South American Latinos with US-born White, non-Latino  
2043 cancer caregivers. *Palliat Med*. 2010;24(4):427-434.
- 2044 16. Morrison RS, Meier DE. High rates of advance care planning in New York City's elderly  
2045 population. *Arch Intern Med*. 2004;164(22):2421-2426.
- 2046 17. Paasche-Orlow MK, Parker RM, Gazmararian JA, Nielsen-Bohlman LT, Rudd RR. The  
2047 prevalence of limited health literacy. *J Gen Intern Med*. 2005;20(2):175-184.
- 2048 18. Kutner M, Greenberg E, Baer J. *A first look at the literacy of America's adults in the 21st*  
2049 *century*. National Center for Education Statistics, U.S. Department of Education. 2005.
- 2050 19. Katz MG, Jacobson TA, Veledar E, Kripalani S. Patient literacy and question-asking  
2051 behavior during the medical encounter: a mixed-methods analysis. *J Gen Intern Med*.  
2052 2007;22(6):782-786.
- 2053 20. Sudore RL, Landefeld CS, Perez-Stable EJ, Bibbins-Domingo K, Williams BA,  
2054 Schillinger D. Unraveling the relationship between literacy, language proficiency, and  
2055 patient-physician communication. *Patient Educ Couns*. 2009;75(3):398-402.
- 2056 21. Schenker Y, Karter AJ, Schillinger D, et al. The impact of limited English proficiency and  
2057 physician language concordance on reports of clinical interactions among patients with  
2058 diabetes: the DISTANCE study. *Patient Educ Couns*. 2010;81(2):222-228.
- 2059 22. Fernandez A, Schillinger D, Warton EM, et al. Language barriers, physician-patient  
2060 language concordance, and glycemic control among insured Latinos with diabetes: the  
2061 Diabetes Study of Northern California (DISTANCE). *J Gen Intern Med*. 2011;26(2):170-  
2062 176.
- 2063 23. Doak CC DL, Root JH. *Teaching patients with low literacy skills*. Philadelphia, PA: JB  
2064 Lippincott; 1996.
- 2065 24. Sudore RL, Fried TR. Redefining the "planning" in advance care planning: preparing for  
2066 end-of-life decision making. *Ann Intern Med*. 2010;153(4):256-261.
- 2067 25. Tulsky JA. Beyond advance directives: importance of communication skills at the end of  
2068 life. *Jama*. 2005;294(3):359-365.

- 2069 26. Goldberg GR, Meier DE. A swinging pendulum: comment on "on patient autonomy and  
2070 physician responsibility in end-of-life care". *Arch Intern Med.* 2011;171(9):854.
- 2071 27. Sudore RL, Knight SJ, McMahan RD, et al. A novel website to prepare diverse older  
2072 adults for decision making and advance care planning: a pilot study. *J Pain Symptom*  
2073 *Manage.* 2014;47(4):674-686.
- 2074 28. Sudore RL, Le GM, McMahan RD, Feuz M, Katen M, Barnes DE. The advance care  
2075 planning PREPARE study among older Veterans with serious and chronic illness: study  
2076 protocol for a randomized controlled trial. *Trials.* 2015;Dec(16):570.
- 2077 29. Sudore RL, Landefeld CS, Williams BA, Barnes DE, Lindquist K, Schillinger D. Use of a  
2078 modified informed consent process among vulnerable patients: a descriptive study. *J*  
2079 *Gen Intern Med.* 2006;21(8):867-873.
- 2080 30. Sudore RL, Schickedanz AD, Landefeld CS, et al. Engagement in multiple steps of the  
2081 advance care planning process: a descriptive study of diverse older adults. *Journal of*  
2082 *the American Geriatrics Society.* 2008;56(6):1006-1013.
- 2083 31. Schickedanz AD, Schillinger D, Landefeld CS, Knight SJ, Williams BA, Sudore RL. A  
2084 clinical framework for improving the advance care planning process: start with patients'  
2085 self-identified barriers. *Journal of the American Geriatrics Society.* 2009;57(1):31-39.
- 2086 32. McMahan RD, Knight SJ, Fried TR, Sudore RL. Advance care planning beyond advance  
2087 directives: perspectives from patients and surrogates. *J Pain Symptom Manage.*  
2088 2013;46(3):355-365.
- 2089 33. Fried TR, Redding CA, Robbins ML, Paiva A, O'Leary JR, Iannone L. Stages of change  
2090 for the component behaviors of advance care planning. *Journal of the American*  
2091 *Geriatrics Society.* 2010;58(12):2329-2336.
- 2092 34. Fried TR, Bullock K, Iannone L, O'Leary JR. Understanding Advance Care Planning as a  
2093 Process of Health Behavior Change. *Journal of the American Geriatrics Society.*  
2094 2009;57(9):1547-1555.
- 2095 35. Sudore RL, Boscardin J, Feuz MA, McMahan RD, Katen MT, Barnes DE. Effect of the  
2096 PREPARE Website vs an Easy-to-Read Advance Directive on Advance Care Planning  
2097 Documentation and Engagement Among Veterans: A Randomized Clinical Trial. *JAMA*  
2098 *Intern Med.* 2017;177(8):1102-1109.
- 2099 36. Sudore RL, Barnes DE, Le GM, et al. Improving advance care planning for English-  
2100 speaking and Spanish-speaking older adults: study protocol for the PREPARE  
2101 randomised controlled trial. *BMJ open.* 2016;6(7):e011705.

- 2102 37. Sudore RL, Stewart AL, Knight SJ, et al. Development and validation of a questionnaire  
2103 to detect behavior change in multiple advance care planning behaviors. *PloS one*.  
2104 2013;8(9):e72465.
- 2105 38. Fried TR, Redding CA, Robbins ML, Paiva A, O'Leary JR, Iannone L. Promoting  
2106 advance care planning as health behavior change: development of scales to assess  
2107 Decisional Balance, Medical and Religious Beliefs, and Processes of Change. *Patient*  
2108 *Educ Couns*. 2012;86(1):25-32.
- 2109 39. Gruenewald TL, Karlamangla AS, Hu P, et al. History of socioeconomic disadvantage  
2110 and allostatic load in later life. *Soc Sci Med*. 2012;74(1):75-83.
- 2111 40. Karlamangla AS, Singer BH, McEwen BS, Rowe JW, Seeman TE. Allostatic load as a  
2112 predictor of functional decline. MacArthur studies of successful aging. *Journal of clinical*  
2113 *epidemiology*. 2002;55(7):696-710.
- 2114 41. Borson S, Scanlan JM, Chen P, Ganguli M. The Mini-Cog as a screen for dementia:  
2115 validation in a population-based sample. *Journal of the American Geriatrics Society*.  
2116 2003;51(10):1451-1454.
- 2117 42. Milne A, Culverwell A, Guss R, Tuppen J, Whelton R. Screening for dementia in primary  
2118 care: a review of the use, efficacy and quality of measures. *Int Psychogeriatr*.  
2119 2008;20(5):911-926.
- 2120 43. Pfeiffer E. A short portable mental status questionnaire for the assessment of organic  
2121 brain deficit in elderly patients. *J Am Geriatr Soc*. 1975;23(10):433-441.
- 2122 44. Sudore RL, Lum HD, You JJ, et al. Defining Advance Care Planning for Adults: A  
2123 Consensus Definition From a Multidisciplinary Delphi Panel. *J Pain Symptom Manage*.  
2124 2017;53(5):821-832.e821.
- 2125 45. Bergman B, Sjostrand J. A longitudinal study of visual acuity and visual rehabilitation  
2126 needs in an urban Swedish population followed from the ages of 70 to 97 years of age.  
2127 *Acta ophthalmologica Scandinavica*. 2002;80(6):598-607.
- 2128 46. Erkinjuntti T, Sulkava R, Wikstrom J, Autio L. Short Portable Mental Status  
2129 Questionnaire as a screening test for dementia and delirium among the elderly. *Journal*  
2130 *of the American Geriatrics Society*. 1987;35(5):412-416.
- 2131 47. Borson S, Scanlan J, Brush M, Vitaliano P, Dokmak A. The mini-cog: a cognitive 'vital  
2132 signs' measure for dementia screening in multi-lingual elderly. *Int J Geriatr Psychiatry*.  
2133 2000;15(11):1021-1027.
- 2134 48. Bandura A. Self-efficacy: toward a unifying theory of behavioral change. *Psychol Rev*.  
2135 1977;84(2):191-215.

- 2136 49. Street RL, Jr. *Interpersonal Communication Skills in Health Care Contexts*. In: Greene  
2137 JO, Burlleson BR, editors. *Handbook of Communication and Social Interaction Skills*. p.  
2138 909-33. Mahwah, New Jersey: Lawrence Erlbaum Associates; 2003.
- 2139 50. Champion VL, Skinner CS. *The health belief model*. In: Glanz K, Rimer BK, Viswanath K,  
2140 editors. *Health behavior and health education: Theory, research, and practice*. 4th ed.  
2141 San Francisco, CA: Jossey-Bass; 2008. p. 45-65.
- 2142 51. Montano DE, Kasprzyk D. *Theory of reasoned Action, Theory of Planned Behavior, and*  
2143 *the Integrated Behavioral Model*. In: Glanz K, Rimer BK, Viswanath K, editors. *Health*  
2144 *behavior and health education: Theory, research, and practice*. 4th ed. San Francisco,  
2145 CA: Jossey-Bass; 2008. p. 67-96.
- 2146 52. Theory at a Glance: A Guide for Health Promotion Practice. National Cancer Institute.  
2147 U.S. Department of Health and Human Services of the National Institutes of Health. 2nd  
2148 Edition. 2005. <http://www.cancer.gov/cancertopics/cancerlibrary/theory.pdf>. Accessed  
2149 July 24th, 2013.
- 2150 53. Street RL, Jr., Slee C, Kalauokalani DK, Dean DE, Tancredi DJ, Kravitz RL. Improving  
2151 physician-patient communication about cancer pain with a tailored education-coaching  
2152 intervention. *Patient Educ Couns*. 2010;80(1):42-47.
- 2153 54. Kravitz RL, Tancredi DJ, Street RL, Jr., et al. Cancer Health Empowerment for Living  
2154 without Pain (Ca-HELP): study design and rationale for a tailored education and  
2155 coaching intervention to enhance care of cancer-related pain. *BMC Cancer*. 2009;9:319.
- 2156 55. Rao JK, Anderson LA, Inui TS, Frankel RM. Communication interventions make a  
2157 difference in conversations between physicians and patients: a systematic review of the  
2158 evidence. *Med Care*. 2007;45(4):340-349.
- 2159 56. Post DM, Cegala DJ, Miser WF. The other half of the whole: teaching patients to  
2160 communicate with physicians. *Fam Med*. 2002;34(5):344-352.
- 2161 57. Harrington J, Noble LM, Newman SP. Improving patients' communication with doctors: a  
2162 systematic review of intervention studies. *Patient Educ Couns*. 2004;52(1):7-16.
- 2163 58. Greenfield S, Kaplan S, Ware JE, Jr. Expanding patient involvement in care. Effects on  
2164 patient outcomes. *Ann Intern Med*. 1985;102(4):520-528.
- 2165 59. Roter DL. Patient question asking in physician-patient interaction. *Health Psychol*.  
2166 1984;3(5):395-409.

- 2167 60. Sepucha KR, Belkora JK, Mutchnick S, Esserman LJ. Consultation planning to help  
2168 breast cancer patients prepare for medical consultations: effect on communication and  
2169 satisfaction for patients and physicians. *J Clin Oncol*. 2002;20(11):2695-2700.
- 2170 61. Volandes AE, Paasche-Orlow MK, Barry MJ, et al. Video decision support tool for  
2171 advance care planning in dementia: randomised controlled trial. *BMJ*. 2009;338:b2159.
- 2172 62. Volandes AE, Lehmann LS, Cook EF, Shaykevich S, Abbo ED, Gillick MR. Using video  
2173 images of dementia in advance care planning. *Arch Intern Med*. 2007;167(8):828-833.
- 2174 63. Davis TC, Berkel HJ, Arnold CL, Nandy I, Jackson RH, Murphy PW. Intervention to  
2175 increase mammography utilization in a public hospital. *J Gen Intern Med*.  
2176 1998;13(4):230-233.
- 2177 64. Volandes AE, Brandeis GH, Davis AD, et al. A randomized controlled trial of a goals-of-  
2178 care video for elderly patients admitted to skilled nursing facilities. *J Palliat Med*.  
2179 2012;15(7):805-811.
- 2180 65. Bickmore TW, Pfeifer LM, Byron D, et al. Usability of conversational agents by patients  
2181 with inadequate health literacy: evidence from two clinical trials. *Journal of health*  
2182 *communication*. 2010;15 Suppl 2:197-210.
- 2183 66. Volandes AE, Barry MJ, Chang Y, Paasche-Orlow MK. Improving Decision Making at  
2184 the End of Life with Video Images. *Med Decis Making*. 2010;30 (1)(1):29-34.
- 2185 67. Wang JH, Schwartz MD, Luta G, Maxwell AE, Mandelblatt JS. Intervention tailoring for  
2186 Chinese American women: comparing the effects of two videos on knowledge, attitudes  
2187 and intentions to obtain a mammogram. *Health Educ Res*. 2012;27(3):523-536.
- 2188 68. MacGregor K, Handley M, Wong S, et al. Behavior-change action plans in primary care:  
2189 a feasibility study of clinicians. *Journal of the American Board of Family Medicine* :  
2190 *JABFM*. 2006;19(3):215-223.
- 2191 69. Handley M, MacGregor K, Schillinger D, Sharifi C, Wong S, Bodenheimer T. Using  
2192 action plans to help primary care patients adopt healthy behaviors: a descriptive study.  
2193 *Journal of the American Board of Family Medicine* : *JABFM*. 2006;19(3):224-231.
- 2194 70. The Institute for Healthcare Advancement: [http://www.iha4health.org/our-](http://www.iha4health.org/our-services/advance-directive/)  
2195 [services/advance-directive/](http://www.iha4health.org/our-services/advance-directive/). Accessed 7/25/15.
- 2196 71. Chew LD, Griffin JM, Partin MR, et al. Validation of screening questions for limited health  
2197 literacy in a large VA outpatient population. *J Gen Intern Med*. 2008;23(5):561-566.
- 2198 72. Volandes AE, Levin TT, Slovin S, et al. Augmenting advance care planning in poor  
2199 prognosis cancer with a video decision aid: a preintervention-postintervention study.  
2200 *Cancer*. 2012;118(17):4331-4338.

- 2201 73. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity  
2202 measure. *J Gen Intern Med.* 2001;16(9):606-613.
- 2203 74. Kroenke K, Strine TW, Spitzer RL, Williams JB, Berry JT, Mokdad AH. The PHQ-8 as a  
2204 measure of current depression in the general population. *J Affect Disord.* 2009;114(1-  
2205 3):163-173.
- 2206 75. Spitzer RL, Kroenke K, Williams JB, Lowe B. A brief measure for assessing generalized  
2207 anxiety disorder: the GAD-7. *Arch Intern Med.* 2006;166(10):1092-1097.
- 2208 76. García-Campayo J, Zamorano E, Ruiz MA, Pérez-Páramo M, Vanessa L-G, Rejas J.  
2209 The assessment of generalized anxiety disorder: psychometric validation of the Spanish  
2210 version of the self-administered GAD-2 scale in daily medical practice. *Health and  
2211 quality of life outcomes.* 2012;10(114):10.
- 2212 77. Baker DW, Williams MV, Parker RM, Gazmararian JA, Nurss J. Development of a brief  
2213 test to measure functional health literacy. *Patient Educ Couns.* 1999;38(1):33-42.
- 2214 78. Degner LF, Sloan JA, Venkatesh P. The Control Preferences Scale. *Can J Nurs Res.*  
2215 1997;29(3):21-43.
- 2216 79. Shadbolt B, Barresi J, Craft P. Self-rated health as a predictor of survival among patients  
2217 with advanced cancer. *J Clin Oncol.* 2002;20(10):2514-2519.
- 2218 80. Lucas-Carrasco R. The WHO quality of life (WHOQOL) questionnaire: Spanish  
2219 development and validation studies. *Qual Life Res.* 2012;21(1):161-165.
- 2220 81. Gordon HS, Street RL, Jr., Sharf BF, Soucek J. Racial differences in doctors'  
2221 information-giving and patients' participation. *Cancer.* 2006;107(6):1313-1320.
- 2222 82. Wulsin L, Somoza E, Heck J. The Feasibility of Using the Spanish PHQ-9 to Screen for  
2223 Depression in Primary Care in Honduras. *Primary care companion to the Journal of  
2224 clinical psychiatry.* 2002;4(5):191-195.
- 2225 83. Christie KM, Meyerowitz BE, Giedzinska-Simons A, Gross M, Agus DB. Predictors of  
2226 affect following treatment decision-making for prostate cancer: conversations, cognitive  
2227 processing, and coping. *Psycho-oncology.* 2008;18(5):508-514.
- 2228 84. Kahn JR, Fazio EM. Economic status over the life course and racial disparities in health.  
2229 *J Gerontol B Psychol Sci Soc Sci.* 2005;60 Spec No 2:76-84.
- 2230 85. Chen B, Covinsky KE, Stijacic Cenzer I, Adler N, Williams BA. Subjective social status  
2231 and functional decline in older adults. *J Gen Intern Med.* 2012;27(6):693-699.
- 2232 86. Aguirre AC, Ebrahim N, Shea JA. Performance of the English and Spanish S-TOFHLA  
2233 among publicly insured Medicaid and Medicare patients. *Patient Educ Couns.*  
2234 2005;56(3):332-339.

- 2235 87. Rosenthal A, Wang F, Schillinger D, Perez Stable EJ, Fernandez A. Accuracy of  
 2236 physician self-report of Spanish language proficiency. *Journal of immigrant and minority*  
 2237 *health / Center for Minority Public Health*. 2011;13(2):239-243.
- 2238 88. Degner LF, Sloan JA. Decision making during serious illness: what role do patients really  
 2239 want to play? *Journal of clinical epidemiology*. 1992;45(9):941-950.
- 2240 89. Gigerenzer G, Gray JAM. *Better Doctors, Better Patients, Better Decisions: Envisioning*  
 2241 *Health Care 2020*. MIT Press; 2011.
- 2242 90. Yennurajalingam S, Parsons HA, Duarte ER, et al. Decisional Control Preferences of  
 2243 Hispanic Patients With Advanced Cancer From the United States and Latin America. *J*  
 2244 *Pain Symptom Manage*. 2012.
- 2245 91. Wright AA, Stieglitz H, Kupersztoch YM, et al. United states acculturation and cancer  
 2246 patients' end-of-life care. *PloS one*. 2013;8(3):e58663.
- 2247 92. Lee SJ, Lindquist K, Segal MR, Covinsky KE. Development and validation of a  
 2248 prognostic index for 4-year mortality in older adults. *JAMA*. 2006;295(7):801-808.
- 2249 93. Samper-Ternent R, Kuo YF, Ray LA, Ottenbacher KJ, Markides KS, Al Snih S.  
 2250 Prevalence of health conditions and predictors of mortality in oldest old Mexican  
 2251 Americans and non-Hispanic whites. *Journal of the American Medical Directors*  
 2252 *Association*. 2012;13(3):254-259.
- 2253 94. Vergara I, Bilbao A, Orive M, Garcia-Gutierrez S, Navarro G, Quintana JM. Validation of  
 2254 the Spanish version of the Lawton IADL Scale for its application in elderly people. *Health*  
 2255 *and quality of life outcomes*. 2012;10:130.
- 2256 95. Moser A, Stuck AE, Silliman RA, Ganz PA, Clough-Gorr KM. The eight-item modified  
 2257 Medical Outcomes Study Social Support Survey: psychometric evaluation showed  
 2258 excellent performance. *J Clin Epidemiol*. 2012.
- 2259 96. Costa Requena G, Salamero M, Gil F. Validity of the questionnaire MOS-SSS of social  
 2260 support in neoplastic patients. *Medicina clinica*. 2007;128(18):687-691.
- 2261 97. Balboni TA, Vanderwerker LC, Block SD, et al. Religiousness and spiritual support  
 2262 among advanced cancer patients and associations with end-of-life treatment  
 2263 preferences and quality of life. *J Clin Oncol*. 2007;25(5):555-560.
- 2264 98. Pocock SJ, Assmann SE, Enos LE, Kasten LE. Subgroup analysis, covariate adjustment  
 2265 and baseline comparisons in clinical trial reporting: current practice and problems. *Stat*  
 2266 *Med*. 2002;21(19):2917-2930.
- 2267 99. Cohen J. *Statistical power analysis for the behavioral sciences (2nd ed.)*. Hillsdale, NJ::  
 2268 Lawrence Earlbaum Associates.; 1988.

- 2269 100. Ramsaroop SD, Reid MC, Adelman RD. Completing an advance directive in the primary  
2270 care setting: what do we need for success? *Journal of the American Geriatrics Society*.  
2271 2007;55(2):277-283.
- 2272 101. Pearlman RA, Starks H, Cain KC, Cole WG. Improvements in advance care planning in  
2273 the Veterans Affairs System: results of a multifaceted intervention. *Arch Intern Med*.  
2274 2005;165(6):667-674.
- 2275