

### NIH Collaboratory Ethics and Regulatory Core: UG3 Consultation Call Improving Completion, Accuracy, and Dissemination of Surgical Advanced Care Planning (I CAN DO Surgical ACP) October 27, 2023; 3:00-4:00 pm ET (via Zoom)

#### Attendees:

- Core, Coordinating Center, and NIH: Joe Ali (Johns Hopkins University), Kevin McBryde (NCCIH), Kayla Mehl (Johns Hopkins University), Stephanie Morain (Johns Hopkins University), Pearl O'Rourke (retired), Caleigh Propes (Johns Hopkins University), Barbara Radziszewska (NIA), Tammy Reece (Duke University), Marcel Salive (NIA), Damon Seils (Duke University), Kayte Spector-Bagdady (University of Michigan), Ben Wilfond (University of Washington)
- Demonstration Project team: Molly Diethelm (University of Minnesota), Elizabeth Wick (University of California, San Francisco)

AGENDA ITEMS	DISCUSSION	ACTION ITEMS	OWNER
Brief review of	Meeting attendees received the Research Strategy and Data and Resource Sharing		
Demonstration Project	Plan for I CAN DO Surgical ACP with the meeting agenda (see supplementary		
	material attached). Pearl O'Rourke facilitated the discussion. Core members, I CAN		
	DO Surgical ACP team members, NIH representatives, and staff from the NIH		
	Pragmatic Trials Collaboratory Coordinating Center introduced themselves. The I		
	CAN DO Surgical ACP team members present included principal investigator		
	Elizabeth Wick and project manager Molly Diethelm.		
	<b>Project overview</b> : Elizabeth Wick gave an overview of the project. The goal of I CAN		
	DO Surgical ACP is to identify a system-based approach to help older adults		
	undergoing elective surgery engage in ACP. The project will leverage the existing		
	electronic health record (EHR) and patient portal, PREPARE for Your Care materials		
	to assist patients with completion of ACP, virtual healthcare navigators, and		
	electronic nudges. Another goal of the study is to understand digital engagement,		
	language, and social drivers of health that drive engagement in the intervention.		
	Healthcare system partners: University of California, San Francisco (UCSF),		
	University of California, Irvine (UCI), University of Minnesota (UMN)		

Approved: December 4, 2023

These minutes were circulated to all participants in the call for review and reflect all corrections that were received. The project's Research Strategy and Data and Resource Sharing Plan are included as supplementary material. Page 1

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	NIH Institute Providing Oversight: National Institute on Aging (NIA)		
	<ul> <li>Study design: The study is proposed to be a 3-arm pragmatic trial of older adults being seen in surgical clinics for new patient visits. ACP engagement is a standard of care in the participating healthcare systems. In arm 1, patients will receive a message through the patient portal ahead of their visit with information and materials for ACP. In arm 2, patients will receive the patient portal message and reminder messages. In arm 3, patients will receive the patient portal message and reminder messages plus a call from a healthcare navigator to help them work through the process. Randomization will be at the patient level.</li> <li>Outcomes: The primary outcome is the presence of an advance directive in the EHR. The secondary outcome is engagement in the ACP intervention as measured by an</li> </ul>		
	11-question survey.		
Status of IRB approval	complete at UCSF, almost complete at UMN, and in process at UCI.		
Risk (Does the project meet regulatory criteria for being considered minimal risk?):	The study team anticipates that the project will meet the regulatory criteria to be considered minimal risk.		
and consent (planned	If considered research, the study will likely have a waiver of consent. Pearl O'Rourke		
processes for relevant subjects)	asked about notification of research at the time of the first contact. Ben Wilfond and Joe Ali agreed that notification is important, even if just in the form of an additional 1 or 2 sentences in the patient portal letter.		
	For the follow-up surveys, consent will be embedded in the electronic survey.		
	The study team will obtain consent for focus groups or one-on-one interviews with an ethnographer.		
	Stephanie Morain shared the reasons Core member Dave Wendler has previously outlined for why to provide notification about research, independent of consent: "(1) Preparation, (2) understand what doing/relationships, (3) understanding what individuals are contributing to, (4) allow participants to express concerns, (5) can		

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	promote participant engagement/support, (6) reduce chances of unethical research, (7) promote public trust."		
Privacy (including HIPAA)	The study team is finalizing the approach to data sharing and how to share data for the natural language processing which will be done in Minnesota.		
Monitoring and oversight	The study team intends to use a data and safety monitoring board (DSMB) and has discussed the membership criteria with NIH representatives. The study will also be reviewed by the UCSF Learning Health System Oversight Committee.		
Issues beyond this project (regulatory and ethics concerns raised by the project, if any)	None.		
Other matters	<ul> <li>Joe Ali shared a recent article and encouraged the study team to consider looking for variability in the study outcomes by race/ethnicity.</li> <li>Mpody et al. Current trends in mortality attributable to racial or ethnic disparities in post-surgical population in the United States: a population-based study. Ann Surg. 2023;4(4):e342. doi:10.1097/AS9.0000000000342.</li> <li>Stephanie Morain encouraged the study team to consider finding a way to share what is learned from the trial with the patients who contributed to that learning.</li> </ul>		

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#### **Specific Aims**

Nearly 20 million older adults undergo major elective surgical procedures annually, yet less than 10% engage in advance care planning (ACP).<sup>1</sup> This is a critical missed opportunity to ensure optimal and patientaligned medical decisions and communications. Major surgery in older adults can be associated with complications or worsening health status, ranging from anticipated impairment to unanticipated major and long-term functional impairment and even death.<sup>2</sup> Before and after surgery, patients and surrogate decision-makers make complex decisions, but many are unprepared to articulate their care goals. <u>Consequently, older adults may</u> <u>undergo surgical and post-surgical treatments inconsistent with their values and goals</u>.<sup>3–5</sup>

The goal of ACP is to ensure patients receive medical care aligned with their goals and preferences.<sup>6</sup> While traditionally applied only to end-of-life decisions, the ACP paradigm has been *expanded* to include preparation for communication and decision-making across the illness trajectory.<sup>7,8</sup> *Expanded ACP* aims to prepare patients to define their preferences and values and to participate more effectively with clinicians in making complex medical decisions over time. Despite ACP being incorporated in Centers for Medicare & Medicaid Services Innovations programs and in several national guidelines, adoption has been limited, particularly in the surgical setting.<sup>6,9–11</sup> Most efforts to date have focused on surgeon communication training, *but barriers remain*, including varying levels of familiarity and comfort to conduct ACP conversations, <u>lack of time</u> in the pre-surgical care episode for these often-delicate conversations, and <u>lack of appropriate patient-facing ACP</u> tools to prepare patients and caregivers for complex decisions about surgical treatment.

Our team has designed and tested a theory-based, interactive patient-facing ACP technology solution based on the new *expanded ACP* paradigm of preparing people for communication and medical decision-making.<sup>12,13</sup> We showed that many patients can complete PREPARE at home on their own. <u>Despite consistent</u> evidence that PREPARE increases ACP engagement and patient and clinician empowerment to discuss ACP,<sup>12,14,15</sup> a gap remains in extending PREPARE's use to pre-surgical populations.<sup>15</sup>

Older adults' use of technology (e.g., patient portals and mobile devices) have been increasing exponentially over the past decade,<sup>16</sup> such as electronic health record (EHR)-driven and other digital interventions, including automated and virtual care modalities. They appear effective in engaging patients in health-related behaviors (e.g., colonoscopy and mammography) when approached in a patient-centric manner.<sup>17</sup> We *hypothesize* that by including PREPARE into the EHR-centric pre-surgery workflow for older adults and including automated reminders, we can empower patients and surgical teams to engage in ACP discussions. Given the limited time and resources in the surgical setting to conduct ACP, we will be testing 3 delivery strategies in increasing resource intensity (PREPARE alone, PREPARE with text/phone reminders, or the additional of a healthcare navigator). To ensure generalizability, we will conduct our work in 3 healthcare systems (HCS): Univ. of CA, San Francisco (UCSF), Univ. of CA, Irvine (UCI) and M Health Fairview (UMN, a collaboration among the Univ. of MN Medical School, Univ of MN Physicians, and Fairview Health Services).<sup>18</sup>

#### UG3 Aims (Establish a trial infrastructure in all 3 healthcare systems):

**Aim 1:** Guided by patient and clinician input, finalize clinics and workflows to implement pre-surgery ACP. **Aim 2:** Optimize and fully define clinically meaningful ACP outcome measures for the surgical setting. **Aim 3:** Pilot-test ACP interventions and outcomes in one clinic in each HCS to ensure feasibility.

#### UH3 Aims (Pragmatic randomized controlled trial (RCT) and evaluation):

**Aim 1:** Conduct an NIH Stage Model III (efficacy-effectiveness)<sup>19</sup> three arm RCT in 3 HCS. Patients aged 65 or older, or with serious illness, who are referred for major elective surgery will be randomized to Arms: (1) Letter about ACP, PREPARE advanced directive (AD), PREPARE website; (2) Letter, AD, PREPARE plus reminder text/phone messages; (3) Letter, AD, PREPARE plus reminders plus a healthcare navigator. *Hypothesis:* Increasingly intense support for surgical patients with regards to ACP will result in increased ACP documentation (discussions and care plans, primary outcome) and patient-reported ACP engagement. **Aim 2:** Use mixed methods to assess patients' and surgical care teams' experience with surgery ACP.

**Aim 3:** Analyze the content of the ACP notes across 3 HCS using natural language processing (NLP) and data mining to begin to identify assess thematic completeness of ACP notes.

*This project is significant, innovative, and feasible.* It uses a model of *expanded* ACP as the foundation to support ACP engagement in older adults undergoing surgery by (1) introducing a <u>patient-directed paradigm</u> for ACP engagement; (2) leveraging <u>existing</u> evidence-based tools in a system-based approach; (3) integrating digital tools including patient portal, text or phone-based reminders and remote healthcare navigators to <u>improve scalability</u>; and (4) involving a <u>transdisciplinary team</u> with expertise in surgery, geriatrics, ACP, implementation science, clinical trials, quality, informatics and data science (with expertise in NLP, datamining, biostatistics), and human factors with a successful track-record of collaboration and HCS embedded research.

# **Research Strategy**

# A. SIGNIFICANCE

**Surgery and the Older Adult:** Everyday, 10,000 people in the U.S. turn 65. The U.S. Census Bureau projects the number of older adults will grow by 55% from 2010 to 2050, eventually making up 21% of the population.<sup>20</sup> Even with current smaller numbers, older adults account for over 40% of inpatient and 33% of outpatient surgical procedures performed annually in the U.S. This is increasingly a public health issue as the number of elderly patients grows, and the need for surgical services rises.<sup>21,22</sup> While operative risk has declined over time, major surgery not infrequently can be associated with complications or worsening health status. This can range from anticipated expected or temporary functional impairment to unanticipated major and long-term functional impairment and even death, particularly in older adults.<sup>23,24</sup> Nearly 20% of patients who die in the U.S. have undergone an invasive surgical procedure in the prior 2 months.<sup>25–27</sup> Risk stratification, predictive tools, and surgeon experience are not reliable in predicting which patients will have major complications.<sup>28</sup> Additionally, although older adults must make major personal decisions in the pre- and postoperative periods, many feel under-prepared and may not be able to de novo articulate their individual care goals well; in some instances, they may not have had a chance to consider or rethink their care goals in the face of a new major diagnosis. As a result, all too often, patients undergo treatments and surgical procedures that are inconsistent with their values and goals.<sup>24,29,3031</sup>

Advance Care Planning (ACP): Advance care planning is the process of understanding and sharing personal values, life goals, and preferences regarding future medical care. Designed to encourage care aligned decisions consistent with patient preference, ACP has traditionally focused on end-of-life treatment preferences (e.g., cardiopulmonary resuscitation (CPR) or mechanical ventilation). Our team and others have worked to expand the ACP paradigm to focus on preparing patients to communicate their medical wishes and make informed medical decisions.<sup>7,8</sup> This *expanded ACP paradigm* (Figure 1997).



1)<sup>32,33</sup> seeks to elicit patients' values about quality of life. These discussions can help align treatment intensity with patient preferences to balance the short-term risks vs. longer-term benefits of surgery and post-surgical complication management.

ACP is also a critical way to support older adults in participating actively with clinicians in making real-time, complex medical decisions so that the medical care they receive is aligned with their goals.<sup>34</sup> Most conversations about patients' goals, values, surrogates, and prognosis, including with palliative care specialists, take place before a medical crisis, as it should be. These conversations, which encompass ACP, focus on preparing patients and surrogates for communication and medical decision-making. There has been some recent controversy over ACP effectiveness due to mixed evidence for care consistent with goals (a historically difficult, unstandardized outcome) and utilization (not a universally accepted patient-centered outcome). However, a recent scoping review of high-quality trials of ACP found decreased anxiety, grief, posttraumatic stress, and burden for surrogate decision makers—a main motivator for patients to engage in ACP.<sup>20</sup> The review found that it is the very individuals who have experience with serious illness decision-making, including patients and surrogate decision makers, who report that ACP is valuable.<sup>20</sup>

**Challenges with Current Implementation of Advance Care Planning in Surgery:** <u>ACP is broadly endorsed</u> <u>as an important quality metric for older adults undergoing surgery</u>. National initiatives and surgical programs have endorsed ACP. Jointly developed guidelines from the American College of Surgeons and the American Geriatric Society delineate that ACP is a care standard for the older adult surgical patient.<sup>10,11</sup> Similarly, the Centers for Medicare & Medicaid Services (CMS) Innovation Center Programs (Innovation Center) through its Bundled Payment Care Initiative Advanced (BPCI-A) Model includes the National Quality Forum ACP measure as one component of the Composite Quality Score calculation to determine participating hospitals' incentive payments.<sup>9</sup> Despite strong evidence and in some cases, financial incentives (e.g., BPCI-A), <u>real-world success is lacking and</u> ACP adoption in surgery remains low.<sup>35,36</sup> Even in clinical trial environments, efforts to effectively integrate ACP into surgical care have repeatedly failed.<sup>37,38</sup> Furthermore, even high-risk individuals undergoing major surgery have low levels of ACP knowledge and engagement.<sup>39,4041</sup> In one study of individuals who died

within 1 year of their surgery, nearly half did not have a designated surrogate decision maker or advanced directive (AD) by the date of their operation.<sup>42</sup> Even with a clinician-directed EHR alert, only 25% of patients who died after undergoing high-risk surgery had completed an ACP.<sup>35</sup> Identified barriers include varying levels of comfort on the part of surgeons for conducting these conversations, lack of dedicated time in the pre-surgical care episode for these often-delicate conversations, and lack of preparedness on the part of the patient, family, and other loved ones before surgery. In some cases, clinicians may rely on the surgical "buy-in" or perception that, by agreeing to surgery, a patient is also agreeing to a variety of life-sustaining treatments.<sup>43</sup> Trials of surgeon-led discussions to elicit patient goals have been done.<sup>44,45</sup> While these can be effective, these interventions require a significant investment of surgeon time for both training and patient-facing discussions and do not appear to be scalable.<sup>37</sup>

**Alignment to National Institute on Aging Goals:** We propose to address these challenges by initiating a transdisciplinary collaboration between surgeons, informaticians, and geriatricians across 3 health systems: University of California, San Francisco (UCSF), University of California, Irvine (UCI) and M Health Fairview (UMN) in Minnesota. We will develop infrastructure and rigorously test a <u>novel approach</u> to integrating ACP into the surgical care episode. Our proposal is also responsive to the NIA Strategic Directions for Research 2020-5 goals C5 (Develop strategies to improve the interaction of older adults with the health system) and G1 (Support the infrastructure and resources needed to promote high-quality research). Our goal is to meaningfully increase the prevalence and quality of pre-surgery ACP for older adults undergoing high risk surgery. Increased ACP discussions and documentation are **essential first steps** in achieving the National Academy of Medicine priority of ensuring goal-concordant surgical care, particularly in the face of post-operative complications.<sup>46</sup>

#### **B. INNOVATION**

This proposal is highly innovative for several reasons. Using the PRagmatic Explanatory Continuum Indicator Summary (PRECIS-2) criteria<sup>47</sup>, the proposed NIH Stage Model III (efficacy-effectiveness) approach is *highly pragmatic*.<sup>1919</sup> Key innovations and the overall impacts of our current proposal are designed to move the surgical and ACP fields forward using pragmatic, technology, and data-driven approaches, including:

**Use of an Expanded ACP paradigm:** We propose to apply and rigorously evaluate a patient-centered, expanded ACP paradigm and existing PREPARE tools (validated in primary care settings) in the novel setting of pre-major elective surgery for older adults and patients with serious illness.<sup>48</sup> We will address historical concerns with ACP (outdated models of a checkbox approach focused on hypothetical end-of-life treatment preferences) by using the <u>expanded the ACP paradigm focused on</u> preparing people and their caregivers for communication and ongoing in-the-moment decision making.<sup>7,8,13,20,35,49–54</sup> The *expanded ACP paradigm* will be **newly applied to the pre-surgical context**.

Leveraging Technology and Digital Approaches to Scale Our Approach: We are leveraging a range of technology-driven approaches including the interactive PREPARE website, reminder automated text-based and/or automated phone calls to nudge patients and remote healthcare navigator to help patients with ACP. The technology solutions proposed will be integrated with the EHR. This is a highly efficient and more cost-effective way to conduct our research and engage patients as well as ensure sustainability of the valuable elements. The goal of this strategy is to enable older adults who are being evaluated for major elective surgery (e.g., referred to a surgeon for evaluation in the clinic) to prepare for and engage in goals of care conversations with their surgical care teams, to re-assess their overarching treatment goals, and ultimately, hopefully, promote goal-concordant surgical care. Ultimately, we will leverage the pragmatic trial data with data science and natural language processing to define and better predict surgical patients in need of additional support (e.g. postal mailed materials and/or healthcare navigator) to engage with ACP and begin to understand the content (and quality) of ACP notes in the EHR.

**Engaging Patients as Change Agents:** Guiding a patient and their proxy(ies) through medical decision-making requires that the care team understand each patient's preferences and values. Despite rigorous efforts to integrate ACP into the surgeons' workflow, very large barriers exist, including varying levels of familiarity and comfort to conduct ACP conversations, lack of dedicated time in the pre-surgical care episode for these often-delicate conversations, and lack of appropriate patient-facing ACP tools to prepare patients and caregivers for complex decisions about surgical treatment.<sup>38</sup> *Our proposed solution is innovative because it is patient-facing and enabled with technology that prepares older adults for conversations with the surgical care team and beyond*. Our approach does not make new demands on care teams but instead empowers the patient by using evidence-based approaches to be an active participant in achieving better care.<sup>2,13,35</sup>

**Pragmatic Intervention:** For the past 10 years, NIH has expanded the footprint of pragmatic trials which help inform a clinical, operational, or policy decision to guide adoption into real-world practice.<sup>55</sup> For this reason, pragmatic trials are ideal for informing population-level interventions such as ACP for which spread will rely heavily on <u>feasibility</u>.<sup>47</sup> However, a major barrier in the field of ACP has been the challenge of moving from small, proof-of-concept studies to large-scale implementation that fits with workflow and can be sustained.

**Scaling Learnings with a Surgical Learning Health System and Informatics-Driven Approaches:** Surgical fields have been slow to embrace data-driven and iterative learning interventions, including pragmatic trials, which is a significant missed opportunity for rapid dissemination and implementation of evidence-based practice and discovery of new knowledge. Surgical disciplines have also been slower to innovate using health IT and advanced analytics approaches to improve care delivery.<sup>41</sup> Our proposed approach is novel in its application of informatics in surgery, with which we have significant experience, including leveraging (1) EHR and digitally-delivered patient "reminders" (previously done to encourage preventive care and to decrease use of opioid in the postoperative setting, UMN) to improve ACP completion, (2) EHR-embedded randomization, at the patient level, for the 3-arm pragmatic trial, and (3) using advanced informatics approaches including natural language processing (NLP) and machine learning to understand both factors associated with ACP discussions and actual documentation including the impact of the interventions on the components of the goals of care documentation.

Overall, many of the learnings from the relatively low-cost and generalizable frameworks and approaches (e.g., learnings on patient readiness around ACP, health IT design and usability for older surgical patients, surgical workflow learnings, organizational change management) will be generalizable to other gaps beyond ACP and/or other specialties beyond surgery and/or scalable to other HCSs.

Similarly, learnings from our proposed work will extend our knowledge and capabilities for NLP in the context of ACP related notes. Current reports around using NLP with ACP related notes have utilized approaches which are primarily rule-based with regular expressions to extract conceptual information related to specific ACP themes.<sup>57</sup> Moreover, this approach, when used to extract information from several sites used different rules, approaches and annotation standards, which ultimately suffers from a lack of reproducibility or external validity. This approach uses a rule-based and deterministic method without ensuring consistency of findings (e.g., reliability of the annotated ACP note gold standard) when applying the NLP tool between clinical sites.<sup>57</sup> We propose using robust and state-of-the-art deep learning approaches expanding upon a gold standard, as well as to conduct external validation at each of the sites, which will be a contribution on its own, to a scalable approach to unlocking content in clinical notes related to ACP. Immediately, as part of the proposed work, the NLP results will provide insight into the quality and completeness of ACP documentation in 3 HCS in general and as an adjunct pragmatic randomized clinical trial finding. Ultimately, as a future direction, we will begin to examine intensity of care to gain deeper insights about associated factors with ACP information elements and goal concordant care.<sup>58–60</sup>

# C. APPROACH

#### C.1. PRELIMINARY DATA

National Leadership in Designing and Testing a Rigorous Interactive ACP Tool, PREPARE for Your Care: PREPARE is a patient-facing, theory-based, interactive online program (prepareforyourcare.org), *developed and* 

evaluated by R. Sudore, MPI, that supports older adults to prepare for and engage in ACP discussions and decision-making for medical care. To reduce cognitive burden, PREPARE was written at a 5th-grade reading level and includes voice-overs of all text, closed-captioning, and culturally sensitive videos that model ACP behaviors (in English and Spanish) and written materials in several languages (i.e., English, Spanish, Mandarin, Cantonese).<sup>50</sup> PREPARE was designed to be used by older adults in primary care <u>before a primary care office visit</u>. The original PREPARE technology solution was co-created in collaboration with patients, caregivers, and providers. Based on extensive developmental work with these key advisors and endusers (including 13 focus groups with 69 ethnically diverse older adults), the PREPARE program was designed to walk patients through the following 5 Steps: 1) Choose a Medical Decision Maker, 2) Decide What Matters Most in Life, 3) Choose



Flexibility for Your Decision Maker, 4) Tell Others About Your Wishes, and 5) Ask Medical Providers the Right Questions (**Figure 2**).

Figure 2: PREPARE

**Rigorous Demonstration in RCTs that PREPARE deployment is Improves ACP Engagement and is Feasible:** In two RCTs with over 1,400 primary care patients (86% retention rate) demonstrated that the PREPARE technology solution plus the PREPARE easy-to-read ADs versus the AD alone resulted in a higher rate of ACP documentation (43% vs 32%; p < 0.001) and higher self-reported ACP engagement scores (98% vs 89.5%; p < 0.001).<sup>12,13,50,61</sup> The PREPARE tools are patient-facing, meaning they <u>needed no additional clinician</u> <u>or system-level interventions</u>. Importantly, these RCTs demonstrate that the PREPARE program: a) can successfully engage patients in general ACP, b) can be completed even in older patients with limited health literacy (nearly 40%), and c) pre-visit patient engagement directly affects primary care visit interactions, ACP documentation, and patient involvement in their own care. Despite the success of PREPARE it has not been tested in a pre-surgical setting.

Experience with system-level real-world incorporation of ACP tools (PREPARE) into primary care workflows at UCSF and UCI sites: Providing access to the PREPARE program through automated EHR patient portal messages has been evaluated in the UCSF primary care setting, demonstrating both feasibility and effectiveness. Messaging was directed to primary care patients  $\geq$ 65 years of age and those with serious illness (identified via EHR algorithm, currently in place and validated at UCSF and UCI)<sup>48</sup> in 3 of the general medicine clinics (~35,000 patients). This population is 45% non-white, 10% Hispanic/Latino, and 60% women spanning 11 clinics. The impact of this has been significant with an increase of ACP documentation (conversations, ADs, and surrogates increasing from 18% to 54% over 1.5 years and from 60% to 86% in patients with serious illness. Based on the positive impact, a pragmatic cluster RCT with primary care patients was approved and is being conducted at UCLA, UCSF, and UCI (R. Sudore, MPI; UCI: L. Gibbs, Co-I, participated; Patient Centered Outcomes Research Institute PLC-1609-36291). The study has completed patient accrual and analysis is ongoing.

Current UCSF Pilot in Older Adult Surgical Patients with Patient Portal ACP Messaging Demonstrates that our Proposed Intervention is Feasible and Acceptable: Recognizing the gap in ACP in surgical patients and the challenges associated with the integration of ACP into the surgeon workflow, we interviewed older surgical patients (n=10, E. Wick, unpublished data) at UCSF to understand barriers, facilitators and potential acceptability of patient portal delivered ACP materials for presurgical patients. Patients were receptive to being messaged prior to the initial consultation, acknowledged the time pressures in surgical clinics, and were open to support from team members other than the surgeon for ACP. Patients that had AD frequently did not share with surgical care teams because the opportunity was not afforded. Patients emphasized the desire to focus on procedural details with the surgeon as opposed to discussing ACP-related items. Advanced practice providers and nurses were identified as potential team members to support ACP completion. Provision of PREPARE through the EHR patient portal has just been initiated in a couple of surgical clinics at UCSF (the arm 1 intervention). Patients ≥65 years, scheduled for surgery receive the messages, with 63% (261 out of 417 letters opened on the day received) of the messages read (compared to 50% in primary care (1,365 out of 2,739 letters)

opened on the day received, p<0.05), suggesting promising patient engagement with ACP messaging. To avoid contamination in the proposed trial, these pilot clinics will be excluded.

**Experience with Clinical Decision Support (CDS) Implementation, Workflow Optimization, and Advanced Methods with Risk Modeling**: We have broad experience with health information technology (IT) including development and implementation of solutions to promote patient engagement in health-related activities and follow-up care<sup>62,63</sup>, evaluation of health IT implementation in terms of usability for care team and patient workflows, as well as development and implementation of CDS to promote adoption of evidence-based care including with patient engagement health IT solutions.<sup>64–66</sup> SCALED (SCaling AcceptabLE cDs) represents an approach for scaling sharable CDS. Recently, UMN used SCALED for a CDS system for thoracic trauma patients that was developed externally.<sup>67</sup> To overcome design and adoption barriers, the CDS was delivered across 6 clinical disciplines and customized to patient factors. Suggestions were risk stratified into one of three pre-checked order sets with tailored recommendations to patient renal function. Evidence was directly delivered to providers and caregivers at the point of care via HTML embeddings within the EHR.

Our team also has substantial expertise in risk modeling with both chronic and acute diseases, including type 2 diabetes, sepsis, postoperative complications including externally validating machine learning models at both UMN and UCSF<sup>68–71</sup>, and a novel COVID-19 predictive model currently in use to triage patients to various levels of care. We have also developed several novel methodologies for most aspects of clinical knowledge discovery and risk modeling, including missing value imputation, data representations, causal phenotypes, consensus modeling quantifying the effect of continuous and binary interventions in heterogeneous subpopulations, and use of external data for improving predictive accuracy.<sup>72,7374–85</sup>

**Promising Natural Language Processing (NLP) Findings with Extracting Core Elements of Serious Illness Conversations and Patient Goals of Care from Palliative Care Notes:** In order to explore the feasibility of utilizing NLP to extract meaningful data elements from ACP documentation, we applied an established framework which defines core dimensions of serious illness conversations.<sup>86</sup> After constructing a set of annotation guidelines for the dimensions of legal documentation, decision-making, goals, abilities, and tradeoffs, a total of 226 palliative care documents were annotated by three annotators (inter-rater reliability Fleiss's Kappa = 0.726 over 50 notes). Using a state-of-the-art sequence deep-learning model (BERT-base-uncased) modified for multi-label classification and fine-tuned for the above data dataset similar to an approach we have used previously<sup>87</sup>, the NLP model demonstrated the ability to extract the various aspects of serious illness conversations (F-scores with 5-fold cross-validation: overall, legal documentation, decision-making of 0.78, 0.90, 0.75, respectively).

When we applied our NLP artificial intelligence/machine learning (AI/ML) model to an overall corpus of 12,946 palliative care notes, we observed variation in the frequency that goals of care were documented for any goal of care with decision-making, abilities, goals, or tradeoffs; or legal documentation documented 94%, 81%, 86%, and 85% of the time, respectively. In anticipation of our upcoming multi-institutional NLP collaborative work, we have also successfully shared a large set of UCSF de-identified ACP notes with UMN for the purposes of research (protocol approved and determined non-human subjects research, respective UMN and UCSF material transfer agreements and data management plans in place). These notes will be used for external validation of our NLP ACP model at UCSF and extended NLP model development for additional high impact data elements and ACP themes.

Low ACP Completion Rates Demonstrating Opportunities with Older Adults Undergoing Surgery: Together, UCSF, UCI and UMN evaluate ~5,600 older adults for major elective surgery (primary study population). The <u>one-year mortality</u> for the proposed population is approximately 9% (Table 1). For older adults undergoing high-risk surgery, <u>enrollment in the patient portal is relatively high (80</u>%) but ACP <u>completion is low</u> (15%) at all three HCS (Table 2, next page) with new and/or updated ACP documentation within 3 months of surgery very low. This data <u>suggests a tremendous opportunity for a systems-based intervention</u> *leveraging the EHR to improve ACP discussions and documentation in this highrisk population*.

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Table 1: UCSF Cumulative mortality (age 65+ elective major surgery, EHR data linked to California death registry								
In-Hospital Mortality	0.73 %							
30-Day Mortality	1.32%							
90-Day Mortality	3.28%							
6-Month Mortality	5.62%							
1-Year Mortality	9.19%							

Institutional Leadership as Age-Friendly Healthcare Systems: Both UCSF and UCI have been recognized by the Institute for Healthcare Improvement (IHI) as an

Age-Friendly Health System - which is the highest level awarded for geriatric care. The Center for Surgery for the Older Adult at UCSF (led by Department of Surgery, UCSF) was a "one stop shop" for functional and cognitive

assessments, prehabilitation, and assistance with ACP before surgery.<sup>88</sup> While evaluations were helpful, patients and caregivers were challenged to travel to additional appointments in the tight presurgery window, and the health system could not support the additional staffing. The clinic was halted in 2017 and <u>new approaches leveraging</u> existing infrastructure are needed.

# C.2. INVESTIGATIVE TEAM

Our team and its expertise, including associated staff at each institution, is depicted in **Figure 3**, **page 8**. The proposed team includes experts in all key project tasks as well as HCS leaders at UCSF, UMN and UCI who are experienced in surgery, perioperative, data and EHR inner workings. The latter being *essential* for timely execution of embedded HCS research. Importantly while the 3 HCS group is new, <u>all team</u> members have collaborated with one or more members of the team from



prior to the proposed work including on federally funded grants. Successful study-related EHR changes and complex data exchanges have been accomplished by all 3 HCS.

# Our team consists of the following core team members <u>who have a history of related collaborations and</u> <u>conducting successful health system embedded research:</u>

# Core Team and Associated Expertise

**E. Wick, MD (MPI):** Professor of Surgery at UCSF and Chief Perioperative Quality and Safety Officer at UCSF Health. She is an expert in quality improvement, change management and organizational culture as it applies to surgery. She was the first to apply the comprehensive unit-based safety program (CUSP) to surgery.<sup>89–93</sup> She has published broadly and <u>scaled efforts</u> in surgical site infection and surgical pathways from one to hundreds of hospitals (in collaboration with American College of Surgeons, letter of support, C. Ko). She leads the AHRQ ACTION III Network, AHRQ Safety Program for Improving Surgical Care and Recovery, a 300+ hospital collaborative aimed at accelerating adoption of evidence-based clinical pathways along the care continuum in surgery.<sup>94–99</sup> Preliminary findings are promising with significant improvements in patient length of stay and complications associated with successful implementation, with extensive evaluation of fidelity to intervention.

**G. Melton, MD, PhD (MPI)**: Professor of Surgery and Health Informatics at UMN, President of the American College of Medical Informatics, Director for the Center for Learning Health System Sciences (CLHSS) and Associate Director of the Clinical NLP program at UMN. Her expertise is in clinical NLP, biomedical standards, real world data for quality and value, in line with her role as Chief Analytics and Care Innovation Officer at M Health Fairview and External Advisory Board Member of National Covid Cohort Collaborative and National Center for Data to Health.<sup>56,62,80,100–108</sup> She has published extensively on social and behavioral health data, leveraging EHR and artificial intelligence/machine learning for research, patient care, and clinical NLP.<sup>67,107–110</sup> She also leads implementation of evidence-based practices at M Health Fairview and the UMN CLHSS, which features the Rapid Prospective Evaluation (RapidEval) Unit, that conducts pragmatic trials to test health care practices at scale in real-world settings.

**R. Sudore, MD (MPI):** Professor of Medicine at UCSF and a geriatrician, palliative medicine physician, implementation scientist, and Director of the Vulnerable Aging Recruitment and Retention Core (VARC) of the NIA-funded Pepper Center and the Innovation and Implementation Center of Aging & Palliative Care research (I-CAP). Her research focuses on aging, health literacy, health disparities, and developing and testing tools to facilitate health communication and informed medical decision making for historically marginalized older adults. For example, she designed and tested easy-to-read advance directives which have been adopted nationally. She also developed modified informed consent procedures for older adults with limited health literacy and limited English proficiency which have been included in national IRB guidelines. In addition, R. Sudore helped to develop a *new expanded advance care planning (ACP) paradigm* that shifts the focus from the pre-specification of life-prolonging procedures to preparing patients and caregivers to participate with clinicians in making in-the-moment decisions. To operationalize this paradigm, she developed the patient-centered ACP PREPARE for Your Care program. PREPARE provides video stories that teach people how to identify what quality of life means to them; how to communicate their ACP wishes with family, friends, and clinicians; and how to make informed medical decisions. She has completed randomized trials of the PREPARE program demonstrating its efficacy among

English- and Spanish-speaking populations and conducted a pilot study among patients with mild cognitive impairment and caregivers. She also has extensive expertise with community engaged research, the inclusion of historically marginalized populations in the research process, the use of implementation science methods to develop interventions and assess their feasibility in real-world settings, and in the recruitment, retention, and informed consent for marginalized, older populations.

J. Carmichael, MD (co-I, site PI UCI): Professor of Surgery and Chief Medical Officer UCI Health. His expertise is in colorectal surgery and has served as the director of perioperative services for UCI and led important health system initiatives including deployment of electronic surgical consents. In addition, he led the University of California Office of the President Surgical Collaborative around dissemination of enhanced recovery pathways. J. Carmichael and E. Wick are collaborating as co-Is with Susan Huang, MD (PI) on the DECREASE SSI trial, funded by AHRQ in 2022. As Chief Medical Officer, J. Carmichael, co-develops UCI Health strategic priorities and currently ACP is a HCS priority.

L. Gibbs, MD (co-I): Regan Endowed Professor of Medicine, Chief of Geriatrics and Director Population Health UCI Health will work closely with J. Carmichael to support the UCI team. She has worked closely with R. Sudore on the UC Health Care Planning study (PCORI) and is the site PI for UCI.

**J. Boscardin, PhD (co-I):** Professor of Medicine and Epidemiology & Biostatistics at UCSF and a biostatistician. He is the Director of the Statistical Laboratory in the UCSF Division of Geriatrics, Co-leader of the UCSF Pepper Center Data and the Data Analytics Core. With R. Sudore, he has led the design and analysis of ACP-related pragmatic clinical trials evaluating effectiveness of interventions for older adults

J. Koopmeiners, PhD (co-I): Mayo Professor and Head of Biostatistics in the School of Public Health at UMN. Dr. Koopmeiners is an expert in Bayesian adaptive methods for clinical trials, biomarker validation, and causal inference. The current focus of his methodological research relates to the development of Bayesian methods for multi-trial data integration and statistical methods for elucidating treatment effect heterogeneity from randomized clinical trials. Currently, he serves as PI of an R01 to develop novel causal inference methodology for tobacco regulatory science. In addition to his methods research, he also has extensive experience in coordination and analysis of multi-site clinical trials. He is the Director of the Biostatistics and Data Management Core for the Center for the Evaluation of Nicotine in Cigarettes (CENIC) and he was previously co-PI of the Data Coordinating Center (DCC) for the Angiotensin receptor blocker-based Lung Protective Strategy for COVID-19 (ALPS-COVID) clinical trials. He was the unblinded statistician for Partnership for Research on Ebola Virus in Liberia II (PREVAIL II) and Accelerating COVID-19 Therapeutics and Vaccines – 3 (ACTIV-3).

<u>Collective Clinical Trials Experience:</u> We have convened a complementary team that has diverse clinical trial (see clinical trial experience table) and implementation experience in advanced care planning, surgery, and health informatics. R. Sudore is a leading ACP clinical trialist and has collaborated with L. Gibbs at UCI in an analogous clinical trial in primary care. J. Carmichael has served as the site PI or co-I for some of the leading clinical trials in colorectal surgery including the ROLARR (Robotic vs Laparoscopic Resection for Rectal Cancer) and OPRA (Organ Preservation in Rectal Cancer) and has recently begun collaborating with E. Wick, UCSF in the DECREASE SSI trial funded by AHRQ (PI, Susan Huang, MD, UCI). G. Melton has led and collaborated on multi-institutional EHR embedded pragmatic trials funded by AHRQ and NIH. Finally, E. Wick has led or co-led two of the largest AHRQ ACTION<sup>111</sup> network surgical implementation and dissemination programs – AHRQ Safety Program for Surgery and AHRQ Improving Surgical Care and Recovery. While not clinical trials, the AHRQ ACTION network programs involve dissemination of surgical quality and safety toolkits to hundreds of hospitals and the ACTION network learnings will inform HCS collaboration and dissemination.

**Project Team Structure for Large Scale Implementation:** Throughout the UG3 and UH3 phases, bi-weekly team meetings consisting of the core team consisting of MPIs (E. Wick, R. Sudore and G. Melton), site-PI UCI surgery (J. Carmichael) and co-I UCI geriatrics (L. Gibbs), and statistical investigators (J. Boscardin and J. Koopmeiners) plus research coordinators from each site will review upcoming project deadlines and coordinate local efforts. Informatics and regulatory leads at each site will be included in the agenda as applicable. This will be complemented by site-specific meetings. We collectively have experience managing complex multi-site projects (E. Wick - Agency for Healthcare Research and Quality (AHRQ) ACTION II Network Safety Program for Surgery and AHRQ ACTION III Network Safety Program for Improving Surgical Care and Recovery; R. Sudore - Patient Centered Outcomes Research Institute (PCORI) and NIH, G. Melton - AHRQ R18 Multi-site Interoperability Pragmatic Trial on Anticoagulation CDS) and recognize the importance of clear communication lines, collaboration/coordination, timeliness and transparency.

# Importantly, we have garnered critical leadership support at each HCS, including members of the project team with leadership positions and other key leadership proponents for the project, including:

## **UCSF Health:**

- E. Wick, Chief Perioperative Quality and Safety Officer UCSF Health
- Letters of Support from Chief Clinical Officer, UCSF Health (J Adler), Chief Health Information Officer UCSF Health (R. Cuccina) and Vice President Population Health UCSF Health (G Intinarelli), Chair of Surgery (J.A. Sosa) and Chair of Anesthesia (M. Gropper).

# UCI Health:

- o J. Carmichael, Chief Medical Officer UCI Health
- L. Gibbs, Director, Population Health UCI Health
- Letters of Support from CEO UCI Healh (C. Lefteris)

# M Health Fairview

- G. Melton, Chief Data and Analytics Officer M Health Fairview
- Letters of Support from CEO Fairview (J Hereford), CQO M Health Fairview (A. Jacob), Chair of Surgery (S. Ikramuddin), Chair of Anesthesia (M. Wall)

Overall, the investigative team has the expertise needed to ensure that the study and its findings will have maximal impact and rigorous evaluation. Our team members also have expertise in data mining and machine learning including NLP (G. Simon, PhD, B Knoll, G. Melton), human factors (J. Marquard, PhD, R. Rizvi, MD, PhD), ethnography/qualitative evaluation (D. Dohan, PhD, R. Rizvi, MD, PhD), and implementation science (D. Peska, PhD, PharmD).



# C.3. RESEARCH DESIGN AND METHODS

The research design and methods for the UG3 phase is described, followed by the UH3 phase. The overarching goal of the proposal is to evaluate 3 related but increasingly resource intensive ACP interventions in a pragmatic randomized controlled trial at the patient level (**Figure 5**).

# C.3.1. UG3 Planning Phase

# Overview of UG3 and its relationship to UH3:

We will establish the **organization**, **processes**, and **infrastructure**, **particularly technology related**, necessary to conducting a pragmatic 3 arm randomized controlled trial (<u>UH3 aim 1</u>) for patients age 65+ referred for major elective surgical intervention (**Table 3**).

Table 3: <u>UH3 Aim 1</u> Pragmatic trial of ACP in surgery <b>overview</b>								
Study Design	Randomized controlled pragmatic clinical trial							
Study	Older Adults (age 65+) or any patient with a serious illness referred for surgical							
Population	evaluation							
Exclusions	1. ACP on file within 6 months prior to surgery							
	2. Prior ACP-related patient portal messages from primary care (UCSF and UCI)							
Intervention	Increasing intensity of ACP-related messaging prior to surgical visit							
	<ul> <li>ACP related letter, AD and PREPARE sent via patient portal and postal mail</li> </ul>							
	• Arm 1 PLUS reminder messages via patients preferred messaging (text or							
	telephone)							
	<ul> <li><u>Arm 2 PLUS</u> healthcare navigator support to complete ACP</li> </ul>							
Randomization	1:1 randomized block design stratified by enrollment site; within enrollment site, further							
	stratified by surgical clinic							
Study Follow Up	Total Duration: 6 months after initial messaging							
Outcomes	PRIMARY: Advanced Directive (Living Will and Durable Power of Attorney) or out of							
	hospital DNR or Physician Orders for Life-Sustaining Treatment or ACP note in EHR*							
	SECONDARY: Patient engagement in ACP (11 question survey)							

First, we will finalize the surgical clinics at UCSF, UCI and UMN to be included in the pragmatic trial and then we will evaluate new patient referral, scheduling, and workflows across the 3 HCS to create a standardized approach to integrating the ACP messaging into the patient portal with follow up reminders. The approach will be aligned with patient and surgical care team workflows and scalable to all the intervention clinics (UH3 aim 1). The UH3 aim 1 trial will use established EHR systems at each HCS to obtain the ACP-related primary outcome and in UG3 aim 2, we will work to ensure they are attainable and accurate in all HCSs. Finally, the EHR tools (patient identification (inclusion/exclusion criteria), patient portal, and reminder messaging developed for administering the trial will be tested in 1 clinic in each HCS to ensure that they are reliable and accurate.

In addition to the UG3 Aims outlined, regulatory approvals will be obtained, and plans reviewed and coordinated with oversight bodies (Data Safety Monitoring Board, National Institute of Aging, NIH Collaboratory) during the UG3 phase.

# Settings for the Proposed Intervention:

<u>UCSF</u>: The intervention will take place in UCSF Health surgical clinics. UCSF Health is a non-profit health system based in the San Francisco Bay Area. The surgical services see patients in the UCSF Health facilities across the City of San Francisco and complete 22,000 adult operations across at three inpatient hospitals with greater than 1,000 licensed beds. Urology, Orthopedics and Neurosurgery specialty services are among the best in the country. Since 2013, UCSF Health has used Epic as its EHR and has supported embedded EHR research and reporting via the Center for Translational Science Investigations subgroup, APeX Enabled Research (see LOS) and researchers can access the clinical data warehouse.

<u>UCI:</u> The intervention will take place in UCI Health surgical clinics. UCI is a non-profit health system in Orange County, California and includes the UCI Hospital (420-beds) and the Chao Family Cancer Center, an NCI-designated comprehensive cancer center. Since 2016, UCI Health has used Epic as its EHR with data flowing

to a clinical data warehouse. Surgical services relevant to the proposed work include cardiac and thoracic, urologic, colorectal, head and neck, endocrine, esophageal, hepatobiliary, gynecologic oncology, vascular, spine, arthroplasty, and brain tumor surgery.

<u>UMN:</u> The intervention will take place primarily in University of Minnesota Physician and Fairview Health Services Medical Group surgical clinics. Fairview Health System and University of Minnesota Physicians are academic and strategic partners. University of Minnesota Physician is the physician group representing the faculty at UMN. Fairview is a non-profit community-based health system based in the Twin Cities and greater Minnesota. Since 2003, Fairview Medical Group has used Epic as its EHR with hospitals implementing Epic since 2012 along with University of Minnesota Physician clinics. As such, all data flow through a shared research infrastructure established through the University of Minnesota Clinical Translational Science Institute which includes the Learning Health System data platform supporting pragmatic interventions, real world data analysis and rapid iterative learning based at Fairview and University of Minnesota Physicians.

#### Infrastructure Development:

**Establishment of Program Infrastructure:** Most broadly, we will adhere to <u>best practices for conducting clinical</u> <u>research</u>. We will register our study on clinicaltrials.gov, pre-specify the primary and secondary outcomes, and pre-specify analytic plans, including any sub-group analyses. We will also record and make public the algorithm that we use for randomizing patients.

**Single Institutional Review Board (IRB) Oversight:** To expedite review and ensure timeline adherence, Advara will serve as the single IRB. UCSF has a reliance agreement with Advarra for low-risk studies and UCI and UMN have agreed to rely on Advarra (see **single IRB plan**). Before the study begins, all sites will sign an authorization/reliance agreement that will clarify the roles and responsibilities of the IRB and participating sites. UCSF will maintain records of the authorization/reliance agreements and of the communication plan. Our investigator group is well versed in multi-center studies and national trials requiring a single IRB with reliance agreements. We anticipate that the pragmatic trial will not require informed consent (UH3 aim 1) but written informed consent will be obtained from patients participating in the ACP engagement survey (baseline and 6 month follow up, UH3 aim 1) and/or interviews (UH3 aim 2). For a full description of IRB considerations, see **Protection of Human Subjects**.

**Data Safety Monitoring Board (DSMB):** The DSMB will meet throughout the life of the grant. It will be convened within the first two months of the grant and will meet quarterly. The DSMB will provide oversight and input to all aspects of trial conduct, specifically addressing HCS barriers and needed pivots in study administration. We fully anticipate that leadership changes, staff turnover, and new local or national policies could occur during the project that may require a change of plan. Therefore, we have identified a small but knowledgeable team to serve in an advisory capacity (see LOS from each member).

#### DSMB External Advisors

- (1) <u>Rebecca Hubbard, PhD</u>, Professor of Biostatics, University of Pennsylvania. Expertise application of methods to improve analyses using real world data sources including from claims and the EHR. She has expertise in large trials in the aging, cancer, and primary care.
- (2) <u>Fabian Johnston, MD</u>, Associate Professor of Surgery, Division Chief GI Surgical Oncology, Johns Hopkins. Expertise – pragmatic trials; community-based research in palliative care and surgery, engaging diverse patient populations in surgical studies.
- (3) <u>Peter Pronovost, MD, PhD</u>, Professor of Anesthesia and Critical Medicine, Chief Quality Officer and Chief Transformation Officer, University Hospitals and Case Western Reserve School of Medicine. He oversees quality and population health for University Hospitals Health System, the largest health system in Northeast Ohio with over 15 hospitals. Expertise - learning health systems, change management, healthcare system safety culture, critical care, preventable harm, scaling quality initiatives via HCS, state and national quality safety collaboratives (central-line associated blood stream infections, comprehensive unit safety program, AHRQ) and real-world data.
- (4) <u>Anne Walling, MD,</u> Associate Professor Medicine, Chief of Palliative Care, UCLA School of Medicine. Expertise advanced care planning, quality improvement, pragmatic trials, quality measurement, and palliative care.

**Patient Advisory Group:** The patient perspective will be essential to incorporate into both the UG3 and UH3 phases. Two to three patients, who have been evaluated in and undergone major elective surgery in the past couple of years, per HCS will be identified by E. Wick (UCSF), G. Melton (UMN) and J. Carmichael (UCI) or team member and invited to serve on the patient advisory group. The Center for Community Engagement in the UCSF Clinical and Translational Science Institute will be consulted (see LOS) to ensure best practices for community engagement are followed and assist in engaging diverse voices. Members of the patient advisory group will be compensated for meetings and material review.

**NIH Collaboratory Workgroup Participation:** The project team looks forward to participating in collaboratory workgroups and anticipate biostatistics and study design (J. Boscardin, J Koopmeiners, and/or R. Sudore), electronic health record (E. Wick and/or G. Melton), healthcare system interactions (E. Wick, G. Melton, J. Carmichael, L. Gibbs and/or R. Sudore), ethics and regulatory (G. Melton and/or R. Sudore) and patient centered outcomes (E. Wick, G. Melton and/or R. Sudore) would be the most relevant.

#### C.2.2. UG3 Aim 1: Guided by patient and clinician input, finalize clinics and workflows to implement presurgery ACP in 3 HCSs.

**Rationale:** In other non-procedural specialties (e.g., primary care, medical oncology, hospital medicine), integrating technology, such as patient portals, has shown promise in helping patients and/or clinicians improve patient engagement in ACP. A systems-based approach using the EHR and PREPARE to increase ACP engagement has been implemented, led by R. Sudore, MPI, in UCSF primary care clinics as both a clinical demonstration project and a PCORI-funded pragmatic trial. Although the investigators are still blinded to the intervention arms, the preliminary impact is promising (see Preliminary Data).

Patients' interactions with the care team in the context of surgery are somewhat different from those of primary

care. The relationship is new and often finite, unlike primary care which is longitudinal. Particularly for older adults, the need for major surgery often signals a change in a health condition that may invoke an added sense of urgency for engaging in ACP discussions and/or documentation or updating their prior ACP preferences. Therefore, <u>we hypothesize that the time-sensitive nature of major elective surgery combined with the change in a health condition associated with the need for surgery presents a **unique** opportunity to "nudge" patients to engage in the ACP conversations and documentation, leading to increased patient-centered ACP documented in the EHR.</u>

Much ACP intervention content (PREPARE and the easy-to-read ADs) is transferable from primary care to surgery. In addition, the EHR build, content, and timing of messages and reminders tailored to the surgical context, and healthcare navigator workflows have been adapted for surgery as part of a UCSF HCS pilot (see preliminary data, above). Based on preliminary qualitative interviews conducted at UCSF, surgical patients are receptive to being prompted for ACP before surgery. Early findings suggested that surgical patients are more comfortable receiving the information **early** in the relationship with their surgeon as opposed to immediately before surgery, but greater insight is needed to refine the timing with regards triggers for initiating the reminder messages as well as the detailed wording of the messages about ACP and reminder messages.

**Approach:** We will first finalize the surgical clinics that will participate in the UH3 trial in each HCS (**Table 4 for preliminary UCSF surgical clinic list, similar data available at UCI and UMN**). The goal is to focus on surgical clinics that (1) evaluate patients for <u>major</u> elective surgery (i.e., surgical procedures that usually require an inpatient hospitalization and/or significant recovery) and (2) have a high number of new patients for which the surgeon recommends major elective surgery

Table 4: Proposed UCSF									
Surgical Clinic (UCSF)	New Patient Visits for Patients Age 65+								
Orthopedic Surgery (arthroplasty and spine)	3,187								
Neurosurgery ( <u>brain</u> and spine)	1,694								
Urologic Oncology	1,556								
Otolaryngology, Head and Neck Surgery	776								
Surgical Oncology	551								
Vascular Surgery	474								
General Surgery	441								
Colorectal Surgery	388								
Thoracic Surgery	311								
Endocrine Surgery	300								
Gynecologic Oncology	266								
Orthopedic Surgical Oncology	219								
Head & Neck Cancer Center	178								
Cardiothoracic Surgery	170								
Total	10,511								

(i.e. a high number of patients referred to the clinic are in need of surgery, termed "yield"). It is anticipated that general, colorectal, endocrine, thoracic, cardiac, vascular, orthopedics (spine and arthroplasty), neurologic, urologic and head and neck surgery clinics will participate in each HCS. Collectively, across the 3 HCSs annual new patient visits in these areas far exceeds the target trial enrollment. Therefore, there is opportunity to further refine the list per input during the UG3 phase to ensure feasibility and engagement in those included in the clinic

final roster for the pragmatic trial. Surgical clinics that offer a significant amount of non-operative management and minor surgical procedures will not be included (e.g. ophthalmology, audiology, hand, foot and ankle, and plastic surgery) and are not included in Table 2 or 4 volume estimates. Transplant surgery will not be included because of the unique workflow and regulatory requirements for new potential transplant patients as well as the long period between initial evaluation and surgery. All 3 HCS have strongly endorsed the work and E. Wick, G. Melton, and J. Carmichael, are knowledgeable and collaborative with their surgical colleagues and have previously done and are able to implement system-level surgical interventions in their respective HCS.

Prior work in the preoperative phase of surgical care (ACTION III Network AHRQ Safety Program for Improving Surgical Care and Recovery) leads us to anticipate that even in a single clinic, there will be variations by surgeon and patient with the <u>timing of decision for surgery</u> (e.g., in clinic or after additional testing) and mechanics of requesting and scheduling surgery (e.g., surgeon, advanced practice provider, surgical resident or fellow, done with patient at time of visit, or asynchronously). With these variations, <u>we will ideally focus reminder messages</u> in a close time frame around the initial surgical consultation visit for the pragmatic trial. The anticipated initial triggering event for the patient portal ACP message will be a new **surgical consultation visit** with the concept that ACP is part of preparing for the visit. This is aligned with the successful pilot initiated in a few UCSF surgery clinics in Spring 2022 (see preliminary data).

Informed by the surgical clinic pilot (Figure 4) and guided by patients and clinicians from surgical clinics that will participate. we will further map the presurgery workflow from the initial consultation to the surgical procedure itself in the 3 HCS, and determine barriers, facilitators, and optimal workflow(s) for the ACP intervention that are aligned across HCS and surgical practices. The overarching goal is to identify a workflow that maximizes patient engagement and minimizes surgical care team burden.



We will then, with patient, surgeon, and surgical care team input, review the ACP-related patient materials (letters, patient portal messages, reminders) and seek input on how to normalize ACP and convey the timeliness and value of engaging in ACP before surgery. Obtaining a range of patient and clinician views will be essential in finalizing the approach. To achieve this, surgeons will be asked to identify older adult patients who had major elective surgery in the past year (approximately 4 to 5 patients per site). The Center for Community Engagement in the UCSF Clinical and Translational Science Institute will be consulted to provide best practices for engaging diverse patient voices. R. Sudore is a Co-I of the UCSF CTSI Research Action Group for Equity, whose goal is to ensure the inclusion of historically marginalized patients in research. This is important because our preliminary data (unpublished, E. Wick) and the literature suggest that language, race, and ethnicity impact ACP engagement.<sup>12,12,112</sup> In collaboration with the surgical care team, we will contact the patients, determine interest, and obtain consent. In addition to patients, we anticipate that 3-4 surgeons and 3-4 representatives from key surgical care team roles (surgery scheduler, medical office assistant, advanced practice provider and/or preanesthesia clinic provider) at UCSF, UCI, and UMN will also be approached to determine interest and obtain consent for participation.

Finally, because we cannot include patients and surgical care team members from all potential surgical specialties, to triangulate, validate, and ensure scalability of our approach, we will analyze EHR metadata patterns from all surgical clinics to shed light on the workflow (e.g., new patient scheduled for consultation, consultation visit, surgical case scheduled, surgery occurrence etc). We will analyze across surgeons, surgical specialties, and clinic sites. We will use our findings and desired workflow to build an initial prototype of the

patient portal message in English and Spanish in a development/test environment and will conduct iterative usability testing to refine the solution (see UG3 Aim 2). Additional languages will be added in UH3 aim 1.

Anticipated Findings and Alternatives: We anticipate the least practice-to-practice and HCS-to-HCS variation associated with new surgical consult scheduling. Therefore, we will ideally focus reminder messages in a close time frame around the initial surgical consultation visit for the pragmatic trial. The anticipated initial triggering event for the patient portal ACP message will be a new surgical consultation visit with the concept that ACP is part of preparing for the visit. At this point, the message, in addition to ACP-specific content, will also be able to reference the surgeon and appointment date, providing context for the communication. Preliminary data from UCSF demonstrates that appointments are created ~10-15 days before the date of a new patient consultation appointment. Possibly, some patients may feel uncertain about receiving an ACP message before meeting the surgeon. Alternatives include triggering ACP messaging at later time points such as at the time of the surgical case request or even at the time of various pre-surgical evaluation appointments (e.g., preoperative clearance/physical, pre-procedure surgical appointment). While a range of time points may allow for concrete information for processing the ACP message, the timeline before surgery may be compressed and difficult, and introducing messaging just prior to the procedure may introduce additional anxiety. We anticipate, to enable scalability, signing the letters from a surgical and/or population health leader in the HCS but it is possible, if desired by patients and surgeons to sign the letters from a specific surgeon. It is possible that the latter approach may increase expectations for surgeon-led ACP discussions during the office visit which may not be possible. We will seek input from patients and the surgical care team on the most patient-centered approach and then will refine and finalize the outcomes collaboratively between the NIA, DSMB, NIH Collaboratory, and the study team.

# C.2.3. UG3 Aim 2: Optimize and fully define clinically meaningful ACP outcome measures for the surgical setting in HCSs.

**Rationale:** Measurement is needed (1) to evaluate effectiveness of the three arms of the pragmatic trial and (2) to sustain and spread the intervention once the trial is complete. To achieve both goals, using the PRECIS-2 Framework, the primary outcome should be part of usual care and relevant to patients. While ultimately ACP aims to improve goal concordant care, goal concordant care has been elusive to measure.<sup>20113</sup> Most trials have used AD completion to signify a patient's engagement in ACP. More recently, an *expanded definition for ACP* has been adopted to include ongoing discussions and documentation of those discussions as well as ADs. UCSF Population Health, in collaboration with R. Sudore's PREPARE team has developed a composite ACP measure of "Clinically Meaningful ACP Documentation." This documentation includes ACP documentation, current procedural terminology (CPT) billing codes, and any notes or problem lists or note "Smartforms<sup>TM</sup>" or "Smartphrases<sup>TM</sup>" used in the Epic EHR for ACP. ACP-specific clinical notes can be written by several care team members (providers, nurses, social workers) and can document ongoing, dynamic discussions between the healthcare team and patient and caregivers. We propose using the expanded definition of ACP and Clinically Meaningful ACP Documentation as our primary outcome in the pragmatic trial.

**Approach**: The planned <u>primary outcome</u> is the presence of **Clinically Meaningful ACP Documentation in the EHR** (ACP-related clinical notes, Advanced Directive, Physician Orders for Life Sustaining Treatment, out of hospital do-not-resuscitate order, living will, CPT billing code for ACP, problem lists, Smartforms or Smartphrases). The components of the proposed metric are available in EHR at UCSF, UMN and UCI as structured data fields. At UCSF, ACP documentation has been monitored closely in primary care practice for over five years both as part of pragmatic trials and quality improvement.

Although all 3 HCS use Epic as their EHR vendor, the user interface and data warehouse for this information often has been customized, including some of the associated structured elements and components. Therefore, to ensure that the data is reliable and measuring similar documents at all 3 HCS, 25 patient charts determined to have clinically meaningful ACP documentation and 25 charts determined to not have documentation be reviewed for accuracy.

**Data availability**: At UCSF, the data required for this analysis will be extracted and analyzed by the Surgery Informatics group. This group is a resource within the Department of Surgery, led by L. Pierce, co-I, that has extensive experience retrieving and working with clinical Health IT data. At UMN, the EHR data needed for the research team to conduct the analysis will be available from the UMN Clinical and Translational Science Institute's (CTSI). The CTSI has a collaborative arrangement with Fairview and UMP that makes the EHR data available to the research team <u>free-of-charge</u> and the CTSI provides user-support for working with the EHR data, including brokering connections between researchers and Fairview staff to answer detailed questions. At UCI,

the data is available via the EHR data warehouse and is readily accessed and used in the Office of Population Health (L. Gibbs, co-I). The transfer process (UCI, UMN→ UCSF and UCSF, UCI→UMN) will also be finalized and tested. UCI and UCSF have experience transferring ACP EHR files to UC, Los Angeles (PCORI) and UCSF has experience transferring EHR files and de-identified clinical notes to UMN (AHRQ, IRBs and materials transfer agreement in place).

**Expected Findings and Alternatives:** Based on preliminary data and local quality improvement efforts around ACP we anticipate that both formal ACP documentation and clinically meaningful ACP documentation outcome measures will be easily obtained and accurate in the 3 HCS. Development of ACP specific notes, ACP centralized dashboards, and advances in organizing ACP-related scanned documents and clinical notes in the EHR have been significant over the past couple of years, partially prompted by the COVID-19 pandemic. It is likely that these functions will continue to improve in the next 12-18 months and further enhancements may be in place when the proposed work starts. We expect that the data will be reliable but, as with any EHR documentation, errors can occur with regards to scanning and note type assignment. However, we anticipate that this will be rare and random between surgical clinics.

The project team leadership collaboratively between the NIA, DSMB and NIH Collaboratory and the project team will review clinically meaningful ACP documentation measures at the 3 HCS and determine if there is alignment across HCS. If inconsistencies are identified, particularly in identifying ACP notes and Epic Smartforms/phrases, this could impact the integrity of the trial outcome measures. In the unlikely event that this would occur, we will then use the traditional ACP outcome measure of advance directive documentation.

# C.2.4. UG3: Aim 3: Usability- and pilot-test ACP interventions in one clinic in each HCS to ensure it works as intended.

**Rationale:** A proof-of-concept study of EHR-enabled PREPARE plus the easy-to-read ADs to enable ACP has been conducted in primary care at UCSF and UCI. We have just initiated testing in a small pilot surgical setting at UCSF but this experience is limited. Therefore, <u>we will conduct formal usability analysis and pilot test this intervention at UCSF, UMN and UCI in surgery to ensure the ACP messaging is appropriate as well as useful to and usable by patients and the surgeon and surgical care team before we conduct the pragmatic trial. Usability and pilot testing are critical to ensure that we have optimized the clinical workflows for <u>identifying</u> patients scheduled for new patient visits and <u>messaging</u> them through the patient portal before the visit and <u>reminding</u> them to complete materials via automated text or telephone reminder. Usability and pilot testing is also crucial to ensure that patients are <u>willing and able to</u> use the EHR-enabled PREPARE tool. Any identified technical problems in the systems used in the intervention will be able to be addressed without disrupting the actual trial. Our design will be iterated as needed, in a coordinated manner between HCS, guided by the project team leadership, with the goal of minimizing burden on clinical staff and patients, unintended consequences, and technical defects.</u>

**Approach:** We will conduct the ACP intervention in one UCSF clinic, followed by one UCI clinic and one UMN clinic. Our usability testing will involve a formative assessment of the system, aimed at iteratively improving the system design.

<u>Test Environment Scenario-Based Usability Testing:</u> Health IT usability experts on the team, (Co-I, J. Marquard, R. Rizvi) in collaboration with implementation science experts (MPI R. Sudore, Co-I D. Peska) will conduct cognitive walkthroughs with patients and clinicians of the portions of the system they interact with, including the patient portal messaging, the PREPARE website links and the advanced directive (AD), direct messaging to patients, and interactions with the healthcare navigator. We will utilize a scenario-based protocol to identify areas for system improvement.

<u>Patients</u>: Patient participants (n=15) will interact with the system in the test environment. We will create scenarios representing each potential way a patient might interact with the system (Study Arms 1, 2, and 3), ensuring that each participant interacts with all elements of the system. Arm 1 includes letter, AD, and PREPARE only (1 scenario), Arm 2 includes letter, AD and PREPARE plus reminder text or phone messages (2 scenarios), and Arm 3 includes letter, AD and PREPARE plus reminder text or phone messages plus a healthcare Navigator (2 scenarios). Once the participant completes their first scenario, they will be shown PREPARE as a part of the remaining scenarios but will no longer complete the entire PREPARE tool. Participants will be asked to 'think aloud' during the scenarios, voicing in real-time their feedback about the system.

We will record sessions with audio and use screen capture software to capture participants' navigation patterns, a typical approach in EHR usability studies. We will assess participants' perceived workload after each scenario, using the validated National Aeronautics and Space Administration Task Load Index (NASA-TLX) instrument.<sup>114</sup> After completing all scenarios, we will conduct a debriefing interview to glean additional open-ended feedback from participants about the system.

After each set of 5 participants, we will identify and implement design improvements. Improvements not able to be immediately corrected (e.g., gross defects identified in the cognitive walkthrough) will be classified according to their severity, root cause, potential solution(s), and recommendation(s). Participation will be voluntary and written informed consent will be obtained from participants prior to participation. Participants will be provided a \$30 gift card as an incentive for participating.

<u>Surgical Care Team</u>: We will complete a parallel assessment as the one described above with surgical care team participants (n=15), focused on scenarios representing each potential way they might interact with the system. Participants will be provided a \$100 gift card as an incentive for participating.

<u>Clinic Pilot Testing</u>: Following test environment usability testing, the UCSF, UMN and UCI pilot clinics will be implemented with the optimized tool. Each of the HCS clinic "areas" or subspecialties tends to support ~5-8 surgeons. We anticipate at least 10 patients per clinic per week will meet enrollment criteria (patient 65+ and/or serious illness<sup>48</sup> referred for new surgical consultation) and to pilot the solution for ~3 months. Details on the serious illness EHR definition and methodology are described in detail UH3 aim1.

Surgeons, surgical care teams (advanced practice providers, RN staff, medical office staff and pre-anesthesia evaluation providers; in total ~ 15 people per site) will be oriented to ACP, AD, PREPARE and the EHR workflow. Using existing materials together with new surgery-oriented materials, R. Sudore (MPI) and/or the PREPARE members of the project team will provide short training sessions with brief background on ACP and frequently asked questions (existing support materials adapted to surgery) to the clinics. For the pilot, we will only test the technology-driven arm (patient portal messaging and reminders Figure 5, arm 2). The navigator model (Figure 5, arm 3) has been tested in primary care and materials for establishing navigator workflow at a HCS and trainings are available but will take additional time and resources to implement and this work will begin in beginning of Year 2 (UH3). We will use standardized semi-structured interview guides that are based off templates used extensively to pilot other PREPARE and ACP interventions (R. Sudore, MPI and team). We will assess patient experience and engagement with ACP, PREPARE and ADs, as well as the surgical care team experience and workflow. We will ask what worked well, what didn't work well, and why and ask for additional suggestions. For the surgical care team and to determine workflow impact, we will interview care team members and measure (1) surgical care team's weekly updates on the burden [including telephone calls, patient portal messages related to ACP, requests to mail in documents for scanning]. To complement survey data, we will measure EHR patient portal access log data to (1) confirm the patient received the message, (2) determine if the patient opened the message and used PREPARE, and will measure ACP completion rates, and (3) patient response to patient reminders. Findings will be reviewed at the project team meetings and with the DSMB if appropriate.

<u>Potential Local Optimization:</u> Given the complexities of surgical care delivery and the intrinsic variability between HCSs and Health IT environments, it is possible that small site-specific modifications to the EHR ACP intervention will be needed. Differences in patient portal interfaces including UMN having an HCS-specific M Health Fairview patient app/portal or other patient portal variations will likely mean that the technical aspects will require local modification. This is consistent with what is often observed during various IT dissemination/implementation strategies. The need for any variation will be balanced with the fidelity of the intervention with the pragmatic trial. Each site will also use, in addition to sharing patient and provider feedback, the Framework for Reporting Adaptations and Modifications to Evidence-based Implementation Strategies (FRAME-IS) template to share modifications made locally.<sup>115</sup> All the above will be reviewed by the project team, DSMB, and NIA prior to proceeding to the UH3 stage to ensure alignment and fidelity to the collective model prior to initiating the pragmatic trial.

**Expected Findings and Alternatives:** We expect the procedures to be feasible and the surgical team (and patients) to find the approach acceptable. We anticipate that there will be some small changes needed to language in messaging and workflow of PREPARE. It is possible that patients may desire additional, non-ACP related information, as part of the message. Some patients may also feel they need more information regarding ACP and AD in the context of their planned surgery. We anticipate surgical care team support will be required for a subset of patients.<sup>70</sup> While some questions may be addressed by the surgical care team, some require

surgeon input. We will begin to quantify the types of questions and burden to refine the surgical care team trainings and support materials for the larger deployment and to inform tailored surgical training for the healthcare navigators (**Figure 5, arm 3**). Patients may prefer to complete the materials on a mobile device. Today, PREPARE is web-based, but we have experience adapting web solutions for mobile platforms and form factors, as well as naive Android and iOS development, which are helpful if web usability is noted to be a barrier. The download/upload functionality for AD could be a barrier; alternatives include EHR questionnaires and forms with options to sign via mobile device (used for electronic surgical consent). R. Sudore, MPI, is knowledgeable with regards to what is legally feasible vs. technically feasible. Finally, we will likely identify a subset of very vulnerable patients who cannot use the self-directed materials. The use of non-clinician facilitators has shown benefit with completing ACP. Given the limited resources in surgical clinics, we can explore the use of non-clinician facilitators such as medical assistants and patient care coordinators to ensure patients receive ACP materials, collect completed materials, scan them into the EHR, and schedule patients who would like additional information or help to complete their AD. In the UH3 aim 1 trial, arm 3 will evaluate the effect of a healthcare navigator, at the HCS level, not specific to a clinic, to address this gap.

# C.3.5. UG3 Milestones and Timeline

Major milestones during the UG3 phase essential for preparedness for UH3 phase (detailed milestones and timelines in **Table 5**, MAJOR milestones in grey):

Table 5: UG3 Timeline												
Administrative Milestones	M1	М2	МЗ	M4	М5	М6	М7	<b>M</b> 8	M9	M10	M11	M12
Biannual project meeting at NIH				х						х		
Establish sIRB completing process at each site for respective reliance	x	x	x	x								
Register trial on clinicaltrials.gov	0			x								
Finalize safety monitoring plan				x	x							
Identify personnel for NIH Pragmatic Trials Collaboratory WG participation					x	x						
Refine study design, timeline, & analytics plan with guidance from NIH							x	x	x			
Finalize UH3 milestones and budget										X	x	x
Pilot Milestones	M1	M2	М3	M4	M5	M6	М7	<b>M</b> 8	M9	M10	M11	M12
Landscape surgical practices and specialties at 3 sites		x	x	x								
Finalize and pilot patient surveys		X	x	x								
Interview on satisfaction and engagement with ACP process								x	X	X	X	x
Build and deploy pilot ACP tools in test environment at UCSF	x	x										
Build and deploy ACP tools at UMN and UCI							х	x				
Cognitive walkthrough with test environment with optimization of ACP tools			x	x	x							
User pilot testing with refinement				х	x	x						
Finalize and perform quality improvement on data extraction							х	x	х			
Finalize study outcomes and verify they can be extracted from EHR					x	x						
Pilot test intervention in one clinic at UCSF							x	x	Х			
Pilot test intervention in one clinic at UMN and UCI									X	Х	х	
Finalize tools for ACP intervention/implementation											X	X

MAJOR Milestone 1 (Complete by month 4): Complete all regulatory approvals to proceed with UG3/UH3:

- 1. sIRB approval with reliance agreements in place at UCSF, UCI and UMN.
- 2. Register at clinicaltrials.gov.

MAJOR Milestone 2 (Complete by month 6): Outcome measures:

- 1. Final review and approval of primary outcome measures by DSMB, NIA, NIH Collaboratory.
- 2. Demonstrate that agreed upon outcome measure can be retrieved from the EHR at UCSF, UCI and UMN accurately.

MAJOR Milestone 3 (Complete by month 8): Implement changes to HCS EHRs to support pilot intervention:

- 1. Build and deploy tools in test environment at UCSF as needed.
- 2. Build and deploy tools in test environment at UCI (modify from primary care).
- 3. Build and deploy tools in test environment at UMN.

MAJOR Milestone 4 (Complete by month 12): Conduct pilot testing in 3 HCS including the following subtasks:

- 1. Verify that the intervention is delivered within the EHR reliably and as intended in each HCS (pilot); share EHR audit logs and message open rates.
- 2. Outcomes data registry developed to monitor impact in each HCS and demonstrate that UCI and UMN data can be shared back with UCSF; share ACP compliance rates in 3 HCS.

# C.3.6. UH3 Conduct and Evaluation of Pragmatic Trial

# Overview of UH3 and relationship to UG3



Using the tools (letters, reminder messages, outcome measures etc.) developed and tested in primary care and adapted and tested for surgery during the UG3 phase, in UH3 Aim 1, we will conduct a NIH Stage Model III (efficacy-effectiveness), 3-arm pragmatic RCT to test the effectiveness of 3 increasingly resource intensive ACP interventions for patients age 65+ or with serious illness<sup>48</sup> who are referred for evaluation for major elective surgery. In UH3 Aims 2 and 3, we will use mixed methods including qualitative interviews, data science and natural language processing to define and better predict surgical patients in need of additional support to engage with ACP and begin to understand the content (and quality) of ACP notes in the EHR. This will inform sustainability of ACP in the pre-surgical setting.

C.3.7. Aim 1: Conduct an NIH Stage Model III (efficacy-effectiveness)<sup>19</sup> three arm RCT in 3 HCS. Patients aged 65 or older, or with serious illness, who are referred for major elective surgery will be randomized to Arms: (1) Letter about ACP, PREPARE advanced directive (AD), PREPARE website; (2) Letter, AD, PREPARE plus reminder text/phone messages; (3) Letter, AD, PREPARE plus reminders plus a healthcare navigator.

<u>*Hypothesis:*</u> Increasingly intense support for surgical patients with regards to ACP will result in increased ACP documentation (discussions and care plans, primary outcome) and patient-reported ACP engagement.

**Rationale:** Real-world, scalable interventions to improve adoption of the ACP in older adults are lacking, especially in older adults in need of surgery. The EHR and associated patient portals are a promising tool for increasing adoption of ACP. *The innovation of the proposed patient-level pragmatic RCT is four-fold:* 

**First**, the trial will allow us to assess whether using the patient-facing PREPARE tools are effective in improving ACP engagement before major elective surgery and *test the comparative effectiveness (and acceptability to patients and care teams) of three increasingly resource intensive delivery models (Figure 5). One-on-one facilitation has been shown to increase ACP documentation and engagement but is often costly and time consuming.<sup>116</sup> Therefore, <i>it is important to understand the relative benefit of each additional level of support as most HCS have limited resources*.

**Second**, the intervention will be coordinated via the EHR at 3 HCS and its integration into the EHR ensures *consistent organization of ACP* information in an easy-to-use format for outpatient and inpatient surgical care teams. This addresses an important need: if a patient undergoes surgery and experiences unanticipated complications, the inpatient care team could easily access ACP documented discussions and advance care planning documents.

<u>Third</u>, work will be conducted in 3 geographically and culturally distinct HCS, with busy surgical practices but different baseline ACP rates, health system strategic goals, and geriatric medicine "footprints".

Consequently, the findings of the trial will be well-positioned for learnings that will help improve the uptake at other HCS with variable baseline ACP efforts.

**Fourth**, since the trial will be conducted in "real world" settings with the associated competing surgical team priorities and strained staffing, the findings have significant promise in terms of *sustainability* and *scalability* to other HCS – important criteria to assess value of the proposed trial. While many of the interventions are system-based, some are more resource intensive (postal mailings and healthcare navigator) and in UH3 aim 2, deeper analyses of the pragmatic trial data will be done to identify particularly high-risk patients who may have gained benefit from these enhancements beyond the EHR-driven tools.

**Population Cohort:** The population cohort (estimated n=6,000) includes patients aged 65 and older who are <u>scheduled for a new patient visit in a surgical clinic</u> at UCSF, UCI and UMN, <u>balanced</u> by surgical clinic-type (see environment, below for proposed surgical clinics to be involved, the plan is to be finalized in UG3 aim 1). We will also include patients of any age with serious illness diagnosis defined by a validated algorithm<sup>48</sup> (i.e., an at-risk medical diagnosis including cancer, heart failure, chronic obstructive pulmonary disease, end-stage liver disease, end-stage renal disease or amyotrophic lateral sclerosis, advanced age or severity of functional or cognitive decline). Because ACP is an iterative process and choices may change over time, we will include patients who have not completed an AD document within the past 6 months. We will exclude patients who were enrolled in the PCORI funded ACP trial in primary care (see Preliminary Data) at UCSF and UCI (<6% of patients at those sites). We will also, to avoid contamination, exclude the few surgical clinics at UCSF that have started to pilot the ACP EHR workflow in 2022.

Patients registered with the EHR patient portal, as well as those who are not registered, will be included in the randomization. Patient portal enrollment at UCSF, UMN and UCI is variable (40-65%), with increases noted over the past 18 months associated with the outreach during the COVID-19 pandemic and vaccine rollout. However, patient enrollment in the EHR portal is not equitable. Given the importance of ACP, patients who meet the enrollment criteria but are <u>not</u> enrolled in the EHR portal <u>will be included</u> in the randomization and the interventions will be delivered by postal mail. Patients whose primary language in the EHR is designated as Chinese (Cantonese or Mandarin), Russian, Hmong, Somali, and Vietnamese <u>will be included</u> but will receive the letters, ADs, and PREPARE pamphlet in their preferred language by postal mail. The online PREPARE program is currently only in English and Spanish as is the Epic EHR portal (~90+% of patients in the 3 HCS have primary language of English or Spanish designated in EHR).

**Environment:** The sites include UCSF Health, UCI Health, and M Health Fairview. We will include the following surgical clinics at these sites: general, colorectal, surgical oncology, otolaryngology, urology, neurosurgery, gynecologic oncology, thoracic, cardiac, and vascular surgery. We will finalize these, and possibly other clinics, as part of UG3 aim 1, as described above. We will plan on excluding the plastic surgery, hand, foot, audiology, and sports medicine specialty clinics because they tend to have a low percentage of new patient consultations that ultimately require surgery and in general, the conditions are lower acuity. We will also exclude the transplant clinics because with the complexity of the pre-transplant work up and requirements, additional messaging could be confusing to the patient. Given our current inclusion/exclusion criteria, at UCSF alone, the annual new patient visits exceed 10,000 and >20,000 across the 3 HCS. Each clinic has a medical director and administrative director who will be engaged to coordinate with local information dissemination (see LOS, HCS leadership). We will offer 20–30-minute ACP educational sessions for each participating surgical clinic with information about ACP basics and ACP conversations, documentation, and billing. These materials have already been developed by the PREPARE Team and adapted for the surgical environment by the surgical team at UCSF.

**Randomization Engine Infrastructure and Processes:** Patients will be randomized in a 1:1:1 ratio to the three treatment groups using block randomization stratified by surgical clinic nested within HCS. We will use an existing and *tested* (University of California Health Care Planning Study funded by Patient-Centered Outcomes Research Institute (PCORI PLC-1609-36291)) relational database management system (RDBMS) that integrates EHR records (new patient clinic visits) and randomization engine infrastructure which has been similarly set-up and utilized at M Health Fairview. Eligible patients will be identified using a structured query language (SQL) stored procedure on the RDBMS. This automated process will run immediately following the nightly Extract, Transform, and Load (ETL) process from the EHR to the RDBMS. The SQL stored procedure will be responsible for evaluating all inclusion and exclusion criteria necessary for identifying patients with eligible upcoming surgical appointments. When the stored procedure is complete, eligible patients are automatically returned to the EHR through a secure connection to the RDBMS. After identification in the RDBMS, patients will be randomized into three intervention groups using the randomization engine developed at UCSF. Randomly generated blocks stratified by surgical clinic within HCS will be used to ensure a balance in sample size across groups at each site

over time. The assigned randomization will be linked to the patient in the EHR and used to generate group specific letter content, send follow up ACP reminders, and group patients for healthcare navigator outreach. Patients who are identified and randomized will be automatically added to a table of the RDBMS which will track metrics related to their randomization, intervention, and outcomes. The data in this table will be updated daily as a part of the SQL stored procedure used to identify eligible patients.



Intervention Arms: As shown in Figure 5, each intervention arm builds on the prior arm:

(1) Introduction letter about ACP, distribution of easy-to-read PREPARE ADs, plus prompting for the

patient to engage with PREPARE website

(2) letter, AD, PREPARE plus reminder text or telephone messages

(3) letter, AD, messaging, PREPARE, reminders <u>plus</u> healthcare navigator engagement with patients and surgical care team.

Our primary analysis is the comparison <u>between</u> study arms. All patients will receive the intervention (letter, easy-to-read AD, and the PREPARE pamphlet in their preferred language) via the postal mail in their preferred language and, if they are active with the patient portal, they will receive the same information via the portal. In Arm 2 and 3, the follow up reminders will be delivered via the patients preferred delivery method – either automated, interactive telephone call or text message. Arm 3 will add one-on-one support from a remote non-clinician healthcare navigator. The role of the healthcare navigator will be to remind patients to engage with the PREPARE materials, help answer questions, encourage patients to speak with their surgeon, and route any pertinent ACP information to the surgical care team. A detailed manual for healthcare navigators has been developed and validated by the PREPARE team and is available for use in this setting. The use of one-on-one facilitation has been shown to increase ACP documentation and engagement, but it is often the most costly and

time-consuming approach.<sup>116</sup> Especially in the resource and workforce constrained environment, it is essential to understand the relative benefit of layering the patient navigator onto a relatively low-cost systems intervention.

All participants will be invited to complete an 10-item survey including the validated 9-item ACP Engagement Survey (see secondary outcome below for details) after the ACP message has been sent. Eligible patients will be messaged via the patient portal introducing the survey, an easy-to-read written consent form (e.g., 5<sup>th</sup> grade reading level). Patients may enroll in the survey study by signing the consent form and completing the survey. Included in the introductory information is an "opt-out" telephone number. Patients who do not return a survey or and do not opt-out may be contacted two weeks after the survey mailing by telephone or e-mail to assess interest in participating (**Figure 6**, overview of survey process). The survey has been validated in English and Spanish therefore, patients whose preferred language is other than English or Spanish will not be included.

Surgical patients, unlike primary care patients are referred in at different intervals from inside and outside the HCS. Therefore, it is not possible to obtain baseline survey data prior to the intervention. However, after patients have received the intervention, and for those patients who followed up with their surgical appointment, we will send out the surveys 1-2 weeks after their surgical appointment. At UCSF, the surgical clinic no-show rate is <2%. Given the intention-to-treat anaysis plan, patients who receive the intervention but fail to attend their new patient surgical clinic visit will be included in the analysis. Because ACP is a process that occurs over time, and surgery may be associated with unexpected events in the post-operative phase or underlying conditions may progress necessitating the need for ongoing ACP conversations, we will also re-assess the ACP Engagement Survey 6 months latter, in the patients that opted into the survey initially. Patients will receive a \$30 dollar gift card for completing each survey.

#### **Intervention Modalities:**

Overall, the interventions are designed to engage patients in ACP and prepare them to share their wishes with their surgical team as appropriate. These interventions are based on studies in *primary care* that first rigorously evaluated one-on-one introduction of PREPARE plus easy-to-read AD in an office setting and then, used system-based approaches and reminders to scale the work (study ongoing, blinded, preliminary data, **Table 2**).

Letter: An introductory letter describing ACP and normalizing it as a part of clinical care at the health system. The letter template was adopted from letters that have been developed by R. Sudore and L. Gibbs and over 100 key patient, caregiver, and clinician advisors. For non-English and non-Spanish speaking patients not registered in the patient portal, they will be sent the letter in their preferred language. Letters will be automatically generated in the EHR and delivered electronically to the patient portal using the appropriate letter template for the assigned randomization group. Letter content will be personalized to the patient using tokens that are dynamically replaced with appointment and demographic details available in the HER, for patients' whose preferred language is English or Spanish. Patients will be automatically notified of the letter by email or text message (short message service [SMS]) depending on their specified communication preferences in the EHR. The registry will be shared with the postal mailing service and all patients will receive the same letter, AD and PREPARE pamphlet via the postal mail, in their preferred language.

**PREPARE:** The PREPARE program easy-to-read ADs and the online program will be provided to all patients through URL links in the patient portal. For non-English and non-Spanish speaking patients not registered in the patient portal, they will be sent the easy-to-read ADs and the PREPARE pamphlet in their preferred language.

<u>Text or Phone Reminder Messages</u>: Using a third-party messaging service, patients randomized to **Arms 2 and 3** will receive a reminder to engage in ACP by automated text or phone message (short messaging service [SMS) depending on their specified communication preferences in the EHR.

**Healthcare Navigator:** Patients randomized to Arm 3 and the "healthcare navigator" will be automatically added to a registry in the EHR which will allow the navigator to identify patients and perform and document ACP outreach. Healthcare navigators will: (1) evaluate AD completion; (2) introduce ACP to the patient and facilitate referral to the PREPARE website, access ADs, and answer basic ACP questions or refer to the patient's surgical care team; (3) facilitate completion and collection of ACP documents; (4) notify surgical care teams about obstacles to ACP. Healthcare navigators will be trained and provided scripts and checklists that have been developed by R. Sudore and the PREPARE team. The 1-2-hour training will introduce ACP and ACP documents.

**Blinding:** The surgeons and care team will be blinded to the intervention, but it is possible that, if the patient is assigned to the health navigator arm, the navigator may need to reach out to the surgeon or surgical care team.

**Primary Outcome:** The primary outcome is **clinically meaningful ACP documentation** (ACP-specific clinical notes, problem lists, Epic Smartforms or Smartphrases, advanced directives, Physician Orders for Life Sustaining Treatment, out of hospital do-not-resuscitate order, living wills, or CPT billing codes) available in the HCS EHR before surgery. If patients do not have surgery, we define ACP documentation as any ACP documentation within 6 months of the intervention (or death if the patient dies within the follow up period). The primary outcome will be reviewed with the DSMB, NIA and NIH Collaboratory as part of UG3 Aim 2 and may be adjusted per discussions.

**Secondary Outcomes: Patient-centered outcomes will be derived from the validated 9-item ACP Engagement Survey.**<sup>117</sup> The survey will be administered with <u>the initial ACP intervention</u> and a follow up survey will be sent <u>6 months later</u>. A \$30 gift card will be provided for each survey (**Figure 6**).



correlation coefficient 0.89, p<0.001).<sup>117–119</sup> Scores do not differ by literacy or race/ethnicity, p>.05.<sup>70</sup> Studies have validated a <u>0.2-point change in scores as clinically meaningful</u> (see Preliminary Data). The Survey has 3 self-efficacy questions (i.e., asking someone to be a medical decision maker, and talking with the decision maker and medical providers about medical wishes). Self-efficacy response options range from "not-at-all confident" to "extremely confident." There are 6 readiness questions (i.e., how ready participants are to: ask a someone to be a surrogate decision maker, discuss the surrogate with clinicians, document the surrogate, talk to surrogates/clinicians about their medical wishes, and document wishes). Readiness response options range from "I've never thought about it" to "I've already done it." We will assess scores at initially after the intevention and 6 months later.

<u>Exploratory Outcomes</u>: The field of ACP is evolving, including its recommendations on appropriate and feasible ACP measures. There are no validated self-reported or chart abstraction measures for goal concordant care, and there is debate about whether this outcome can be measured effectively.<sup>51,135,136</sup> One recommendation is to measure whether the interventions met individuals' needs. Participants may have engaged in the self-directed materials, the visits, or both. Therefore, we will ask, "Did the materials we gave you and the visits you may have attended meet your needs for ACP information?" Response options include, "It was less than I needed," "It was as much as I needed," and "It was more than I needed." In the holistic view of ACP as a systems-level intervention, we will explore additional implementation-related factors in UH3 aim 2.

**Sample Size and Power Analysis:** It is expected, based on the number of historical annual surgical clinic new patient visits that we will complete enrollment of approximately 6,000 patients in 12-18 months in 3 HCS. Prior studies suggest that similar interventions result in new AD completion rates of between 25% and 50%. Consistent with these studies, the PREPARE trial demonstrated an effect size of 0.5; to account for the pragmatic nature of the proposed trial, a conservative estimate would be a 25% absolute increase in clinically meaningful ACP completion from baseline. We expect that the clinically meaningful ACP documentation rates will be 20%, 35% and 45% for arms 1, arm 2 and arm 3, respectively. As described below analyses will account for intraclinic correlation of responses, however based on our previous studies<sup>113</sup> we anticipate a minimal design effect of 1.3 or less. If we conservatively assume an effective sample size of n=1500 patients in each arm, we will have 80%

power to detect a difference of 20% vs 25% completion rate and better than 99% power to detect 10% differences in completion rates (e.g., 20% vs 30%; 35% vs 45%) between arms (two-sided Bonferonni-corrected alpha of 0.016=0.05/3). We will thus have more than ample power to detect our anticipated pairwise differences.

We anticipate a 20% response rate (1,200 patients) to the initial survey and a 50% (600 patients) follow up survey response rate (600 patients with baseline and follow up surveys). The estimate is based on the survey response rate associated with the PREPARE trial in primary care. We anticipate that ~5% of patients will die during the 6 month follow up period (~300 patients). For the secondary analyses, we will have n=200 subjects per arm with negligible design effect. We will have 80% power (two-sided alpha of 0.016) to detect differences of approximately one third of a Likert scale point in mean change from baseline to 6 months between two arms.

Analysis Plan: We will estimate the effect of the three treatment groups on our primary and secondary outcomes using a parallel, randomized control design. Approximately 6,000 patients will be enrolled in total at UCSF, UCI and UMN and randomized at a 1:1:1 ratio to one of the three study arms. Randomization will be stratified by HCS and surgical clinic. We will compare treatment groups by important baseline covariates to assure that treatment groups are balanced after randomization. For purposes of this analysis, the baseline data will be defined as 6 months prior to initiating the intervention. Continuous covariates will be summarized by the mean and standard deviation or median and interguartile range, as appropriate, and categorical covariates will be summarized by frequencies and the sample proportions. The primary outcome is ACP documentation from baseline to 6 months (or death). The rate of ACP documentation will be compared between treatment groups using generalized estimating equation (GEE) logistic regression models to account for patients clustered within clinics. Covariates included in the model, a priori, include patient age, gender, race/ethnicity, serious illness category, clinic baseline AD completion rate, site, and study arm. As this is a randomized design, we anticipate that treatment groups will be balanced for baseline covariates and include these covariates in the model to improve the precision of our treatment effect estimates. A secondary analysis will be completed that includes other baseline covariates that are systematically different between treatment groups. As per clinical trial guidelines, all primary analyses will follow the intention-to-treat principle. Recent CONSORT guideline extension recommends against multiple comparisons adjustment when comparing the active arms versus control arm in a multi-arm trial.<sup>120</sup> As our interest lies in comparing all pairwise comparisons (i.e. not only the comparison of active arms to the control), we include a conservative Bonferroni adjustment, such a p-value of 0.016 = 0.05/3 will be used to declare statistical significance. Given that the primary outcome will be collected via the EHR in this pragmatic trial, we anticipate only small amounts of missing data. Missing outcome data will be analyzed using multiple imputation and we will complete sensitivity analyses to evaluate the robustness of our conclusions to various assumptions regarding the missing data mechanism.

Secondary analyses of the 9-item ACP Engagement Survey will be done to compare change in engagement (using both the 9-item composite score and the individual items) as measured in average change in 5-point Likert scores between initial contact and 6 months between 3 arms. Means, medians, and ranges will be used to quantify the changes descriptively. Formal analysis will employ GEE models (with normal distribution and identity link for the 9-item composite measure as used in our past studies<sup>12</sup>; individual item models will use GEE logistic for dichotomized versions of the items and GEE log Poisson models for the 5 item scales).

**Ensuring Fidelity to the Intervention Across Sites:** The proposed intervention depends on the participation of a diverse cadre of surgical clinics and a build in the EHR to implement consistent interventions across sites. The sites use the same EHR (Epic) but have varying degrees of customization. It is possible that the EHR builds will be slightly different across the 3 HCS) but will still deliver the same patient-facing intervention (as it currently does in the PCORI funded primary care trial at UCSF and UCI). As part of the UG3 phase (aims 1 and 3), collectively the approaches will be developed, compared, and finalized. The pilot and the trial implementation and fidelity will be evaluated using the RE-AIM framework as described previously for the primary care ACP trial.

The intervention includes both the messaging about ACP, the PREPARE easy-to-read ADs, as well as the online program. Some patients will prefer to engage in some or all these materials yet will still obtain ACP information. To monitor fidelity to the intervention during the pragmatic trial, we will monitor the number of letters that are sent through the patient portal and physically mailed, the number of ADs and PREPARE pamphlets mailed via postal service, and the number of patients who click on the study-specific URL links in the EHR portal. We will also assess the healthcare navigator call logs and EHR notes documenting interactions with patients and surgical care teams recording patient contact as well as meaningful ACP engagement rates.

Finally, with our knowledge on state of the science with ACP changing and adapting over time, and it is probable over the study period that the EHR might roll out new ACP-related features, additional HCS efforts will be initiated

around ACP, commercial and government payers may introduce incentives or mandates to improve ACP in the study population. In each HCS, the environmental changes will be recorded to help with understanding secular trends.

**Data Safety Monitoring Plan and Stopping the Study:** The intervention is aiming to enable patients to engage with ACP which is the standard of care and therefore, is minimal risk. Data will be stored behind each HCS firewall on secure servers. Survey data will be collected via electronic link to REDCap database and each entry will be assigned a unique study identifier. If the patient does not engage via the electronic link, a small subset will be collected via telephone and entered by study team into REDCap. The research team reporting to the DSMB will regularly review protocol fidelity, adverse events, and unintended side-effects.

Expecting Findings and Alternatives: We expect that we will see incremental benefit with additional reminders and support and that Arm 3 will be associated with the highest clinically meaningful ACP documentation (documented ACP discussions, problem lists, smartphrases, ADs, POLSTs, living will or CPT codes) rates. We hypothesize that the least resource intensive intervention of sending out messages about ACP and PREPARE and the easy-to-read AD (Arm 1) will improve ACP completion rates in the surgical population over baseline. While it is possible that we may not be able to accrue 6,000 patients over 18 months, UCSF, UCI and UMN continue to expand surgical services with almost a 10% growth year over year. Therefore, the baseline surgical new patient volumes may be conservative estimates for the proposed study period. Because UMN and UCI have lower surgical volumes than UCSF, UCSF may stop enrolling earlier. UMN, since the entire M Health Fairview System is on a single instance of the EHR, could include additional community surgical practices if they are not on track to complete accrual. UMN has 9 community-based hospitals, of which (St. Joseph's Hospital, M Health Fairview) is ideal, with several others very small and some of the larger hospitals have largely independently employed providers on separate ambulatory EHR systems making implementation of the proposed intervention more difficult. It is also possible that there could be a regional or national disruption in elective surgical practice as was seen in March 2020 COVID-19 pandemic and intermittently in the subsequent time. Given the advances with telehealth as was as the recognition of the implications of disruption of surgical care on patient outcomes it is probable that, while some operations could be curtailed, cessation would be avoided.

As the intervention is randomized at the patient level, arms may not be balanced with regards to surgeons, diagnoses, and surgical care team. Although progress in surgery with regards to ACP has been exceptionally difficult, it is possible that the overall intervention may have a more powerful effect with certain clinicians or specialties/practices, and a few may begin to integrate elements of ACP more into their patient interactions. Furthermore, adoption of ACP across diverse populations has been uneven with lower completion noted in patients with limited English proficiency as well as those from diverse racial and ethnic groups. This will be a potentially positive impact of the proposed work but could confound the findings and at the same time contribute to some of the broader dissemination and implementation strategies that we identify.

C.3.8. UH3 Aim 2: Use mixed methods to assess patients' and surgical care teams' experience with surgery ACP. <u>Hypothesis</u>: A subset of surgical patients will require more support to engage in ACP; predictive analytics could allow resources to be directed to those in need of additional support.

**Rationale:** Older adults referred for surgery are a heterogeneous and vulnerable population and while we hypothesize that the system-level approach to improving pre-surgery ACP tested in the pragmatic trial (aim 1) will improve engagement in ACP, significant gaps will remain and, to inform the sustainability phase as well as future surgical ACP research questions, a deeper understanding of the gaps is required. The UCSF/UCI/UMN data registry (primary and secondary outcome data) developed and populated as part of the pragmatic trial will represent a powerful, diverse, real-world dataset to identify opportunities to further refine the intervention particularly about (1) engaging diverse patients and (2) deploying limited resources (e.g., postal mailings and healthcare navigator) in a sustainable and scalable manner. This is essential in the face of competing priorities and staffing shortages in U.S. HCSs.

In addition to informing the sustainability, dissemination and resource sharing, the findings will inform future directions such as (1) iterations of the system-level intervention including, possible clinical decision support (CDS) directed toward the surgical care team that might prompt additional contact with particularly vulnerable patients (2) data-driven healthcare navigator support for those at highest risk of failing to engage in the system-based intervention and (3) tailoring of patient-facing PREPARE materials to surgery.

**Approach:** Informed by the quantitative analysis of the primary and secondary outcomes conducted in UH3 as well as the deeper dive described above, we will conduct ethnographic interviews to better understand *who* engaged in PREPARE and ACP, *why* they did (or did not engage) and *how* the intervention was perceived by patients and/or caregivers and their perceptions of their surgical care and alignment with personal goals, particularly in the event of unexpected post-operative complications.

Quantitative: The ACP outcome data registry will be linked to the patient, provider, and procedure-related information in the EHR. To identify risk factors for failing to engage with PREPARE and ACP, we will construct linear and logistic regression models, adjusted for patient characteristics (age, sex, race/ethnicity, serious illness, and language), HCS and, if relevant, procedure characteristics (oncologic vs. cardiovascular, complexity [duration and intensity]), surgical care team (surgeon, surgery clinic) and post-operative course (inpatient length of stay, intensive care unit stay). We will stratify patients by intervention arm location to understand if the patient group who failed to respond to each intervention arm differed. We will utilize bipartite network analysis<sup>121,122</sup> to help visualize patient subgroups and the frequently co-occurring elements associated with patients failing to complete ACP. We anticipate that these analyses would assist in designing future interventions either in the EHR (e.g., targeted clinical decision support) or new operational workflows (e.g., data-driven deployment of healthcare navigator to those most in need of help and targeted ACP postal mailings to those unlikely to engage with patient portal despite being an active member). As an exploratory analysis, we will evaluate heterogeneity in the effect of the treatments on the prevalence of clinically meaningful ACP. This analysis will allow us to identify baseline covariates associated with differential responses to the treatment effect and, potentially, subgroups of the population for which the more intense intervention is needed to achieve high rates of ACP, as well as subgroups for which other interventions could be considered. Our analysis will use a modified version of the Virtual Twins (VT) algorithm.<sup>123</sup> We will implement the standard VT algorithm with the exception that we will use super learner.<sup>124</sup> instead of random forests during the first stage of the algorithm, which is an ensemble learning approach that is more robust to different forms of the response surface. This will result in a response surface, whereby individual level responses to the treatment are estimated as a function of baseline covariates. In the second stage of VT, we will use tree-based methods to identify subgroups of the population with differential treatment effects, while using a permutation testing approach that allows for family-wise control of the type-1 error rate for the entire VT algorithm.<sup>125</sup>

<u>Qualitative:</u> Led by D. Dohan (Co-I), qualitative work will be partially informed by the primary outcome (ACP completion) and secondary outcome (ACP engagement survey) data as well as the deeper dive of our quantitative analyses described in the paragraph above. Using purposeful sampling, we will identify patients with high and low ACP engagement scores (secondary outcome) by survey and patients who did and did not complete ACP (primary outcome) from each HCS and then from this list, each site with select 20 patients total (5 per group) for qualitative interviews (total n=60). Caregivers will be included as desired. We will ensure diversity with respect to age, race/ethnicity, gender. Due to the complexities in involving an interpreter, we will limit our recruitment to English-speaking participants.

Informed by previous studies of ACP and older adults conducted by R. Sudore and D. Dohan<sup>126</sup>, we will develop a semi-structured interview guide to include open-ended guestions related to their experience with ACP, preparing for surgery, post-operative course, and expectations vs. experience with surgical care. The team will be extended by Co-I's D Peska and R Rizvi who will assist in assessments at UMN and perform virtual interviews with UCI patients. The 3 HCS are unique in their care coordination and culture, case mix, provider mix, and patient racial, ethnic, and economic diversity and we hypothesize that barriers and facilitators to this process may different based on patient and HCS characteristics. We will assess experience navigating the patient portal, PREPARE, pre-surgery communications with surgical and perioperative team as well as post-operative course. Questions will be designed incorporating themes from Capability, Opportunity and Motivation, Behavior (COM-B)<sup>1</sup> implementation science theory.<sup>126,128</sup> Our interview guide will include broad, open-ended questions, allowing participants to direct the course of discussion, and use probes to clarify concepts and elicit detail. We anticipate, based on prior similar analysis, reaching thematic saturation with 15 patients per group (5 per HCS) but if this does not occur, additional interviews in each subgroup will be added. Each interview will be recorded, professionally transcribed, and the interviewer will then verify its accuracy. We will analyze transcript data using an iterative framework approach which includes familiarization with data, coding data, and combining codes into larger themes by comparisons within and across transcripts.<sup>129</sup> We will resolve any discrepancies using the constant comparative method, a systematic process used in gualitative research.<sup>130</sup> The gualitative ratings by reviewers will be assessed across a core group of notes

and inter-rater reliability will be assessed using Fleiss' kappa. Thematic emergence will then be analyzed and discussed by all team members to refine their understanding of the conceptual content.<sup>131,132</sup> Dedoose Version 8.0.35 (Los Angeles, CA: SocioCultural Research Consultants, LLC) will be used for data organization and retrieval.

In addition to the patient interviews, we will lead focus groups of 3-5 surgical care team providers from each HCS as well as the healthcare navigators from each HCS. We will assess barriers and facilitators to ACP completion in the surgical patients, with a focus on these specific domains: training, education, documentation and burden of administrative related tasks, sense of responsibility, experience with older adults (for stakeholders).

**Expected Findings and Alternatives:** We anticipated that we will be able to predict the small but critical subgroup patients who need the intervention via the postal mail and/or require additional support from the remote healthcare navigator to engage in ACP. Ideally, we would integrate predictive analytics into the EHR to automate sending postal mailings for those patients not likely to engage via the patient portal. Similarly for those patients predicted to need healthcare navigator support, automatically populating a work list for the healthcare navigator would improve efficiency and scalability. Our team has broad experience in both predictive analytics as well as clinical decision support (an alternative strategy to support those patients more hesitant to engage, especially if the support must come from the surgical care team as opposed to a ACP-specific healthcare navigator). Targeted, focused deployment of postal mailings and the healthcare navigator (expensive and finite resources) will increase the HCS ability to sustain the work after the study period ends. We anticipate that there will be moderate burden on the surgical care teams with regards to guestions related to ACP and documentation but much of these is able to be alleviated by the healthcare navigator. It is possible that over the study period, the laws around AD as well as the EHR vendors may have evolve allowing for the approaches to be further streamlined as compared to what is proposed in the UG3/UH3, R. Sudore and G. Melton regularly work with legal groups and EHR vendors. Finally, if the pragmatic trial does not show incremental benefit with increasingly intense ACP interventions, the qualitative interviews will be critical to better understand why the intervention was not transferable to surgical clinics and to identify future directions for system-level interventions to engage patients in surgical ACP.

C.3.9. UH3 Aim 3: Analyze the content of the ACP notes across 3 HCS using natural language processing (NLP) and data mining to begin to identify and assess thematic completeness of ACP notes. <u>Hypothesis:</u> ACP notes represent a newer and more dynamic marker of patient-care team interactions around ACP and deeper understanding of the variation in content and completeness (e.g., surrogate, preferences with life-sustaining treatments, and goals of care) will inform impact of UH3 trial and future directions.

Rationale: We propose, highly consistent with and supporting the premise of the expanded definition of ACP and Clinically Meaningful ACP Documentation, to explore the content of ACP documentation including presence or absence of various elements of serious illness conversations and to understand the detailed content at a broader level. This will help us move more dynamically towards making expanded ACP a dynamic ("living and breathing") document. While the primary outcome (ACP completion) and secondary outcome (patient engagement in ACP) are defined for the pragmatic trial, these measures over-simplify the complex nature of ACP and do not address the dynamic nature of ACP and the expanded ACP definition (see significance). Particularly in surgery, ACP will be dynamic. Goals and wishes may evolve as patient learns about initial diagnosis, treatment options (new surgical clinic evaluation, timing of intervention in aim 1) and then elects to undergo surgery (or not), learns of operating room and pathologic findings, and convalesces in the hospital and beyond. Formal documentation (AD, POLST, living wills etc.) frequently lack important clinically meaningful aspects of ACP discussions and, with the associated legal requirements with regards to signatures and notaries, are not easily amended as a patient's condition, situation or wishes would evolve. ACP notes in the EHR are a living document that reflect discussions between the patient and the HCS care team, are easily accessible and amended, aligned with expanded ACP definition, and will likely continue to become more prevalent. While there is no standard as to what should be in the ACP notes, it has been suggested that key components might include surrogate decision maker, desire for life sustaining treatment, and overall health goals, (personal values, life goals, and preferences regarding future medical care including various informed decisions related to quality of life as well as the influence of the duration of physical/cognitive disability and pain on guality of life).

Our preliminary data demonstrate variability in documentation of these elements in palliative care notes. In UH3 aim 3, this work will be extended to ACP notes completed by providers other than those trained in palliative care e.g., the surgical care team to begin to unlock elements of expanded ACP and patient-surgical care team

discussions and, hopefully begin to understand the relationship between engagement in the intervention and robust ACP notes.

Our approach to NLP will also use state-of-the-art deep-learning recurrent neural networks to build more robust AI/ML models. This is in contrast to recent work disseminating findings aimed to ascertain ACP elements from clinical notes, using basic regular expressions which were then tested on a small set of 60 clinical notes.<sup>57</sup> Further, this work will not only develop robust NLP AI/ML models for various aspects of ACP documentation, but also we plan to ensure our developed NLP tools are externally validated (across multiple sites) and shared. We expect that the pragmatic trial will result in a significant increase in clinical ACP notes for surgical patients and anticipate that our findings will serve as a supplemental sub analysis of the effectiveness of each of the trial arms. This work, as alluded to previously, will also serve as a foundation for understanding and ascertaining the provision of goal-concordant care in future studies.

**Approach:** Our overarching approach will be split into NLP and data mining tool development and optimization and clinical trial analysis. This work will be led by the UMN informatics team (G. Melton, G. Simon, B. Knoll in collaboration with Fairview IT, UCI EHR analyst, L. Pierce UCSF Informatics) which will interface with the biostatistics team (J Boscardin and J Koopmeiners) for the supplemental clinical trial analysis. The NLP and data mining tool development and optimization include the following high-level steps:

Expand the ACP documentation corpora and annotations for NLP AI/ML tools: We will focus on ACP documentation for our corpora but will plan to expand our analysis to other high-value data sources (including nursing assessments and other data sources in later phases and gold standard expansion). To date, we have successfully shared a large set of deidentified UCSF ACP notes with UMN for additional analyses and NLP model development as well as have a history of externally validating by running AI/ML tools separately at each site when data sharing has been less feasible. Transfer of notes has been accomplished by establishing a material transfer agreement and IRB approval for de-identified note sharing and NLP AI/ML model development. We will expand this arrangement to include UCI early in the UH3 study. Additional annotators will be trained using our ACP annotation codebook with annotation guidelines and information on how to use our annotation tool, INCEpTION. Annotation guidelines for various data elements will be adapted and illustrative examples will be added to help coders, as needed. Inter-rater agreement assessment of annotation quality will be assessed using Fleiss's kappa for multiple raters. We estimate performing inter-rater reliability on a subset of approximately 10% of the corpus used for training and validation (maximum of 50 notes overlap) to ensure a reliable and high-quality gold standard. We expect to work exclusively with ACP documentation to start for a total of 1,000 notes across the three sites. We will expand our corpora and annotations to other assessments (e.g., semistructured/unstructured nursing assessments stored in flowsheets, physical therapy notes, and occupational therapy notes) as our study progresses and core ACP note NLP AI/ML models are complete.

NLP AI/ML model development and optimization: Our preliminary work was performed on palliative care notes and the associated annotations will be leveraged for training our NLP AI/ML models on surgical ACP notes. To maximize the performance and robustness of our NLP AI/ML models, we will use a range of techniques to ensure we consider the range of language variability and levels of granularity. For example, we will apply standard techniques to identify misspellings, abbreviations, and other regular expressions. Importantly, we will use word embeddings to strengthen the performance of our NLP AI/ML models. Word embeddings are a form of word representation that allows words with similar meanings to have a similar representation (e.g., both "substance use disorder" and its abbreviation, "SUD" are represented as having similar meanings). We have used them in term expansion projects.<sup>133,134</sup> In our prior work.<sup>40</sup> we have demonstrated that deep learning techniques can capture deep semantics of medical concepts from a large clinical corpus to extract a variety of semantically similar words or synonyms. For example, using word embedding models trained on a large scale of clinical notes, we could identify between 1 to 12 semantically similar terms for a group of dietary supplements, including misspellings (e.g., "melotonin" is a misspelling of "melatonin") and semantically similar words (e.g., "ginkgo" is similar to "gingko"). This enabled us to average 8.4% more clinical notes and 11.7% more patients for each supplement compared with simply expanding terms using the Unified Medical Language System (UMLS) as an ontology of related terms. For this reason, we propose to use expert consultation and word embedding models to expand our approach. We will plan to use deep learning techniques such as attention-based neural network or Bidirectional Encoder Representations from Transformers (BERT)<sup>135</sup> and its variants such as ClinicalBERT, PubMedBERT, and BlueBERT, to resolve ambiguity.<sup>136,137</sup> Similar

to our prior work,<sup>40</sup> we will fine tune hyperparameters in pre-trained BERT models on 80% of our annotated corpus and evaluate on the remaining 20%.

<u>NLP AI/ML model evaluation</u>: We will train our NLP AI/ML model on the core set of ACP notes (anticipated to be approximately 800 ACP notes plus the 226 already annotated palliative care notes) and a fully held out evaluation set (at least 200 ACP notes) so as not to bias our results. We will ensure that our validation and training sets have a mixture of notes from all sites. The NLP AI/ML models will be trained on goals of care. Our training set will also have performance metrics (ceiling maximal performance) using 10-fold cross-validation and will report F1-measure to characterize model performance, expecting acceptable performance to be 0.85 or better for use for extraction of each of the ACP note components. We expect that for themes with frequent content (e.g., surrogate decision maker) or likely low variability in language (e.g., information about power of attorney), that our approach may work well. We also anticipate that addition NLP AI/ML model optimizations may be needed for less frequent themes or themes with a greater degree of variability in expression (e.g., expressions around goals of care), including the need to expand our training set or enrich model training using techniques provide additional training examples, including using silver standards for training our models.<sup>138</sup> These results will allow us overall to describe the relative completeness of ACP notes (e.g., whether each of the key components of serious illness conversations is included).

<u>Topic model on ACP note content</u>: As we have previously done with other applications such as clinical text with remote patient monitoring<sup>139</sup> and with text around learner evaluations,<sup>140</sup> we will use topic modeling techniques, both Latent Dirichlet Allocation (LDA<sup>141</sup>) and the Correlation Explanation (CorEx<sup>142</sup>) algorithms to automatically infer topics from ACP text. Study team reviewers will evaluate the performance of the topic modeling and assignments of various topics to various categories. From this, we will characterize various areas of importance to patients for each of the various ACP components (e.g., what is the topic and/or content that patients provide around social support).

<u>Sub-analysis of ACP content with clinical trial arms:</u> With NLP AI/ML models developed and evaluated with adequate performance, our models will be run on ACP clinical notes for all arms of the trial to characterize the presence or abscess of content across the expected domains including <u>surrogate decision maker</u>, <u>desire for life</u> <u>sustaining treatment</u>, and <u>overall health goals</u>, (personal values, life goals, and preferences regarding future medical care including various informed decisions related to quality of life as well as the influence of the duration of physical/cognitive disability and pain on quality of life). In addition to measuring each dimension, we will also develop an ACP documentation quality score based on the completeness of documentation across multiple dimensions, starting with a proportion of completeness or possibly a weighted proportion (e.g., potentially weighting more important elements higher and less important elements lower). As a surrogate sub-analysis of the UH3 aim 1 trial, we will correlate the quality of ACP documentation and ACP content with each Arm of the trial, by the surgeon, and over time with the trial.

**Expecting Findings and Alternatives:** We expect that there will be greater rates of meaningful ACP documentation across trial arms with increasing intensity of the intervention and that other individualized factors in the notes will also increase (e.g., ACP completion previously, beyond the 6-month period, social support factors, other personal factors). It is possible that we may encounter data challenges for which we have substantial experience, including missing values, complex data representations, the need for consensus modeling if there are challenges with data sharing, or the need to recognize and deal with heterogeneous subpopulations, or to use external data for improving predictive accuracy. As a follow-up step, we expect to expand our corpus beyond "official" ACP documentation to include other data sources of high value for associated information (e.g., nursing assessments, occupational therapy or physical therapy notes, patient questionnaires, and others) to assess the additional value of these sources. In the later phases of the study, we will also explore automated methods to extract the intensity of care in the perioperative period (e.g., CPR, vasopressors, prolonged intubation) relying on a combination of structured and unstructured data sources and begin to explore care intensity to be able to understand more about the *provision of goal concordant care*.

#### C.3.10. UH3 Project Timeline and Milestones

The UH3 project timeline is tight but the groundwork has been laid for the UG3 phase, R. Sudore, PI, and L. Gibbs, co-I have integrated ACP into the EHR patient portal for the primary care encounter and administered a pragmatic clinical trial. E. Wick has pilot-tested ACP integration into the surgical care episode at UCSF. E. Wick, G. Melton, and J. Carmichael are knowledgeable about the surgical encounter and surgical HCS barriers. J. Carmichael and G. Melton hold major HCS leadership roles at UCI (Chief Medical Officer) and UMN (Chief Data and Analytics Officer), respectively. E. Wick, G. Melton, and R. Sudore have navigated the learning health system

at UCSF and UMN, understand the oversight and building and testing protocols, <u>and</u> have coordinated pragmatic EHR clinical trials like the one proposed. The primary and secondary outcomes are measurable and have been measured by members of the study team under clinical trial conditions. Furthermore, under the existing UCSF/UMN collaboration around surgical outcome measurement and the EHR, the combined team has standing weekly meetings, IRB approvals for similar work, and standard operating procedures for cross-testing work in the two health systems. Below (**Table 5**) is the timeline for the U H3 phase (details following the table on NLP and AI/ML,Aim 3). For the UG3 project timeline, refer to **Table 5**.

Table 6: UH3 Timeline						_		_				_						
Administrative Milestones		AR 1			YE	AR 2	2		YEAR 3				YEAR 4					
c	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4		
Develop detailed site implementation plans including site staff, method of ID & randomization	x	x	x															
Annual project meeting at NIH				x				x				x				x		
Interim data to report to DSMB			X		X		X		X		x		x					
3 HCS patient advisory board		x		X		x		x		x		x		x				
Final report to DSMB and NIH				0												x		
Trial Milestones	YEAR 1		YEAR 1					YEAR 2				AR :	3		YEAR 4			
	Q1 Y	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4		
Translate PREPARE for Your Care into additional languages	×			9														
Train virtual ACP navigators at 3 HCS	×		Y	•											<u> </u>			
Build and integrate Cipher messaging tool at 3 HCS	× ×		^															
Finalize participating surgical clinics at 3 HCS		x	Y												<u> </u>			
Onboard surgical practices and leadership to ACP and trial at 3 HCS	x	×	×												<u> </u>			
Finalize randomization engine at 3 HCS	~	^	~	¥	x	x	¥	x	¥	x	x	x			<u> </u>			
Intervention period of the trial (including 6 months follow-up)				×	×	×	~ ×	×	^ V	×	×	^						
Monitor trial accrual at 3 HCS				^	^	×	^	×	^	×	^							
Obtain interim study data from 3 HCS (EHR and survey)						^ ~		^ ~		^ ~								
Interim data cleaning and management (EHR and survey)						^		^		^			v	v	$\vdash$			
Obtain final study data from 3 HCS													^ V	^ ~	<u> </u>			
Conduct healthcare team interviews												v	^ _	^	<u> </u>			
Conduct patient interviews												X	X					
Analyze EHR, survey and interview data				<u> </u>		<u> </u>		<u> </u>			<u> </u>	<u> </u>	X	X	X	X		
Sustainability & Dissemination Milestones	YE	AR 1		1	YEAR 2				YE	YEAR 3			YE	YEAR 4				
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4		
Draft and submit manuscript describing study protocol		x																
Submit abstracts for scientific meetings			X		X	X	X		X	x	X		X	X	x			

Draft, submit, revise manuscripts		x	x	x	x	x	х	x	x	X	x	
Present research at scientific meetings			х	х		х	х		Χ	x		
Present findings at local organization grand rounds				х			х			x		
Finalize toolkit for broad dissemination									x	х	x	x
Finalize sustainability plans at 3 HCS									X	X	x	x

#### Milestones for Year 1:

- 1. Complete final preparations for trial at 3 HCS:
- 2. Translate PREPARE and ADs into additional languages for Minneapolis-St. Paul population
- 3. Set up and test trial elements that are <u>outside of EHR</u> (postal mailings, Cipher calls and SMS text messaging)
- 4. Identify, hire, and train healthcare navigator at each HCS
- 5. Finalize randomization engine and test with files from UCSF, UMN and UCI
- 6. Finalize surgical practices at each HCS that will participate in trial
- 7. Onboard surgical practices at each HCS
- 8. Initiate NLP Analyses
  - a. Finalize agreements (business associates agreements) and de-identified note transfer from 3 HCS to UMN for NLP analysis (agreement in place between UCSF and UMN for note sharing)
  - b. Initiate NLP analysis including dataset, training annotators and ensuring high quality annotations, and expand ACP documentation information extraction

#### Milestone Year 2:

Launch (end of Year 1) and meet first milestones for pragmatic trial at 3 HCS:

- 1. Review in detail fidelity of intervention to plan at each HCS
  - a. Audit 100 random patient charts at each HCS to ensure population identification logic is functioning correctly
  - b. Review access log data with regards to patient portal message receipt and opening
  - c. Review PREPARE website access data to confirm access
  - d. Review healthcare navigator feedback from 3 HCS on initial patients contacted
- 2. Interim data analysis with 1,000 patients:
  - a. Obtain interim data from 3 HCS
    - b. Clean data
  - c. Analyze primary outcome data
- 3. Conduct NLP information extraction process for ACP note areas; begin ACP note topic modeling. Report and disseminate initial NLP results.

# Milestone Year 3:

- 1. Complete pragmatic trial and follow-up surveys (ACP engagement survey at 6 months)
- 2. Conduct interviews (patients and surgical care team members) in 3 HCS
- 3. (Both Year 3 and 4) Additional maturation and dissemination in Year 4. Optimize NLP information extraction and topic modeling; apply state of the art Al/ML approaches to each, as appropriate. Disseminate findings and consider additional external validation approaches (even beyond the 3 HCS). Begin to explore supplemental analyses of ACP to goal concordant care.

#### Milestone Year 4:

- 1. Quantitative analyses for primary and secondary outcomes
- 2. Qualitative analyses and identification of themes from patients and surgical care teams about areas to improve surgical ACP
- 3. Dissemination via presentation, publication, and collaboration with professional societies
- 4. See NLP AI/ML model Aim 3 (Year 3), Milestone #3.

# D. FUTURE DIRECTIONS

We anticipate that the work will continue both "operationally" and as "research". Operationally, the need to improve adoption of ACP aligns with institutional (UCSF, UMN and UCI). For example, at UCSF and UCI, ACP is a metric followed on the executive scorecards. Additionally, and national quality and pay-for-performance metrics. Future directions can be divided into (1) optimizing the intervention including addressing inequities in

ACP completion rates, (2) understanding and improving how the surgical care team *uses* the preoperative ACP information if the patient has an unexpected post-operative course, and (3) beginning to understand how to use preoperative ACP information to measure goal concordant surgical care. UMN has not used PREPARE or easy-to-read ADs, therefore, the UMN evaluation will be particularly helpful in understanding scalability—a key goal.

#### E. EXPECTED IMPACT, IMPLEMENTATION, AND DISSEMINATION PLAN

This work is urgently needed and innovative. Immediately, it will accelerate adoption of evidence-based surgical care for older adults in two large health systems. Beyond, UMN, UCI and UCSF, the proposed work is pragmatic, using real-world data and will efficiently provide practical and scalable solutions for hospitals, surgeons, and surgical care teams to accelerate integration of ACP into surgery. In the final year, the trial materials will be refined informed by best practices identified in the final analyses and it is anticipated that the collaborations developed as part of the proposed work between the 3 HCS will be leveraged for future innovations in surgical system-level embedded research.

The ACP-related modified as part of the proposed work will be assimilated into a dissemination package or toolkit. We will have an example postal mail and patient portal letters, detailed EHR logic to help information technology experts in a HCS initiate patient portal messages and/or patient reminders, training materials for ACP specific healthcare navigator as a well as details on the specific definition of clinically meaningful ACP outcome measurement in the pragmatic trial. The PREPARE website provides the easy-to-read ADs and the PREPARE materials for individual use and avenues for HCS to license for large-scale adoption.

The American College of Surgeons (ACS) will serve as a critical dissemination pathway for the findings (Letter of Support, C. Ko). ACS was founded in 1913 and comprised of surgeon members. Its mission is to improve the quality of care for surgical patients by setting standards for education and practice for surgeons. The ACS has 104 chapters and 80,000 members in the U.S. and abroad, making it the most significant global organization of surgeons. The ACS is influential in the surgical community and has a robust community base of local chapters across the U.S. This structure offers wide dissemination of information about ACS priorities and quality initiatives, such as the proposed program from trusted, local surgeon peers. The ACS's current portfolio of quality programs spans the spectrum of disease indications, from trauma to cancer, obesity, and breast disease. A flagship program at the ACS is National Surgical Quality Improvement Program (NSQIP), a nationally validated, risk-adjusted, outcomes-based approach to measuring and improving surgical care and is among the foremost clinical registries in Medicine. E. Wick and C. Ko (Director, Division of Research and Continuous Quality Improvement, ACS) have successfully collaborated to accelerate the scale and adoption of surgical site infection bundles as well as enhanced recovery pathways in hundreds of hospitals (Agency for Healthcare Research and Quality ACTION III network, Safety Program for Surgery and Improving Surgical Care and Recovery Program).

E. Wick also has relationships with state hospital associations and/or state surgical quality improvement collaboratives (lowa, Hawaii, Tennessee, Michigan, and Illinois, amongst others). These groups convene and support quality improvement in surgery at the hospital level. E. Wick has also successfully collaborated with these groups to disseminate the Agency for Healthcare Research and Quality ACTION III network contracts. E. Wick, G. Melton, and R. Sudore are committed to presenting and publishing both the study design as well as the findings (positive or negative) and have a strong track record of presenting and disseminating in surgical, informatics, palliative care, and geriatrics meetings and journals.

Currently, older adults account for more than 40 percent of all inpatient operations performed annually in the U.S. This number will likely grow accordingly as the population ages, and the need for surgical services will rise concurrently. While operative risk has declined over time, major surgery can be associated with complications or worsening health status, ranging from anticipated straightforward impairment to unanticipated significant and long-term functional impairment and even death, particularly in older adults. Major elective surgery is a unique moment in time, one in which a patient and their caregivers naturally reflect on their quality of life and goals. Therefore, it is highly promising that, using <u>evidence-based</u>, <u>patient-facing tools</u>, we can enable patients to complete ADs and communicate their goals more effectively to their care team. This is an essential first step to ensuring goal-concordant surgical care, a priority of the National Academy of Medicine. Follow-up work will focus on deeper analyses of surgical encounters to better understand the association between ACP and goal concordant care and healthcare utilization.

#### DATA AND RESOURCE SHARING PLAN

UCSF endorses and supports the rationale of the NIH that sharing data from all NIH-supported studies reinforces open scientific inquiry, encourages diversity of analysis and opinion, and promotes new research. Sharing data from all NIH-supported studies also allows the testing of new or alternative hypotheses and methods of analysis, supports studies on data collection methods and measurement, facilitates the education of new researchers, enables the exploration of topics not envisioned by the initial investigators, and permits the creation of new data sets when data from multiple sources are combined.

To do so, we will deposit data from the proposed project in the National Archive of Computerized Data on Aging (NACDA), maintained by ICPSR at the University of Michigan. To minimize disclosure risk, our research team will remove direct and indirect identifiers from data. To encourage data sharing, our publications from the proposed project will highlight the availability of data of the proposed project.

# <u>All 3 HCS have agreed to share the data from the proposed work as required by the UG3/UH3</u> mechanism, see letters of support from HCS leaders at UCSF (J. Adler, Chief Clinical Officer, UCSF Health), UCI (C. Lefteris, CEO UCI) and M Health Fairview (J. Hereford, CEO).

#### Pragmatic Trial Data Sharing

Access and Sharing: ICPSR will make the research data from this project available to the broader research community. These files may be accessed directly through the NACDA website. After agreeing to Terms of Use, users with an ICPSR MyData account and an authorized IP address from a member institution may download the data, and non-members may purchase the files. Timeline: The research data from this project will be supplied to ICPSR by the end of the project so that any issues surrounding the usability of the data can be resolved. We will prepare the data appropriately, following NACDA best practices, to allow the NACDA/ICPSR staff to disseminate the data in a variety of media formats.

Intellectual Property Rights: The research team and their institutions hold the copyright for the research data they generate. By depositing with ICPSR, investigators do not transfer copyright but instead grant permission for ICPSR to re-disseminate the data and to transform the data as necessary to protect respondent confidentiality, improve usefulness, and facilitate preservation.

Ethics, Privacy, and Procedures: The proposed research will include data from approximately 6,000 surgical patients

From UCSF, UCI and UMN, and will be managed jointly by Drs. Wick, Sudore and Melton. The final quantitative dataset will include demographic information, ACP outcomes and ACP engagement survey results. We will redact the final quantitative dataset of identifiers prior to release for sharing including any identifying information.

Informed consent: For this project, informed consent statements will include language that allows for the survey data to be shared with the research community.

Disclosure risk management: The research team will remove any direct identifiers in the data before depositing with ICPSR. Once deposited, the data will undergo further procedures to protect participants' confidentiality. These include: 1) rigorous review to assess disclosure risk, 2) modifying data if necessary to protect confidentiality, 3) limiting access to datasets in which risk of disclosure remains high, and 4) consultation with data producers to manage disclosure risk. ICPSR will assign a qualified data manager certified in disclosure risk management to act as steward for the data while they are being processed. The data will be processed and managed in a secure non-networked environment using virtual desktop technology.

Format – Submission: The data and documentation will be submitted to ICPSR in recommended formats. Access: ICPSR will make the data files available in several widely used formats, including ASCII, tab-delimited (for use with Excel), SAS, SPSS, and Stata. Documentation will be provided as PDF.

Preservation: Data will be stored in accordance with prevailing standards and practice. Currently, ICPSR

stores quantitative data as ASCII along with setup files for the statistical software packages, and documentation is preserved using XML and PDF/A.

Archiving and Preservation – ICPSR is a data archive with a nearly 50-year track record for preserving and making data available over several generational shifts in technology. ICPSR will accept responsibility for long-term preservation of the research data upon receipt of a signed deposit form. This responsibility includes a commitment to manage successive iterations of the data if new waves or versions are deposited. ICPSR will ensure that the research data are migrated to new formats, platforms, and storage media as required by good practice in the digital preservation community. Good practice for digital preservation requires that an organization address succession planning for digital assets. ICPSR has a commitment to designate a successor in the unlikely event that such a need arises. Storage and Backup – Research has shown that multiple locally and geographically distributed copies of digital files are required to keep information safe. Accordingly, ICPSR will place a master copy of each digital file (i.e., research data files, documentation, and other related files) in ICPSR's Archival Storage, with several copies stored with partner organizations at designated locations and synchronized with the master.

**Code Sharing.** Relevant resources, such as code used for data processing and analyses, will be made publicly available through GitHub (https://github.com), a code repository service also used by the NIH. GitHub is a web-based platform that host source codes, documentation, and project-related web content for research projects. Code documentation will include instructions on how to access data, the name of a contact person for questions, and all relevant references to publications. To ensure long-term accessibility, a copy of the GitHub code repository will be archived in Zenodo (<u>https://zenodo.org/</u>) at the time of publication. Zenodo is an open access repository that specializes in preserving software and issues DOIs for code. The code DOI will be included in each resulting publication.

**Implementation Tool Sharing.** In addition to the data collected as part of the trial, all the tools created will be freely available. This includes: patient facing materials (letters, telephone and text scripts, PREPARE materials) as well as EHR build information (randomization engine, outcome measurement data queries etc.)

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