Study Population:	Patients: Adult (21+) Kaiser Permanente Southern California members diagnosed and treated for first primary early-stage breast (stage 0, I, II) or colorectal (stage I, II) cancer within Kaiser Permanente Southern California. Patients will be at low-risk for recurrence and treatment-related toxicities, as determined by our risk algorithm. Physicians: For centers in the embedded PCP model, PCPs selected to participate must be Board Certified in a relevant primary care specialty; hold a valid and current MD or advanced practitioner license; and be employed by the Southern California Permanente Medical Group.
Phase* or Stage:	This is a single site phase III National Institutes of Health Clinical Trial
Description of Sites/Facilities Enrolling Participants:	This trial will be conducted in a community-based integrated system, Kaiser Permanente Southern California (KPSC). KPSC medical oncology departments in the intervention group will enroll eligible patients into the intervention. KPSC oncology departments in the control group will passively enroll patients for tracking of utilization.
Description of Study Intervention/Experimental Manipulation:	Embedded PCPs will provide comprehensive care for eligible survivors at intervention sites, including cancer surveillance services, preventive care, and management of long-term therapy and associated side effects (e.g., endocrine therapy in breast survivors). A comprehensive multilevel approach will prepare survivors and PCPs. Intervention: Embedded PCP. Embedded PCPs will be enrolled in a 4-month course of initial training and education, followed by ongoing education via tailored survivorship information for low-risk survivors transitioning to their care. Initial training features 3 core components to build capacity, skill, and knowledge: 1) Individual didactic learning; 2) Small in-person group sessions; and 3) Observation. Intervention: Patient-level. Eligible patients in the embedded PCP model will be provided with tailored education regarding the planned transition prior to the transition. After cessation of active treatment, the care team will provide printed information including the planned course of survivorship care, what to expect from embedded PCP care, when the transition will occur, and reassurance that the oncology team will be available via telephone and email, and that PCPs will refer back to the oncologist for any concerning signs or symptoms. Intervention: System-level. Tailored alerts in the electronic medical record for recommended cancer surveillance and preventive care services that include rationale, links to guidelines, and references for questions (scheduled to fire when survivors have an outpatient office visit with their embedded PCP, following the same rationale for the alerts to fire during oncology visits).
Study Duration*:	60-months
Participant Duration:	36-months

2 INTRODUCTION

2.1 STUDY RATIONALE

Advances in treatment and detection of cancer have led to a rapidly growing population of cancer survivors. Significant growth of cancer patients, particularly those ≥65 years, is predicted within the U.S over the next 20 years.[1] The majority of these patients will enter into a prolonged post-treatment phase of care and considered cancer survivors.[2] *Cancer survivor* is commonly defined as from the time of diagnosis through the balance of his or her life, as originally articulated by the National Coalition for Cancer Survivorship.[3] For this proposal, we are focusing on the transition from the end of active cancer treatment (e.g., surgery, chemotherapy, radiation) to the post-treatment survivorship phase, which may include extended hormonal or other chronic therapy. Survivors require coordinated, comprehensive care addressing the major domains of survivorship as described by National Academy of Medicine, the American Society for Clinical Oncology (ASCO) and others, including surveillance for recurrence, screening for new cancers, screening and management for long-term and late effects, symptom management, and preventive care (e.g., vaccinations, screening for other diseases).[4-13] Older survivors (>65 years), who make up the majority of cancer survivors, also have a higher prevalence of comorbid conditions requiring management and coordination of care.[1]

We are facing unprecedented challenges in survivorship care delivery. Currently, survivorship care delivery is unsystematic, occurs in a variety of settings, and is often poorly coordinated.[14-16] Serious gaps in survivorship care have been identified, including underuse of guideline-recommended cancer surveillance services, such as annual mammography for breast cancer survivors and colonoscopy for colorectal cancer (CRC) survivors,[17-22] and underuse of recommended preventive care services such as vaccinations, lipid testing and cardiovascular risk management, and cancer screenings.[23-27] In addition, the frequent overuse of non-recommended services that provide limited benefit exposes patients to significant harms, as exemplified by use of non-recommended serum tumor marker tests and high-intensity imaging for surveillance of early stage CRC and breast cancer.[17, 28-36] Breast and CRC survivors have characterized their survivorship care as lacking in information for follow-up and providing inadequate support to address their needs.[37] Compounding these issues, our current oncology workforce is insufficient to care for the rapidly growing population of survivors.[1, 38, 39] Estimates from ASCO show a projected growth in demand of approximately 50% and only 14% growth in clinician supply, with demand exceeding supply as soon as 2020.[40, 41] This demand is increasing wait times for oncology services across the U.S.[42] The current approach to delivering survivorship care, which is typically with oncology specialists with limited or no coordination with primary care, is inadequate and fails to meet the needs of many survivors.[6] In this study, we will evaluate a new approach to survivorship care that embeds survivorship-trained primary care providers (PCPs) into the oncology setting to provide survivorship care for low-risk survivors, potentially alleviating demand for oncology services while maintaining quality care.

PCP-led survivorship care is feasible, but critical barriers must be addressed. In observational studies, survivors who receive care that involves PCPs (whether physicians or advance practice providers) received

OBJECTIVES	ENDPOINTS	JUSTIFICATION FOR ENDPOINTS
	health decisions as important covariates.	
To determine the efficacy of an ePCP model (experimental condition) compared to usual care on utilization of emergency, urgent, hospital, and non-recommended care.	Utilization: Unplanned care (hospitalizations, emergency department, and urgent care); and receipt of non-recommended cancer surveillance care as described by clinical practice guidelines (e.g., ASCO Choosing Wisely)	ePCPs trained to provide care to cancer survivors may have different rates of patients with unplanned care or non-recommended care.
Tertiary/Exploratory		
To explore knowledge and confidence in survivorship care between ePCPs and PCPs at usual care centers.	Confidence in delivery of survivorship care and knowledge of survivorship care guidelines, assesses using validated survey questions.	Causal mechanism: ePCPs exposed to our multi-level intervention of education, training, and support will demonstrate superior knowledge and confidence in delivery of survivorship care compared to PCPs at the usual care centers, who are not exposed.

4 STUDY DESIGN

4.1 OVERALL DESIGN

Our study was originally designed as a cluster randomized trial of two models of cancer survivorship care. However, as a result of the SARS-CoV-2 pandemic (COVID) and the overwhelming clinical demands experienced by out study sites from multiple COVID surges, we re-designed our study from a cluster randomized trial to a quasi-experimental pre/post with control group design. This design allows us to meet our originally proposed aims and scop*e.*

As a result of the pandemic and the overwhelming COVID surges in the Southern California region, Kaiser Permanente Southern California (KPSC) clinical and administrative staff and facilities entered into 'surge' mode. Surge plans, which are prepared to cope with emergencies such as this pandemic, re-deploy clinical and administrative staff as needed to new positions and assess and redistribute/close medical facilities. During the initial 6 months of the pandemic, many KPSC medical office buildings were closed or had limited services and primary care physicians were re-deployed as hospitalists, ICU relief staff, and as virtual care consultants. Nursing teams from both primary care and oncology were re-deployed into hospital care, urgent care, virtual care, and into new roles such as COVID education and COVID testing. This had a serious impact on our study as medical centers that had committed to participate in our originally proposed design were no longer confident that they had the primary care resources and staff to participate, as our study requires significant clinical time from primary care for training and patient care. Several of our centers informed us they could only participate if they could be assigned to the control condition.

To address these extraordinary circumstances, and to preserve our ability to meet our study aims and scope, we re-designed our study from a cluster randomized trial to a quasi-experimental pre/post with control group design. As we no longer have the element of randomization, we have increased the number of participating medical centers from 8 to 14 (4 intervention, 10 control). This increases our projected number of prospective patient participants from 2,000 to an estimated minimum of 2,450. We have also added a 'pre' data collection period to collect retrospective patient utilization data from all participating centers to allow for comparison of pre-intervention and post-intervention outcomes (Aims 1 and 3). Additionally, to address the potential differences between our intervention and control sites, we have fielded a brief survey to all center Medical Directors about the impact of COVID and other factors that may have contributed to their decision/ability to participate in the study. We are also collecting data on clinician, patient, and geographic factors. This adaptation to the study design was approved via telephone discussion by our program officer at the National Cancer Institute in accordance with NIH Grants Policy Statement, 8.1.2 on October 5, 2020.

Updated Design. This is a single site (KPSC), multi-center (multiple KPSC medical centers) trial using a non-randomized pre/post control group design to compare the effectiveness of 2 risk-stratified models of survivorship care, an ePCP model with a survivorship-trained PCP providing cancer surveillance, symptom management, and preventive care, compared to an oncology-led model, where the survivor stays with their oncology team (usual care within the KPSC system). We will address the barriers to PCP involvement from the empirical literature and propose to measure recommended quality outcomes including receipt of recommended care, PROs, and utilization of hospital, urgent, and non-recommended care.

This trial will evaluate the efficacy of 2 models of cancer survivorship care on receipt of recommended care for early-stage, low-risk colorectal and breast cancer survivors (primary outcome), PROs (secondary outcome), and use of unplanned and non-recommended care (secondary outcomes). This trial will be conducted in a community-based integrated system, KPSC, with medical centers non-randomly assigned to the ePCP or usual care model, with the models running for up to 36 months. We will retrospectively (pre-period) and prospectively (post-period) identify early-stage breast and colorectal cancer patients at

Collectively, this evidence demonstrates the feasibility and capability of PCPs assuming the primary role in providing survivorship care for early-stage, low-risk survivors, as well as the need for evaluation of survivorship care models. Thus, we will conduct a non-randomized pre/post with control trial to compare the effectiveness of an embedded PCP model, with a survivorship-trained PCP embedded into the oncology clinic to provide comprehensive survivorship care (e.g., cancer surveillance, symptom management, preventive care) as compared to an oncology-led model (usual care), where the survivor stays with their treating oncology team and sees their regular PCP in parallel, but in an uncoordinated fashion. We will address the barriers to PCP involvement identified in the empirical literature in the development of the intervention. Guided by the Framework for Quality Survivorship Care,[11] we propose to measure highly relevant outcomes including receipt of recommended care, PROs, including patient-provider communication and quality of life, and utilization of hospital, urgent, and non-recommended care.

4.4 END-OF-STUDY DEFINITION

A participant is considered to have completed the study if he or she has:

- Been identified and enrolled into either the ePCP or the oncology model of care
- Completed the 36-month follow-up period after enrollment into the intervention
- Completed the survey at 12-months post-transition (rolling recruitment)
- Truncated person-time will be accounted for in case of membership end or death

5 STUDY POPULATION

5.1 INCLUSION CRITERIA

In order to be eligible to participate in this study, an individual must meet all of the following criteria:

Provider population:
PCPs selected to participate must be Board Certified in a relevant specialty; hold a valid and current MD or advanced practitioner license; and be employed by the Southern California Permanente Medical Group (SCPMG).

Patient population:
- Adult (21+) KPSC members diagnosed and treated for pathologically-confirmed first primary early-stage breast (stage 0, I, II) or colorectal (stage I, II) cancer within KPSC
- Completed active cancer treatment within the past 6-36 months; active treatment includes cancer-directed surgery, chemotherapy (includes Herceptin (trastuzumab)), radiation therapy, and ovarian suppression therapy (e.g., Goserelin (Zoladex))
- Completed at least one office visit within KPSC medical oncology

The data to be collected at the time of study intervention discontinuation will include the following:

- The reason(s) for discontinuing the participant from the intervention, and methods for determining the need to discontinue
- Where the participant will be receiving survivorship care.

7.2 PARTICIPANT DISCONTINUATION/WITHDRAWAL FROM THE STUDY

Participants are free to withdraw from participation in the study at any time. An investigator may discontinue a participant from the study for the following reasons:

- Significant study intervention non-compliance, unless varying compliance is an aspect of the study objectives;
- Lost-to-follow up; unable to contact subject (see **Section 7.3, Lost to Follow-Up**)
- Any event or medical condition or situation occurs such that continued collection of follow-up study data would not be in the best interest of the participant or might require an additional treatment that would confound the interpretation of the study;
- The participant meets an exclusion criterion (either newly developed or not previously recognized) that precludes further study participation.

The reason for participant discontinuation or withdrawal from the study will be recorded on the EPICS Case Report Form (CRF). Subjects who receive the study intervention, and subsequently withdraw, or are discontinued from the study, will not be replaced.

7.3 LOST TO FOLLOW-UP

For our utilization aims (Aim 1, 3) we will track all utilization within KPSC until disenrollment or death.

For the participant survey, a participant will be considered lost to follow-up if he or she does not respond to multiple contacts to complete the survey after agreeing to do so.

The following actions must be taken if a participant fails to return the survey:

- The site will attempt to contact the participant, resend the survey, and ascertain if the participant wishes to and/or should continue in the study
- Before a participant is deemed lost to follow-up, the investigator or designee will make every effort to regain contact with the participant (where possible, 3 telephone calls and, if necessary, a certified letter to the participant's last known mailing address or local equivalent methods). These contact attempts will be documented in the participant's study file.
- Should the participant continue to be unreachable, he or she will be considered to have withdrawn from the study aim with a primary reason of lost to follow-up.

scale evaluates discussions about: 1) cancer follow-up care; 2) late or long-term treatment effects; 3) lifestyle recommendations; and 4) emotional or social needs, with response options discussed in detail, briefly discussed, did not discuss, and I don't remember. We will also examine CAHPS care coordination that includes six items on how often providers had appropriate information about: care provided by specialists; medical records and information about care; patient prescriptions and medications; follow-up regarding patient labs, X-rays, or other tests; and managing care between different providers. The response set for these items is a 4-point Likert scale ranging from "Never" to "Sometimes" to "Usually" to "Always." We will use design principles of Dillman et al. to order questions to minimize testing order effects, ensure the survey is appropriately and consistently designed for multiple modes, and minimize participant burden.[105]

Measures for Key Constructs for Patient Survey All measures have been previously validated and used in cancer research	
Construct	**Measure**
Patient-provider communication about survivorship care	Medical Expenditure Panel Survey (MEPS) 2016, Experiences with Cancer Supplement, Section 7, Medical Care for Cancer[106]
Quality of life	European Organisation for the Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC)[107]
Coordination and continuity of cancer care	Cancer Consumer Assessment of Healthcare Providers and Systems (CAHPS)[108]
Self-efficacy	PROMIS self-efficacy for managing symptoms[109]
Overall health	PROMIS Global Health Scale[109]
Receipt of treatment summary and/or care plan	Receipt of treatment summary from Health Information and National Trends Survey (HINTS 4, Cycle 2)[110, 111]
Delivery of survivorship care	Delivery of Survivorship Care Scale[63]
Symptom burden	Patient-Reported Bother From Side Effects of Cancer Therapy[112]
Satisfaction with health care decisions	Patient satisfaction with health care decisions: the satisfaction with decision scale[113]
Confidence in care	Questions adapted from 'Confidence in managing survivorship care' Casillas et al[114]

Utilization of unplanned hospitalizations, urgent care, and non-recommended cancer surveillance services (Aim 3). Using a similar approach to Aim 1, we will use CPT and ICD codes to identify hospitalizations related to cancer, using primary ICD code to identify reason for admission, as well as use of urgent care and use of non-recommended care. Non-recommended care measures are identified from relevant guidelines (e.g., ASCO Choosing Wisely, ACS Survivorship).[115-117] For early-stage breast cancer, this includes serum tumor markers and high-intensity imaging (e.g., CT and PET scans); for CRC, PET scans.

Exploratory Aim. We will explore PCP knowledge of and confidence in providing survivorship care, comparing the embedded PCPs to PCPs practicing at centers assigned to the usual care model.

AE/SAE Attribution Scale. We will calculate overall rates of occurrence of SAEs (number of SAEs per person-month) by extracting EMR/administrative data monthly to identify signals that might indicate potential harm.

Expected Risks. Based on data from randomized controlled trials and observational studies, [81, 82, 84, 121-123] we expect the SAEs rate to be comparable across study arms. These clinical events are risks inherent in the population and would occur regardless of study enrollment. We do not expect that the risk of adverse outcomes is heightened as a function of being enrolled in the study. Risks associated with collection of PRO data and potential loss of confidentiality and study procedures to minimize such risks were reviewed above.

8.3.2 DEFINITION OF SERIOUS ADVERSE EVENTS

As defined by the KPSC IRB, a serious adverse event (SAE) includes:

- Death
- Life threatening condition/situation
- An enduring or significant incapacity or substantial disruption of the ability to conduct normal life functions
- The delivery of a child with congenital anomaly or birth defect
- Other medical events that the PI determines require intervention to prevent the above outcomes

8.3.3 CLASSIFICATION OF AN ADVERSE EVENT

8.3.3.1 SEVERITY OF EVENT

The Principal Investigator must take action to protect the study participant(s) or others from the unexpected risk of harm. For AEs not included in the protocol defined grading system, the following guidelines will be used to describe severity:

- **Mild** - Events require minimal or no treatment and do not interfere with the participant's daily activities.
- **Moderate** – Events result in a low level of inconvenience or concern with the intervention measures. Moderate events may cause some interference with functioning.
- **Severe** – Events interrupt a participant's usual daily activity and may require systemic drug therapy or other treatment. Severe events are usually potentially life-threatening or incapacitating. Of note, the term "severe" does not necessarily equate to "serious

8.3.3.2 RELATIONSHIP TO STUDY INTERVENTION/EXPERIMENTAL MANIPULATION

All AEs will have their relationship to study procedures, including the intervention, assessed by an appropriately-trained clinician based on temporal relationship and his/her clinical judgment. The degree of certainty about causality will be graded using the categories below.

- **Related** – The AE is known to occur with the study procedures, there is a reasonable possibility that the study procedures caused the AE, or there is a temporal relationship between the study procedures and the event. Reasonable possibility means that there is evidence to suggest a causal relationship between the study procedures and the AE.
- **Not Related** – There is not a reasonable possibility that the study procedures caused the event, there is no temporal relationship between the study procedures and event onset, or an alternate etiology has been established.

8.3.3.3 EXPECTEDNESS

The Principal Investigator will determine if the event or incident is unexpected in nature, severity, or frequency, taking into consideration:

- The protocol-related documents, including: 1) IRB-approved research protocol or research application; or 2) other sources of information
- The Principal Investigator's knowledge of the characteristics of the study population
- The expected progression of any underlying diseases or conditions of the participants
- The participant's pre-existing conditions and risk profile for the event

8.3.4 TIME PERIOD AND FREQUENCY FOR EVENT ASSESSMENT AND FOLLOW-UP

The occurrence of an AE or SAE may come to the attention of study personnel from review of electronic medical record data or from a study participant presenting for medical care within the embedded PCP or the oncology model.

All AEs, not otherwise precluded per the protocol, will be captured on the appropriate CRF. Information to be collected includes event description, time of onset, clinician's assessment of severity, relationship to study procedures (assessed only by those with the training and authority to make a diagnosis), and time of resolution/stabilization of the event. All AEs occurring while on study will be documented appropriately regardless of relationship. All AEs will be followed to adequate resolution.

Any medical or psychiatric condition that is present at the time that the participant is screened will be considered as baseline and not reported as an AE. However, if the study participant's condition deteriorates at any time during the study, it will be recorded as an AE.

Changes in the severity of an AE will be documented to allow an assessment of the duration of the event at each level of severity to be performed. Documentation of onset and duration of each episode will be maintained for AEs characterized as intermittent.

The Principal Investigator and/or project manager will record events with start dates occurring any time after informed consent is obtained until 7 (for non-serious AEs) or 30 days (for SAEs) after the last day of study participation.

8.3.5 ADVERSE EVENT REPORTING

The Principal Investigator will report AEs that are determined to be unanticipated problems to the KPSC IRB within 10 business days of discovery and at the continuing review period.

8.3.6 SERIOUS ADVERSE EVENT REPORTING

The Principal Investigator will be responsible for conducting an evaluation of a SAE based on the unanticipated problem analysis and shall report the results of such evaluation to the NIH and the KPSC IRB as soon as possible, but no event later than 10 working days after the investigator first learns of the event. In the event of the death of a study participant, reporting will fall under one of the following pathways:

1. Death of an intervention study participant + unanticipated problem determination – the Principal Investigator will report to the Institutional Review Board within 1 business day of discovery and at continuing review
2. Death of an intervention study participant + NOT an unanticipated problem – the Principal Investigator will report at continuing review
3. Death of a non-interventional study participant – the event is not reportable

8.3.7 REPORTING EVENTS TO PARTICIPANTS

N/A

8.3.8 EVENTS OF SPECIAL INTEREST

N/A

8.3.9 REPORTING OF PREGNANCY

N/A

8.4 UNANTICIPATED PROBLEMS

8.4.1 DEFINITION OF UNANTICIPATED PROBLEMS

As per the definition provided by the KPSC IRB we will consider any AE under this protocol a reportable UP if the event meets all three criteria:

- Unexpected in nature, severity, or frequency
- Related or possibly related to participation in the research
- Suggests greater risk to participants or others than previously known

Corrective actions or changes that may be considered in response to a UP are:

- Modification of inclusion or exclusion criteria to mitigate the newly identified risks
- Implementation of additional safety monitoring procedures
- Suspension of consenting/enrollment of new participants or halting of study procedures for consented/enrolled participants
- Modification of informed consent documents to include a description of newly recognized risks
- Provision of additional information about newly recognized risks to previously consented/enrolled participants

8.4.2 UNANTICIPATED PROBLEMS REPORTING

The Principal Investigator will report UPs to the reviewing KPSC IRB. The UP report will include the following information:

- Protocol identifying information: protocol title and number, Principal Investigator's name, and the IRB project number
- A detailed description of the event, incident, experience, or outcome
- An explanation of the basis for determining that the event, incident, experience, or outcome represents an UP
- A description of any changes to the protocol or other corrective actions that have been taken or are proposed in response to the UP

To satisfy the requirement for prompt reporting, UPs will be reported using the following timeline:

- UPs that are SAEs will be reported to the IRB and the study funding agency within 10 business days of the investigator becoming aware of the event; within one day in the event of the death of a participant if determined a UP.
- Any other UP will be reported to the IRB and to the funding agency within 10 business days of the investigator becoming aware of the problem

behaviors, and prior care (e.g., for breast cancer survivors ≥50, colonoscopy every 10 years or annual FIT Kit for CRC cancer screening). We will use validated algorithms from our prior work based on CPT and ICD codes to identify use of services.[17, 31, 32, 99-102] We will identify receipt of recommended care for up to 36 months, starting approximately 12 months after cessation of active treatment (see Study Timeline, section 2.7 of the Study Record). Recommended care will be assessed in 12-month periods, with a binary outcome of received/did not receive for recommended cancer surveillance and for preventive care. We will also compare rates of individual services (e.g., rates of vaccination). Survivors with a pattern indicative of recurrence, based on validated recurrence algorithms,[103, 104] will be excluded from analysis of recommended cancer care. We will identify use of services from oncology, embedded PCP, and the member's assigned KPSC PCP to evaluate the impact of the model on utilization of services.

For the primary outcomes, we will use the DID framework (see equation 1) with different link functions to address the different types of outcomes (continuous, categorical, or counts). Outcome measurements are denoted yijkt, where i indexes the individual patients, j indexes the providers with whom patients had follow-up visit at site k, and during study time period t. The first two parameters on the right-hand side of equation 1 denote a random clinician intercept (δ0j) to represent the baseline variation between physicians in receiving recommended care, and δ1 denotes the level difference for the Oncology-led model of care at the beginning of the post-implementation follow-up period. The other two DID parameters δ2 and δ3 specify the average difference between Embedded-PCP and Oncology-led models at baseline and the difference-in-differences, the latter of which is the main quantity of interest. The remaining parameters correspond to a flexible function of time, and fixed effects for respective patient, provider, and site characteristics.

Equation 1: $f(\mathrm{E}(y_{ijkt})) = \delta_{0j} + \delta_1 I(post=1) + \delta_2 \boldsymbol{I}(Embedded\ PCP=1) + \delta_3 \boldsymbol{I}(post=1)\boldsymbol{I}(Embedded\ PCP=1) + f(t) + \boldsymbol{X_i\alpha + X_j\beta + X_k\gamma}$

Aim 1: n1=800, n2=2000

		Minimum δ by Superiority Margin										
Subscore	Mu_0	0	0.01	0.02	0.03	0.04	0.05	0.06	0.07	0.08	0.09	0.1
Breast, F	0.65	0.055	0.065	0.074	0.084	0.094	0.103	0.113	0.122	0.132	0.141	0.151
Colorectal, F	0.657	0.055	0.064	0.074	0.084	0.093	0.103	0.112	0.122	0.131	0.141	0.150
Colorectal, M	0.592	0.057	0.067	0.077	0.086	0.096	0.106	0.115	0.125	0.135	0.144	0.154
General, F	0.654	0.055	0.064	0.074	0.084	0.093	0.103	0.112	0.122	0.132	0.141	0.151
General, M	0.554	0.058	0.068	0.078	0.087	0.097	0.107	0.117	0.126	0.136	0.146	0.156

9.4.3 ANALYSIS OF THE SECONDARY ENDPOINT(S)

The main outcomes for Aim 2 will be analyzed using the same general modeling approach outlined in Equation 1, but dropping the parameters for the time difference and difference-in-difference(δ_1 and δ_3) since we will only be measuring those items once during follow-up. In this case, for example, yijk could denote the probability that patient i reports 'high quality' patient-provider communication during study period k. Other parameters in the model may be interpreted in the same manner as described above.

Aim 2: n1=240, n2=600

Subscore	Mu_0	0	0.01	0.02	0.03	0.04	0.05	0.06	0.07	0.08	0.09	0.1
Pat-Prov Communication	0.32	0.103	0.113	0.123	0.134	0.144	0.154	0.164	0.175	0.185	0.195	0.205
Surveillance	0.62	0.101	0.110	0.120	0.129	0.138	0.148	0.157	0.166	0.175	0.185	0.194
Late Effects	0.43	0.106	0.116	0.126	0.136	0.146	0.155	0.165	0.175	0.185	0.194	0.204
Emotional Concerns	0.29	0.102	0.113	0.123	0.133	0.143	0.154	0.164	0.174	0.184	0.194	0.204
Lifestyle Behaviors	0.39	0.106	0.116	0.126	0.136	0.146	0.156	0.166	0.176	0.185	0.195	0.205

Outcomes for Aim 3 will follow the same approach as Aim 1, but for categorical outcomes such as any inpatient visits, while using linear or log link functions where needed for continuous or count outcomes.

9.4.4 SAFETY ANALYSES

N/A

9.4.5 BASELINE DESCRIPTIVE STATISTICS

Demographic information (e.g., age, race, ethnicity, census-level education, and income) and clinical information (e.g., date of cancer diagnosis, age at diagnosis, disease stage, cancer treatment, endocrine therapy) will be collected from the EMR for all participants and compared between intervention and control groups.

9.4.6 PLANNED INTERIM ANALYSES

N/A

9.4.7 SUB-GROUP ANALYSES

We will test for differences by gender and race/ethnicity between the intervention and control groups on utilization and patient-reported outcomes. Prior studies of utilization in cancer survivors do not suggest or negate significant differences in intervention effect among subgroups; thus, it is important for our study to examine potential differences.

9.4.8 TABULATION OF INDIVIDUAL PARTICIPANT DATA

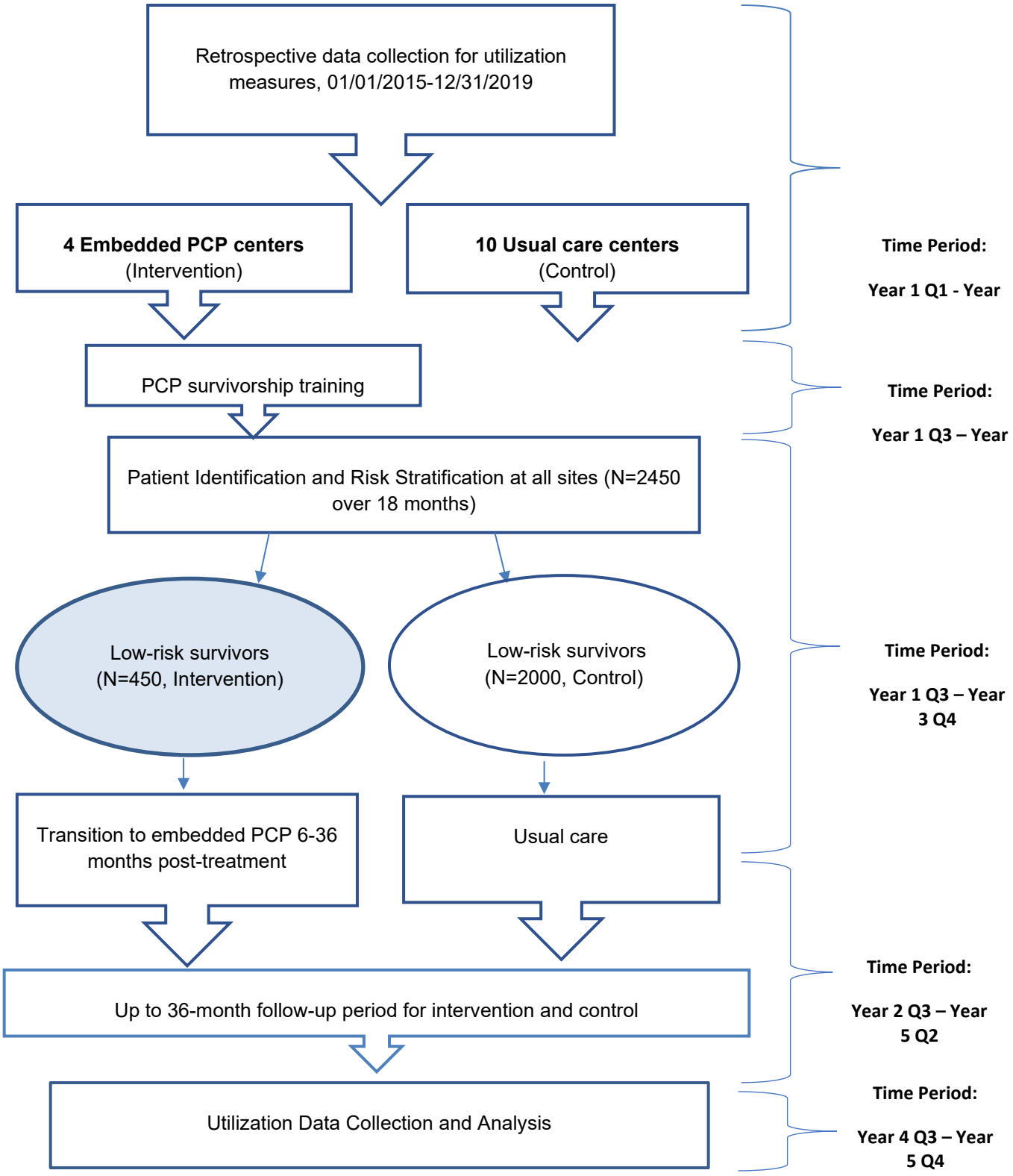
We will not tabulate individual participant data.

NCI	National Cancer Institute
NIH	National Institutes of Health
OHRP	Office for Human Research Protections
PCORI	Patient-Centered Outcomes Research Institute
PET	Positron Emission Tomography
PHI	Protected Health Information
PO	Project Officer
PROs	Patient-Reported Outcomes
PROMIS	Patient-Reported Outcomes Measurement Information Systems
QA	Quality Assurance
QC	Quality Control
RCT	Randomized-Controlled Trial
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SAS	Statistical Analysis Software
SCPs	Survivorship Care Plans
SCPMG	Southern California Permanente Medical Group
SMC	Safety Monitoring Committee
SO	Safety Officer
UK	United Kingdom
UP	Unanticipated Problem
URL	Uniform Resource Locator
US	United States

10.4 PROTOCOL AMENDMENT HISTORY

Version	Date	Description of Change	Brief Rationale
1.0	01-14-2021	N/A; First version	
2.0	07-28-2021	Updates to: 1) study design and statistical analysis plan; 2) Intervention components; 3) risk stratification	In response to the Covid pandemic, we had to change the study design from a randomized trial to a non-randomized quasi-experimental design; 2) We adapted the intervention materials in response to clinician request, including live webinars (rather than just pre-recorded); 3) Updated risk stratification/exclusions based on clinician feedback
3.0		Updates to: 1) Patient eligibility window; 2) Recruitment timeline; 3) Power and statistical analysis	Impacts from COVID have resulted in fewer early stage breast cancer and CRC patients diagnosed at early stage during

1.2 SCHEMA


Retrospective data collection for utilization measures, 01/01/2015-12/31/2019
4 Embedded PCP centers (Intervention)
10 Usual care centers (Control)
PCP survivorship training
Patient Identification and Risk Stratification at all sites (N=2450 over 18 months)
Low-risk survivors (N=450, Intervention)
Low-risk survivors (N=2000, Control)
Transition to embedded PCP 6-36 months post-treatment
Usual care
Up to 36-month follow-up period for intervention and control
Utilization Data Collection and Analysis
Time Period: Year 1 Q1 - Year
Time Period: Year 1 Q3 – Year
Time Period: Year 1 Q3 – Year 3 Q4
Time Period: Year 2 Q3 – Year 5 Q2
Time Period: Year 4 Q3 – Year 5 Q4

higher quality of care. [23, 25, 43-46] Most survivors expect PCPs to manage their general preventive care.[47] PCPs are well-positioned to counsel survivors regarding lifestyle choices such as physical activity,[48] disease prevention,[49] screening for psychosocial health needs,[50] and tobacco cessation.[51] Receipt of CVD preventive care in cancer survivors was strongly associated with PCP involvement.[52] PCPs receive high ratings on care coordination and comprehensive care during survivorship.[53] However, lack of knowledge and other barriers must be addressed for PCPs to assume primary responsibility for survivorship care; for example, a recent survey of PCPs found that less than half of guideline-recommended services for breast cancer survivors were routinely used.[54] Additionally, survivors may not be comfortable transitioning to a PCP for survivorship.[55, 56] Some survivors may prefer oncology-led cancer surveillance based on emotional reasons and feeling connected to their oncology team.[57, 58] Other barriers perceived by clinicians and survivors include poor communication with oncology,[59] lack of knowledge regarding existing guidelines,[60] limitations of health information technology and support,[61] and inadequate survivorship training and education.[58, 60, 62-66] Survivorship care plans (SCPs), summative documents intended to help improve communication and coordination of survivorship care,[7] may be a necessary but insufficient tool to address these issues. SCPs have been shown to help PCPs feel more prepared and knowledgeable about survivorship care delivery,[67] improve PCP-reported care coordination and communication,[68] and may improve quality of survivorship care[69-71] and patient self-efficacy.[72] However, results from most randomized controlled trials (RCTs) have found little to no effect of SCPs on distress, quality of life, or satisfaction with care.[73, 74] Thus, SCPs alone may be a necessary but insufficient component to engage PCPs and improve quality of survivorship care.[73, 75-77] We will address these barriers identified in the empirical literature in our study with multi-level interventions (patient, provider, system) incorporating robust education, training, and support for survivorship care.

The need for risk-stratified survivorship care. Risk-stratified survivorship care has been suggested as a potential model for U.S. survivors.[10, 41, 78-80] Risk-stratification involves evaluation of cancer and treatment characteristics, risk of complications, comorbid conditions, and other patient characteristics. In this approach, survivors with less complicated cancer treatments and at low-risk for recurrence or treatment toxicities are triaged to a less intense pathway (e.g., PCP-led or self-management) and patients with more complex cancer treatments/stage of disease are triaged to specialist oncology care for ongoing follow-up.[41, 80] This type of stratification has been implemented within the National Health Service in the U.K.,[81-83] and a similar approach has been implemented in Northern Ireland.[84] Recent data show successful triage of half of CRC survivors and approximately 80% of breast survivors to a low-intensity survivorship pathway.[82] In the U.K. the stratified pathways have been found to improve access to oncology specialists and are projected to save approximately £90 million over 5 years.[80] We will integrate a risk-stratified approach in our study to identify and triage low-risk CRC and breast cancer survivors, incorporating these evidence-based recommendations.

To address these issues, we will conduct a pre/post with control trial of two models of cancer survivorship care in early-stage colorectal and breast cancer survivors cared for in a community-based, integrated health care setting. Building on our pilot work[57] and drawing on the empirical literature, we will test the efficacy of an embedded PCP model (experimental condition) in which PCPs are embedded within an

all sites during their initial cancer treatment using a combination of pathology data and text information extraction algorithms. Potentially eligible survivors will be assigned a binary risk score (low risk/non-low risk) based on data readily available in the EMR including cancer stage, risk of recurrence, and other factors derived from current consensus-based recommendations. Embedded PCP participants will be transitioned to a trained PCP at 6-36 months after the cessation of active treatment. Multi-level components for this model include empirically-derived survivorship care interventions, such as provider education and training, using established training curriculum for PCPs engaging in survivorship care, health IT support (e.g., proactive office encounter alerts, links to guidelines), and patient education on the transition in care, signs and symptoms to be aware of, and what to expect from their PCP for surveillance and prevention. Usual care participants will be followed by their treating oncologist or surgeon, which is current "usual care" within KPSC.

Our specific aims and hypotheses (H) are:

Aim 1. To determine the efficacy of the PCP model relative to the usual care control group on receipt of recommended care (primary outcome). We will construct a composite measure of guideline-recommended cancer surveillance and age-appropriate preventive care services for the 18-month pre-period and 18-month post-period, identifying utilization from EMR data.

> H1. Patients in the PCP model will have superior receipt of recommended care compared to usual care.

Aim 2. To compare patient-centered outcomes on coordination of survivorship care, self-efficacy in managing care, and confidence in their PCP to provide survivorship care between the 2 models (secondary outcomes).

> H2. Patients in the PCP model will perceive significantly better care coordination, self-efficacy, and confidence in their PCP compared to usual care

Aim 3. To assess utilization of unplanned hospitalizations, use of urgent care, and receipt of non-recommended cancer surveillance services between the 2 models (secondary outcomes).

> H3. Use of unplanned and non-recommended care will be significantly less in the PCP model compared to usual care.

Exploratory Aim. We will explore PCP knowledge of and confidence in providing survivorship care, comparing PCPs who participate in the embedded PCP model to PCPs practicing at centers assigned to the usual care model.

Assignment and consent. Selection of participating centers will occur prior to PCP educational interventions and enrollment of patients. A scientifically valid comparison of the embedded PCP model to current usual care would only be possible with population-based enrollment and outcome assessment of low-risk survivors. Consequently, a waiver of the usual requirement for informed consent will be required. We believe that such a waiver of consent is not only widely recognized as necessary and appropriate but is also scientifically necessary and ethically justified given the minimal risk of the proposed research based

- At low-risk for cancer recurrence and treatment-related toxicities based on stage of disease and treatment modalities

For our Aim 2 survey:

- Primary language of English or Spanish (although we will assess our Aim 1 participants for recorded preferred spoken language and adjust translations as needed)
- Ability to complete surveys of patient-reported outcomes

Individuals of all races, ethnicities, and genders are eligible for this study. Children will not be included in the study, because they are rarely, if ever, affected by breast or colorectal cancer.

5.2 EXCLUSION CRITERIA

An individual who meets any of the following criteria will be excluded from participation in this study:

- Pre-existing cancer diagnosis (other than non-melanoma skin cancer)
- Less than 120 days of KPSC membership after index diagnosis of primary breast cancer or colorectal cancer
- Patient undergoing workup for suspected primary cancer recurrence or new primary cancer
- Enrollment on other cancer clinical trial
- Received treatment indicative of metastatic or high-risk disease including breast cancer patients treated with neoadjuvent chemotherapy
- Serious medical or psychiatric condition that would detract from study participation and measurement of PROs

For the provider survey, there are no exclusions; all sex/gender, racial, and ethnic group members are eligible to participate.

5.3 LIFESTYLE CONSIDERATIONS

N/A

5.4 SCREEN FAILURES

We will retrospectively (pre-period) and prospectively (post-period) identify early-stage (stage 0-II) breast and early-stage (stage I, II) colorectal patients at our assigned intervention condition medical centers early in their treatment course using our comprehensive pathology database, Co-Path, combined with a text-information extraction system. We will identify the end of active treatment (surgery, chemotherapy, radiation, ovarian suppression injection treatment) using our treatment databases (e.g., Beacon chemotherapy, Mosaiq radiation) and EMR data. At the end of treatment, we will assess salient risk factors based on recent recommendations for stratifying low-risk survivors. We will create a risk-score (low

8 STUDY ASSESSMENTS AND PROCEDURES

8.1 ENDPOINT AND OTHER NON-SAFETY ASSESSMENTS

Background Characteristics and Potential Confounders. Demographic information (e.g., age, race, ethnicity, census-level education and income) and clinical information (e.g., date of cancer diagnosis, age at diagnosis, disease stage, cancer treatment, endocrine therapy) will be collected from the EMR for all participants. Self-reported demographics will be collected from those who participate in the PRO survey. We will collect for clinician variables such as clinician gender, race, and years in practice from the EMR. Sex as a potentially important biologic factor will be included in all analyses.

Receipt of Recommended Care (Aim 1). We will construct composite measures of recommended care for cancer surveillance and for preventive care, based on recommendations from the NCCN survivorship guideline. Cancer surveillance for early-stage breast cancer includes annual mammography and 2-4 physician visits with history and physical (H&P) for the first 3 years; CRC surveillance includes colonoscopy within first year, annual chest/abdominal/pelvic CT, and 2-4 H&P visits and CEA lab tests annually for the first 3 years. Preventive care measures will be based on United States Preventive Task Force recommendations including appropriate cancer screening (other than for surveillance of primary cancer) for CRC, cervical, breast, and lung cancers, vaccinations (flu, pneumococcal), counseling for smoking cessation, and management of hyperlipidemia and hypercholesterolemia. These recommendations will be tailored to individual age, cancer type, health behaviors, and prior care (e.g., for breast cancer survivors ≥50, colonoscopy every 10 years or annual FIT Kit for CRC cancer screening). We will use validated algorithms from our prior work based on CPT and ICD codes to identify use of services.[17, 31, 32, 99-102] We will identify receipt of recommended care for up to 36 months, starting 12 months after cessation of active treatment. Recommended care will be assessed in 12-month periods, with a binary outcome of received/did not receive for recommended cancer surveillance and for preventive care. We will also compare rates of individual services (e.g., rates of vaccination). Survivors with a pattern indicative of recurrence, based on validated recurrence algorithms,[103, 104] will be excluded from analysis of recommended cancer care. We will identify use of services from oncology, ePCP, and the member's assigned KPSC PCP to evaluate the impact of the model on utilization of services.

Patient Reported Outcomes (Aim 2). We will use validated, reliable measures from existing national surveys that have been used in our target population. Most measures come from well-established surveys such as the Medical Expenditure Panel Survey (MEPS), the European Organisation for the Research and Treatment of Cancer (EORTC) Quality of Life, the Consumer Assessment of Healthcare Providers and Systems (CAHPS), and the Patient-Reported Outcomes Measurement Information System (PROMIS). We will assess patient-reported coordination of care, patient-provider communication, physical and mental health, assessment of survivorship care delivery, satisfaction with health decisions, and other measures relevant to survivorship care. We will also collect socioeconomic, demographic, and health behavior data (e.g. smoking). To evaluate our secondary outcome of patient-provider communication and coordination, we will use validated measures from the MEPS Experiences with Cancer Supplement CAHPS surveys (i.e., Patient-Centered Medical Home CAHPS coordination items). The MEPS patient-provider communication

8.2 SAFETY ASSESSMENTS

Collection of observational data from administrative and clinical databases, self-reported demographics from the PRO surveys, and intervention activities at the KPSC medical centers will be collected and discussed at weekly project meetings. During monthly investigator meetings, data and recruitment summary reports of demographic and clinical information will be presented. Recruitment strategies will be brainstormed for optimization as needed. Recruitment success by racial/ethnic categories will be monitored closely and reported in National Institutes of Health (NIH) progress reports and to the Project Officer (PO)/Data Safety Monitoring Board (DSMB) no less than annually.

8.3 ADVERSE EVENTS AND SERIOUS ADVERSE EVENTS

8.3.1 DEFINITION OF ADVERSE EVENTS

We believe this study poses no more than minimal risk to subjects and the protocol uses the definition of adverse event (AE) from the KPSC IRB: (a) any unfavorable medical or psychological events experienced by a study participant during clinical research, including: a) a new symptom; b) worsening of an existing condition; or a clinically significant abnormal lab finding. AEs are considered a reportable unanticipated problem (UP) -- e.g., reportable to the KPSC IRB -- if they meet all three criteria for an unanticipated problem:

- Unexpected in nature, severity, or frequency
- Related or possibly related to participation in the research
- Suggests greater risk to participants or others than previously known

In the event that an AE is determined, it must be reported to the IRB within 10 business days and at the continuing review period.

Because patients with early stage cancer will be enrolled in the study, we expect that approximately 2-5% of breast cancer survivors will have a breast cancer recurrence [118], and 5-15% of colon and rectal cancer survivors will have a recurrence. [119] We expect this rate to be comparable across study arms. In terms of cancer-related mortality, the 5-year relative survival for localized breast cancer is 99% and regional is 86%; for colon and rectal cancers the localized 5-year relative survival is 91% and regional is 72%. [120] Our study will follow patients for up to 36 months, thus we anticipate cancer-related mortality in each arm; again, we expect these to be comparable in both arms. Cancer-related hospitalization outside of hospitalization related to cancer recurrence will be very rare, as these patients will be 12 months out from their active treatment (surgery, chemotherapy, radiation, ovarian suppression injection). We will capture metrics on cancer recurrence, mortality, and hospitalizations as part of our safety monitoring plan.

8.4.3 REPORTING UNANTICIPATED PROBLEMS TO PARTICIPANTS

N/A

9 STATISTICAL CONSIDERATIONS

9.1 STATISTICAL HYPOTHESES

Primary Endpoint(s):
To determine the efficacy of the ePCP model relative to the usual care group on receipt of recommended care. We will construct a composite measure of guideline-recommended cancer surveillance and age-appropriate preventive care services, identifying utilization from EMR data. We hypothesize that patients in the ePCP model will have superior receipt of recommended care compared to usual care.

Secondary Endpoint(s):

1) To compare patient-reported outcomes (PROs) including patient-provider communication, coordination of survivorship care, and quality of life between the two models. We hypothesize that patients in the ePCP model will perceive significantly better care communication, self-efficacy, and confidence in delivery of survivorship care compared to usual care, as collected by PRO surveys.

2) To compare utilization of unplanned hospitalizations, use of urgent care, and receipt of non-recommended cancer surveillance services between the two models. We hypothesize that use of unplanned and non-recommended care will be significantly less in the ePCP model compared to usual care.

9.2 SAMPLE SIZE DETERMINATION

Based on recent literature, expected prevalence of surveillance items in the first year of breast cancer survivorship range from 15% for assessment of bone health to 80% for mammography.[124] For CRC surveillance, a meta-analysis has shown that adherence ranged from 18-61% for colonoscopy and 17-71% for CEA tests. For preventive measures, Snyder et al. found that 30% of breast cancer survivors received recommended CRC screening, 32% received lipid testing, and 53% received an influenza vaccine. In our original cluster randomized design, we had 8 total medical centers, 4 intervention and 4 control, and anticipated 2,000 patients (approximately 250 per site). Under the original design, we modeled a range of expected values from 15% to 80% and found that a study this size would provide 90% power to reject the null hypothesis when the mean difference between groups is between 5.5% and 7.2%, with computed minimum detectable effect sizes for fixed power (0.8) and level of significance (0.025), using superiority hypotheses for the primary (receipt of recommended care) and secondary (patient-reported) outcomes.

9.4.9 EXPLORATORY ANALYSES

We will explore PCP knowledge of and confidence in providing survivorship care, comparing the embedded PCPs to PCPs practicing at centers non-randomly assigned to the usual care model. We will compare embedded PCPs to usual care PCPs using 2-sided chi-square tests.

10 SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

10.1 REGULATORY, ETHICAL, AND STUDY OVERSIGHT CONSIDERATIONS

10.1.1 INFORMED CONSENT PROCESS

10.1.1.1 CONSENT/ASSENT AND OTHER INFORMATIONAL DOCUMENTS PROVIDED TO PARTICIPANTS

For this study, a waiver for informed consent will be required to ensure a scientifically valid comparison of the ePCP model to current usual care. We do not foresee any risks to potential participants by not directly consenting them to participate in the trial. This study poses minimal risk to the patient because survivorship cancer care will be performed as part of routine medical care, and both the ePCP and the oncology-based model for survivorship cancer care are consistent with guidelines from professional societies and organizations with regard to the delivery of safe, appropriate, and usual care practices. We also believe that such a waiver of consent is not only widely recognized as necessary and appropriate, but also scientifically necessary and ethically justifiable under the “Common Rule” for protection of research participants (45 CFR 46.116d).

Patients will be recruited for PRO surveys under Aim 2. We will obtain written or oral consent from all participants for participation in the surveys. Survey consents and opt out options will be built into an electronic template as part of the initial survey screens. Consent forms describing in detail the survey procedures, and risks will be given to the participant and written or oral documentation of informed consent will be completed prior to completing the survey. The following consent materials are submitted with this protocol [none at this time; however, all written or oral consenting procedures will be submitted to our IRB prior to conducting any patient contact for the surveys under this Aim.

For utilization data captured under Aim 3 from the EMR, individual patients will not be recruited or consented (falling under the waiver of informed consent for Aim 1).

10.1.1.2 CONSENT PROCEDURES AND DOCUMENTATION

For Aims 1 and 3, consenting procedures are not applicable.

			2020-2021, necessitating changes to our eligibility and power/analysis plan; COVID has also impacted clinical staff availability, necessitating a longer recruitment timeline