Cover Page

Official Study Title:

Symptomatic FIT for Colon Cancer Detection, a Pilot Study

UCSD IRB#814209

Principal Investigator: Dr. Samir Gupta, MD, MSCS, AGAF

Professor, Division of Gastroenterology, Department of Internal Medicine

Co-Lead, Cancer Control Program, Moores Cancer Center

University of California San Diego

NCT Number: To Be Assigned

Document Date: November 4, 2026

Study Protocol and Statistical Analysis Plan

PROTOCOLS

#814209 - Symptomatic FIT for Colon Cancer Detection, a Pilot Study

Protocol Information

Review Type	Status	Submission Number	Approval Date
Expedited	**Approved**	**7**	**Oct 30, 2026**

Continuing Review Date	Expiration Date	Initial Approval Date	Initial Review Type
Mar 30, 2026	**--**	**Mar 30, 2026**	**Expedited**

Feedback

Approval Comment

Kuali version 22:

The consents/assents were revised. Re-consent is not required as no participants have been enrolled in the research.

Protocol Amendment Form

Amendment

UCSD AMENDMENT APPLICATION

All changes to an approved research study must be approved by the IRB prior to implementation, except when changes are necessary to avoid an immediate, apparent hazard to a study participant.

In general, changes to exempt research do not require submission of an amendment except for change in PI. However, changes in study procedures whereby the study no longer qualifies as exempt research requires a new submission.

SECTION A: Study Classification

Is this study subject to coverage analysis review by OCAA?

Yes

Are you submitting documents for an updated coverage analysis review by OCAA?

No

SECTION B: Multi-Site Research

Is the research a multi-site study?

No

Is UCSD relying on an external IRB?

No

Are other site(s) relying on UCSD IRB as their IRB of record?

No

Does the amendment include any changes that are not being implemented at UCSD/RCHSD?

No

SECTION C: Current Study Status

Indicate the current status of research participant enrollment:

Open for Enrollment (or plan to restart enrollment)

Indicate the current status of the research activities:

Research activities have not yet begun

SECTION D: Type of Amendment

NOTE: The OIA staff manage administrative changes. Changes to studies originally approved by the full board may require approval by the full board.

Type of Amendment (select all that apply)

Administrative changes - Revisions to previously approved studies that do not alter the risk–benefit assessment of the research.
For example:

- Additions or changes in Study personnel
- Correcting typographical errors, grammar, change phone number
- Changing document formatting
- Translations of approved documents
- Adding approvals from other sites

Change in Study Design

For example changes in:

- Study purpose and objectives
- Study design (e.g., adding a new treatment arm, long-term observational component)
- Inclusion/exclusion criteria or subject populations (including vulnerable populations)
- Sample Size
- Data/Safety Monitoring Plan
- Early Termination of Study

Changes in Study Procedures

For example changes in:

- Recruitment process and/or materials
- Informed consent process or waivers of consent
- Increase/Decrease in Study visits
- Data collection procedures
- Early Termination of Study

Changes in Study Procedures

Changes to consent, parental permission or assent documents

SECTION E: Changes/Modifications

The proposed changes(s)/modification(s) were initiated by *(select all that apply):*

Principal Investigator

Briefly describe the proposed changes to the research and rationale for the change, as applicable:

The discontinuation of Polymedco's OC-Light FIT, currently used by the UCSD laboratory, was announced approximately six months ago. We propose transitioning our research fecal immunochemical testing (FIT) to quantitative FIT performed by Polymedco. Fecal specimens will be prospectively collected from consented participants, labeled with study IDs, and sent to Polymedco for testing. The study-ID linkage key will remain at UCSD and will not be accessible to Polymedco. Polymedco will perform the testing and provide supplies and shipping at no charge to the study; no funds will be exchanged. Polymedco is the testing vendor, not the study funder. The FIT is for research use. The existing protocol safety provision will be retained: if six months have passed following a positive FIT result and no colonoscopy has been completed, the study team will prompt the participant's primary care provider to advise the participant to obtain a colonoscopy. The protocol, consent form, and relevant application sections will be updated to describe the testing procedure, specimen transfer, confidentiality protections, and handling of results. The revised documents are also being submitted for updated OCAA coverage analysis review. SPO has been contacted regarding the appropriate institutional agreement for the samples being sent. No participants have been enrolled, and research activities have not yet begun.

How will research participants (current or past) be notified of this change? (Select all that apply)

Not applicable – No participants enrolled in the research

Will the amendment/changes, in the opinion of the UCSD PI, increase or decrease the risk to research participants?

Neither

User Assurance

By submitting this form, I confirm that the information within this form is accurate and complete.

I am submitting with the awareness and permission of the Principal Investigator.

Upload the following documents:

For projects relying on OIA IRB:

- **Revised versions of previously approved documents affected by the proposed changes** *(e.g., Research Plan, Consent/Assent, or Recruitment Materials). Include a Word tracked-changes version as well as a clean PDF copy.*
  - **Note:** If revising currently approved documents, please use the "Replace" feature in Kuali to stack new versions of the document on top of the currently approved version. For step by step directions, please see step 8 in our KBA.
- **New documents** *(e.g., new Consent/Assent form or recruitment materials – PDF versions).*
- **Supporting materials relevant to the proposed changes** *(e.g., Master Protocol (MP), Investigators Brochure (IB)), Audit finding. Include a PDF tracked-changes version (or a detailed summary of the changes) and a clean PDF copy.*

For projects relying on an external IRB:

- **Revised versions of previously approved documents affected by the proposed changes** *(e.g., Protocol, Consent/Assent, or Site-specific Recruitment Materials). For Consent/Assent forms, include a Word tracked-changes version of all updated Consent/Assent forms and, if already approved by the reviewing IRB, include the IRB-stamped version.*
  - **Note:** If revising currently approved documents, please use the "Replace" feature in Kuali to stack new versions of the document on top of the currently approved version. For step by step directions, please see step 8 in our KBA.
- **New documents** *(e.g., new Consent/Assent form or site-specific recruitment materials). For Consent/Assent forms, include Word versions).*
- **Supporting materials relevant to the proposed changes** *(e.g., Master Protocol (MP), Investigators Brochure (IB)). Include a PDF tracked-changes version (or a detailed summary of the changes) and a clean PDF copy.*
- **Reviewing IRB approval letter** *if the amendment has already been approved by the reviewing IRB.*

Please make all protocol changes that are part of this amendment below.

Project Basics

STUDY TITLE

Symptomatic FIT for Colon Cancer Detection, a Pilot Study

PRINCIPAL INVESTIGATOR

GUPTA, SAMIR

Lead Department:

Medicine

Facesheet Inclusion

Study Personnel

List the names of all UCSD/RCHSD employees conducting the research or acting as a point of contact on the study.

Instructions to add or update person.

- Click "+ Add Line" to insert additional person.
- Select the Edit Pencil next to a person to edit or update. Be sure to choose Permission as Full Permissions or Read Only for each person.

Person

GUPTA, SAMIR

Home Unit

Medicine

Institutional Title

Professor, Division of Gastroenterology, Department of Internal Medicine Co-Lead, Cancer Control Program, Moores Cancer Center

Researcher Role

Principal Investigator

Permissions

Please choose ONLY ONE option from the below.

Full Access

Person

Boussina, Aaron

Home Unit

Medicine

Institutional Title

Assistant Adjunct Professor

Researcher Role

Key Person

Permissions

Please choose **ONLY ONE** option from the below.

Read-Only

Person

Lew, Kaitlyn

Home Unit

Medicine

Institutional Title

Medical Student Researcher

Researcher Role

Key Person

Permissions

Please choose **ONLY ONE** option from the below.

Full Access

Person

LIU, LIN

Home Unit

Medicine

Institutional Title

Assistant Professor

Researcher Role

Key Person

Permissions

Please choose **ONLY ONE** option from the below.

Full Access

Person

Le, Yi

Home Unit

Medicine

Institutional Title

Statistician

Researcher Role

Key Person

Permissions

Please choose ONLY ONE option from the below.

Full Access

Person

SUTTON, LEISA

Home Unit

Radiation Medicine and Applied Sciences

Institutional Title

project coordinator

Researcher Role

Key Person

Permissions

Please choose **ONLY ONE** option from the below.

Full Access

Person

Rodriguez, Katheryn

Home Unit

Radiation Medicine and Applied Sciences

Institutional Title

project manager

Researcher Role

Key Person

Permissions

Please choose **ONLY ONE** option from the below.

Full Access

Person

MANDVI, AMMAR

Home Unit

Family Medicine

Institutional Title

Professor

Researcher Role

Co-Investigator

Permissions

Please choose ONLY ONE option from the below.

Read-Only

Person

LYNCH, ALLISON

Home Unit

Family Medicine

Institutional Title

professor

Researcher Role

Co-Investigator

Permissions

Please choose **ONLY ONE** option from the below.

Read-Only

Person

Khan, Ayesha

Home Unit

Family Medicine

Institutional Title

Clinical Informatics Fellow

Researcher Role

Co-Investigator

Permissions

Please choose **ONLY ONE** option from the below.

Read-Only

eRegulatory/Florence Study Personnel

List all personnel who should have a role assigned in Florence for this study.

WARNING: You must add at least one eRegulatory/Florence user and role to this protocol in the 'Study Peronnel' section to automatically send this study folder over to Florence eBinders.

Personnel
GUPTA, SAMIR

Florence Role
Investigator

Florence End Date
No date entered

Personnel
SUTTON, LEISA

Florence Role
Research Coordinator

Florence End Date
No date entered

Personnel
Rodriguez, Katheryn

Florence Role

Project Manager/Lab Manager

Florence End Date

No date entered

Will any of the personnel listed above NOT be involved in the consent process?

Yes

List all personnel who will NOT be involved in the consent process.

Personnel

Boussina, Aaron

Personnel

LIU, LIN

Personnel

Le, Yi

Do any of the personnel listed above have any potential conflict of interest related to the research?

No

Unnamed personnel will help conduct the research at or under the direction of UCSD/RCHSD, such as:

- Residents or students who rotate through for short periods
- Volunteers

Yes

Briefly describe each type/group of unnamed personnel, including the expected frequency of rotation and the general scope of duties.

We plan to have coordinators assist with the consent process through the UCSD Moores Cancer Center Clinical Trials Office (CTO). We expect this pilot to have a short turnaround within a few weeks to complete, so the frequency of rotation of unnamed coordinators will be minimal. Generally, their duties would include approaching patients, assisting with data collection and cleanup, and coordinating patient follow up.

For unnamed personnel desribed above, the PI is responsible for:

- Proper delegation and oversight of tasks.
- Ensuring training appropriate to tasks.
- Verifying either no potential conflicts of interest or that conflicts have been disclosed and managed.
- Meeting any applicable institutional standards and permissions (e.g., liability, IT access, badging, HIPAA BAA)

I have read and understand the above

General Information

SUBMISSION TYPE

IRB Review

Submission for IRB Review.

Human Subjects Research – Expedited/Full Board

Please be advised that the timeline for initial Expedited reviews is generally 4-6 weeks from the date of submission of the Kuali application.

Full Board reviews generally receive initial review within 4-8 weeks from the date of submission of the Kuali application.

Once submitted an OIA analyst will be in touch should revisions be needed. If revisions are needed, the study team will be notified through an automatic notification from the Kuali IRB system.

PI is a PI-eligible UCSD employee

Yes

LOCATION WHERE ACTIVITY(IES) WILL BE PERFORMED

ACTRI La Jolla

UCSD Facilities or Sites (e.g., school, hospital or clinics, etc. but excluding ACTRI clinics)

Off-Campus (In California)

UCSD Facilites or Sites

Licensed Clinical Space

Other

Licensed Clinical Space

Outpatient

Other Facility or Site

Moores Cancer Center room 3069. This research office will be used to conduct recruitment calls and recruitment and follow up activities that do not require face to face interaction.

LAY LANGUAGE SYNOPSIS OF THE PROPOSED ACTIVITY

Colorectal cancer (CRC) incidence is sharply rising among successive generations born after 1960, reflecting a striking birth cohort effect (birth cohort CRC, BCCRC). CRC patients voice concerns about delays in diagnosis after symptoms develop, uncertainty regarding causes, and lack of actionable strategies to ensure timely diagnosis and risk mitigation. Current U.S. evaluation of CRC-related symptoms is inconsistent, with no systematic rule-out approach. A strategy of using a fecal immunochemical test (FIT) with high sensitivity for hemoglobin as a “rule out” test for CRC for people with symptoms has shown promise abroad, and novel blood-based cell free DNA (cfDNA) assays are now available, yet neither strategy has been evaluated for symptomatic patients in the United States.

Will UCSD serve as the IRB of Record for other institutions/organizations?

Yes, UCSD IRB will be IRB of record for other sites. (Please complete the Participating Site Section.)

Funding

Choose the option that describes the funding for this project.

Funding to UCSD planned , but not yet in Proposal Development, IP or Award stage (Department or Fiscal contact plans to submit Proposal, IP or Award record in the Grants Module)

Type of Funding

Non-Federal

Non Federal

Non-Profit/Foundation

For funding that is not or will not be in the UCSD Grants Module, briefly describe type of funding.

A Curebound Gift for a project titled "Birth cohort colorectal cancer" is in progress of being processed. Award amount is $250,000 for 2 years.

Study Population

Indicate the projected number of participants expected to be enrolled (i.e. sign consent) or the projected number of existing records/data/biospecimens to be accessed/collected/received by UCSD Study Team

40

Indicate the projected number of participants expected to be enrolled (i.e. sign consent) or the projected number of existing records/data/biospecimens to be accessed/collected/received by RCHSD Study Team

0

If UCSD will be the IRB for non-UCSD/RCHSD site(s), list the number of participants expected to be enrolled (i.e. sign consent) or the projected number of existing records/data/biospecimens to be accessed/collected **by all sites relying on UCSD IRB.**

0

Indicate whether any of the following populations will be specifically recruited:

Participants 18 years old or older

Research Characteristics

The research will involve the following. Carefully review then select all that apply or "None of the Above."

Collection of Biospecimens from Subjects

Compensation or Costs to Participants

Interview/Focus Groups/Surveys/Questionnaires

This research is, or involves, the following. Carefully review then select all that apply or "None of the Above."

Cancer-Related Research

Services/procedures billed to the sponsor/insurance/research participant (eg: labs, imaging, and tests that are performed at a UCSD Health facility). Selection will initiate a Coverage Analysis review from OCAA. Not selecting may result in improper billing to your research patients.

Will biospecimens be collected or processed at UCSD/RCHSD in a clinical site?

Yes

Informed Consent

Specify how informed consent will be obtained:

Signed consent/parental permission

Indicate the setting(s) in which the consent process will be conducted:

By telephone

Private setting

Informed Consent Confirmation:

Confirm that the research team will perform all of the following:

1. Provide the prospective participant(s) the informed consent document and as much time as needed to make a decision;
2. Ensure there is no threat of harm or adverse consequences to the prospective participant(s) if the decision is not to take part in the research;
3. Evaluate whether the prospective participant(s) is being coerced or unduly influenced by others to take part in the research, and if so, not enroll the prospective participant, even if the person agrees to be in the research;
4. Communicate in the preferred language of the prospective participant(s);
5. Adapt the presentation of the information to the person's capacities in terms of intelligence, rationality, maturity, and language;
6. Encourage and answer questions from the prospective participant(s);
7. Evaluate whether the prospective participant(s) understands the information being presented, and not enroll person(s) who does not understand, even if that person agrees to be in the research;
8. Ensure that no information provided is made to waive or appear to waive any of the prospective participant's legal rights, or releases or appears to release the investigator, the sponsor, the institution, or its agents from liability for negligence;
9. Communicate all the information in the consent document or script approved by the IRB; and
10. Not enroll a prospective participant(s) when the person providing informed consent is unwilling to listen to or consider the information, even if the person agrees to be in the research.

I confirm

Compensation/Costs

Will participants be compensated for their participation?

Gift cards

If research volunteers will receive financial or other forms of compensation, please describe the total amount of compensation that research volunteers or group may receive and the schedule of payments (e.g., after each study session/visit, at the end of the study). Also, if applicable, explain how payments, items or services will be apportioned if families or children will be involved.

Participants will receive compensation for each completed study activity: $25 for the study stool test, $25 for the blood draw, $25 for the study questionnaire, and $75 for the colonoscopy, up to a total of $150 in gift cards for completing all study activities. They will receive compensation in the form of a gift card after each completed study activity.

Will subjects incur any financial obligations from participating in the study?

Yes (specify below)

Describe financial obligations

Study materials and research procedures, including the research FIT/stool sample kit, quantitative FIT testing by Polymedco, and specimen shipping, will be provided at no cost to participants. Polymedco will perform the FIT testing and provide supplies and shipping at no charge to the study. However, participants and/or their health plan/insurance company may be responsible for costs associated with standard clinical care, including a usual-care colonoscopy; usual-care blood draw such as a complete blood count and iron studies; and any evaluation or treatment recommended by their clinician for their symptoms. Participants will not be reimbursed for out-of-pocket expenses, such as travel costs.

Screening/Recruitment

Does the research require that you conduct a preliminary assessment to determine eligibility?

Yes

How will screening be performed.

Review of UCSD/RCHSD medical records

Describe the medical records to be reviewed.

An algorithm developed for identifying individuals with signs/symptoms of colorectal cancer (CRC) will be utilized to generate a weekly query of individuals seen in outpatient primary care and urgent care settings with potential signs and symptoms of CRC. Charts for these individuals will be reviewed by a research team member to confirm eligibility. Next, these patients and their primary care clinicians will be contacted to consider the study following the procedures documented below. In collaboration with Dr. Aaron Boussina, a specialist in bioinformatics at UCSD, to develop the screening algorithm, we will access the UCSD Epic Clarity data base to identify adult patients born 1960 and later seen for outpatient primary care, or urgent care, visits between 1/1/16 and 12/31/25. The data will be saved into a pipe-delimited .csv format according to the data format requirements of the System. Once finalized, the algorithm will be applied on an ongoing basis to facilitate identification of potentially eligible individuals for screening by the study team.

Is this study limited to use of existing identifiable information/data/biospecimens, and will not involve any direct contact with research participants?

No

Specify the recruitment methods to be employed:

Face-to-Face Interaction
Print Media - Advertisements, Flyers, Brochures
Telephone or E-mail
Other

Other Recruitment Method

MyChart messages.

Risks & Benefits

Risks to Participants

Does the research involve any physical, psychological, social, legal, economic risks or any other foreseen risks to participants.

Yes

Briefly describe the risk to the participants.

Some minor risks from the blood draw include temporary pain, bruising, and bleeding. Additional minor risks include inconvenience from stool sample collection and minor embarrassment. The most serious risks from the blood draw include infection, nerve injury, excessive bleeding or blood collecting under the skin from the blood draw, all of which are extremely rare occurring in about one in 21,000 blood draws. Other most serious risks include psychological discomfort and embarrassment, and contamination in collection, transport, and storage of stool samples, which is very rare with good practices.

Do the research activities offer potential direct benefits to research participants?

Yes

Please describe potential direct benefit to the participants.

Note: Payment to participants, whether as an incentive to participate or as compensation for time and inconvenience, is not considered a "benefit." Also providing incidental care is also not to be considered a benefit.

Participants will have a usual care colonoscopy for symptom/sign work up facilitated by the research team. This usual care colonoscopy may result in diagnosis or treatment that advances the patient's clinical care and health.

Describe the potential societal benefits of the proposed research (e.g., knowledge to be gained):

The knowledge gained from this study is valuable. This pilot will enable the successful implementation of a full-scale cohort study to evaluate FIT and cfDNA as rule-out strategies for CRC detection.

Privacy/Confidentiality

Indicate the measures that will be taken to protect the privacy of participants. Privacy is about people. Privacy refers to a person's wish to control the access of others to themselves.

Procedures will be performed in a private setting.

Private information collected will be limited to that necessary to conduct the research.

Protected Health Information (PHI) identifiers will be collected or received

Yes

Indicate what Protected Health Information (PHI) identifiers will be collected or received.

Note: Only the "minimum necessary" participant identifiers/sensitive information should be collected.

Name(s)

Account numbers(MRN, health plan number, student ID number, etc.)

Address (street address, city, county, precinct, zip code) and/or equivalent geocodes

Phone/Fax numbers

All elements of dates, except year (including birth date, admission date, discharge date, treatment dates, date of death, etc.)

Any ages over 89 years and elements of dates (including year) indicative of such age, except if combined into a single category (e.g. 90 and above)

E-mail addresses

Please provide a justification for why the PHI identifiers indicated above need to be used for this research.

These PHI identifiers are necessary because demographics (i.e., name, DOB, race, ethnicity), medical conditions, medications, and gastrointestinal conditions and dates, are needed for determining whether the participant fulfills the inclusion criteria and does not have any of the exclusion criteria. Addresses are necessary for the mailed FIT kit collection and to obtain research related study predictor/outcome data.

Indicate the measures that will be taken to help maintain confidentiality of identifiable data, records, and/or biospecimens. Confidentiality refers to the researcher's plan to handle, manage, and disseminate data/records/biospecimens.

Coding of data with separate storage of the key and coded data
Password protection of research files
Password protection of research devices (e.g., computers, hard drives, cell phones, other portable media)
Restricted Access limited to those who have a need to know for performance of their responsibilities
Removal of identifiers as soon as possible
Training of research personnel
Secure network server will be used
Locked access to cabinet, freezer and/or room
Use of REDCap or Velos
Identifiers destroyed upon study closure

Will identifiable information transmitted over the internet be encrypted?

Yes

Is there a plan to share data/specimens from this study outside of the study team?

Yes

Is it possible that sharing of data/specimens from this study will be desirable in the future?

No

In what format will data/specimens be shared?

Data/specimens will be stripped of identifiers but will be labelled with a code. The recipient will not have access to the link between the code and identifiers (coded)

NOTE: If data/specimens will leave UCSD/RCHSD, an agreement must be in place first. Studies with a Clinical Trial Agreement or Grant award should have their study teams contact the appropriate office if they aren't sure whether the specific contract/award covers data/specimen sharing.

Unfunded studies at UCSD will need to obtain a DUA/MTA from OCGA before data or specimens are shared outside of UCSD.

RCHSD researchers should reach out to research@rchsd.org to establish data/specimen sharing agreements.

Non-English Speaking Individuals

While not targeted for enrollment, will this study include non-English speaking individuals who otherwise qualify for the study?

Yes

Indicate the method that you use to conduct the consent process with participants who do not speak English.

The consent form and other study documents will be available in the participants' primary language.

Confirm that the following statements are true.

1. Study staff or qualified translators will discuss the study in the participants' language;
2. The study will maintain the ability to communicate with non-English speakers throughout their participation in the study; and
3. When conducting research for which there is a real or foreseeable risk of biomedical harm in the state of California, the investigator will provide the participants who do not read, speak, or understand English a copy of the Research Participants Bill of Rights in a language in which they are fluent.

I confirm that the preceding statements apply to the proposed research.

HIPAA Research Authorization

Select all that apply to the use of or disclosure of PHI.

HIPAA research authorization will be obtained

Request for partial waiver of HIPAA research authorization (e.g., for recruitment)

If you selected more than one option above, indicate the process to be used with each group or activity.

We will conduct weekly screening of patients seen at UCSD clinics who have gastrointestinal symptoms that could be red flag symptoms of early onset colorectal cancer. These patients are ≥18 years-old and born after 1960. This screening is for the purpose of recruitment. We will obtain HIPAA Authorization upon consent of the patient while on study as well.

Confirm that the following statements are true:

1. The requested PHI is the minimum necessary to meet the research objectives;
2. The PHI that is obtained will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research, or for other research for which the use or disclosure of the PHI would be permitted; and
3. PHI will be protected as outlined in the “Privacy/Confidentiality" section.

I confirm.

HIPAA Waiver

If you are requesting a partial waiver, please describe the activity(ies) applicable to the partial waiver.

This study needs access to EPIC and personal health information for eligibility and recruitment purposes.

Will the use or disclosure of protected health information involve no more than a minimal risk to the privacy of individual?

Yes

Could the research be practicably conducted without the waiver?

No

Could the research practicably be conducted without access to, use or disclosure of the PHI?

No

Will identifiers collected under the HIPAA waiver be destroyed at the earliest opportunity?

Yes

Explain why the research could not a) practicably be done without the waiver, and/or b) be done without access to, use, or disclosure of the PHI.

Screening and recruitment of eligible patients requires looking at their personal health information in EPIC to determine whether they meet full inclusion criteria and/or any exclusion criteria.

Supporting Information

Upload the following documents, as applicable

- Protocol (i.e., UCSD Research Protocol or Sponsor Master Protocol)
- Investigators Brochure/Drug Package Insert
- Device Instructions
- Data and Safety Monitoring Plan, if separate from Protocol
- Consent/Assent Forms
- Non-standardized assessments
- Site-Specific Recruitment Materials
- Multi-Site Communication Plan, if separate from Protocol

Supporting Document

Protocol - 1. BCCRC Cohort_UCSD IRB_v14_tracked.docx

Attachment Type

Protocol

Name/Version

Revised Protocol Tracked Changes

Supporting Document

Recruitment Materials - 2. Appendix A_MyChart Template Message_Final_v2.docx

Attachment Type

Recruitment Materials

Name/Version

MyChart Template Message Clean

Supporting Document

Recruitment Materials - Recruitment Materials - 3. Appendix B_Emailed consent form invite_Pilot Study_Final_v2.docx

Attachment Type

Recruitment Materials

Name/Version

Clean copy of Emailed consent form invite

Supporting Document

Recruitment Materials - Recruitment Materials - Study Flyer_Finalv12_SG.pdf

Attachment Type

Recruitment Materials

Name/Version

Clean Copy of Recruitment Flyer

Supporting Document

Data Collection Instruments - 5. Appendix E_REDCap DataDictionary_Final_v2.xlsx

Attachment Type

Data Collection Instruments

Name/Version

Supporting Document

IRB 814209 v21 Consent tracked.docx

Attachment Type

Informed Consent/Parental Permission

Name/Version

Revised Informed Consent Form Tracked Changes

Supporting Document

NIH Sister Study Questionnaire Modified_v2_tracked.docx

Attachment Type

Data Collection Instruments

Name/Version

NIH Sister Study Questionnaire modified to include both sexes and additional questions specific to colorectal cancer risk.

Supporting Document

IRB 814209 v21 Consent clean.pdf

Attachment Type

Informed Consent/Parental Permission

Name/Version

Revised Informed Consent Clean

Supporting Document

NIH Sister Study Questionnaire Modified_v2 Clean.pdf

Attachment Type

Data Collection Instruments

Name/Version

Clean NIH Sister Study Modified Questionnaire

Supporting Document

IRB Revision Cover Letter_03042026.pdf

Attachment Type

Other

Name/Version

IRB Revisions 1 Cover Letter

Supporting Document

Protocol - 1. BCCRC Cohort_UCSD IRB_v14_clean.pdf

Attachment Type

Protocol

Name/Version

Revised Protocol Clean

Supporting Document

IRB Revision 2 Cover Letter_03102026.docx

Attachment Type

Other

Name/Version

IRB Revisions 2 Cover Letter

Supporting Document

Re IRB Submission and PRMC Inquiry.pdf

Attachment Type

Ancillary Approvals (e.g., HERC, COI, PRMC, IBC)

Name/Version

PRMC Exempt Correspondence

Supporting Document

Symptomatic_FIT_Pilot_After_Visit_Summary_Patient_Handout_v1.docx

Attachment Type

Recruitment Materials

Name/Version

Recruitment Materials - After Visit Summary for Clinician Referral v1

Supporting Document

Recruitment Materials - Recruitment Materials - 3. Appendix B_Emailed consent form invite_Pilot Study_Final tracked.docx

Attachment Type

Recruitment Materials

Name/Version

Tracked changes of Emailed consent form invite

Supporting Document

02 Recruitment Materials - 2. Appendix A_MyChart Template Message_Final_SG_tracked.docx

Attachment Type

Recruitment Materials

Name/Version

MyChart Template Message Tracked

Supporting Document

Recruitment Flyer Summary of Changes 100826.docx

Attachment Type

Recruitment Materials

Name/Version

Summary of Changes on Recruitment Flyer

Added Information - Optional

Include any additional information that you want to communicate about the study.

We are adding a post-bac scholar who has joined the lab, Isaac Cesena (icesena@health.ucsd.edu), to the study team.

Assurance/Acknowledgement

By submitting this form, I confirm that the information within this form is accurate and complete.

I am submitting with the awareness and permission of the Principal Investigator

Administrative Details Form

Determinations

Review Type

Expedited

Expedited Category(ies)

Category 2(a)
Category 2(b)
Category 5
Category 7

Risk Level

Study Status

Approved Enrollment

Approved at UCSD	Approved at Rady	Approved at All Sites

Special Considerations

Were any of the following special considerations included in this approval?

Note: Applies to this submission only. Do not include considerations previously approved that were not included in this submission.

UC San Diego

Office of IRB Administration (OIA)
Biomedical Non-Intervention Protocol
Version Date 12.08.21

Detailed instructions are included for each section. All instructions must be removed, and all sections completed. "Not Applicable" is an acceptable response if the section does not apply to the research.

1. STUDY TITLE

Symptomatic FIT for Colon Cancer Detection, a Pilot Study

2. PRINCIPAL INVESTIGATOR

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3. STUDY RATIONALE

Colorectal cancer (CRC) incidence is sharply rising among successive generations born after 1960, reflecting a striking birth cohort effect (birth cohort CRC, BCCRC). CRC patients voice concerns about delays in diagnosis after symptoms develop, uncertainty regarding causes, and lack of actionable strategies to ensure timely diagnosis and risk mitigation. Current U.S. evaluation of CRC-related symptoms is inconsistent, with no systematic rule-out approach. A strategy of using a fecal immunochemical test (FIT) with high sensitivity for hemoglobin as a "rule out" test for CRC for people with symptoms has shown promise abroad, yet the strategy has not been evaluated for symptomatic patients in the United States.

4. SPECIFIC AIMS/HYPOTHESES

Aim. Conduct a pilot study of a clinical diagnostic strategy for BCCRC diagnosis: symptomatic FIT. We will establish a Symptomatic BCCRC Risk Cohort pilot of 40 primary care patients age ≥ 18 years, born 1960 and later, presenting with new CRC-related symptoms to undergo quantitative FIT, blood draw, and reference standard usual care colonoscopy for work up of symptoms to determine diagnostic accuracy.

5. BACKGROUND AND SIGNIFICANCE

- Recent changes in the epidemiology of colorectal cancer (CRC) reflect a striking birth cohort effect, which we conceptualize as birth cohort colorectal cancer (BCCRC).
- Survivors and advocates consistently identify developing actionable CRC detection strategies as a priority area.
- Symptoms are well characterized, yet diagnostic delays remain common.
- Timely diagnosis is a patient-centered priority.
- Current U.S. guidelines leave major gaps in evaluation of CRC symptoms.
- Clinicians face a needle-in-a-haystack challenge in symptomatic CRC diagnosis.
- Symptomatic FIT is a promising triage strategy supported by robust evidence abroad but has not been tested in the U.S.
- Critical evidence gaps must be addressed to implement triage testing in the U.S.
- This project focuses on the lack of actionable strategies for addressing BCCRC detection
- The proposed pilot will support extramural grant applications for a much larger, fully powered study to determine the accuracy and acceptability of symptomatic FIT strategies for diagnosis of CRC.

6. RESEARCH DESIGN AND METHODS

- This is a pilot study recruiting patients from the UC Health system at UC San Diego.
- As part of this proposed pilot, we will recruit 40 primary care patients born in 1960 and later with new CRC symptoms. An overview of the Study Flow is provided in Figure 1.
- Study screening will be conducted through electronic health record (EHR) systems, including
    - EHR-based queries for symptomatic patients in clinics including primary care, internal medicine, family medicine, gynecology, urgent care, and advanced practice provider (APP) clinics.
    - EHR-based strategies for recruitment, such as sending the flyer to eligible patients through MyChart.
- We will develop dissemination/awareness strategies for primary care including internal medicine, family medicine, gynecology, PA and NP primary care, and urgent care.

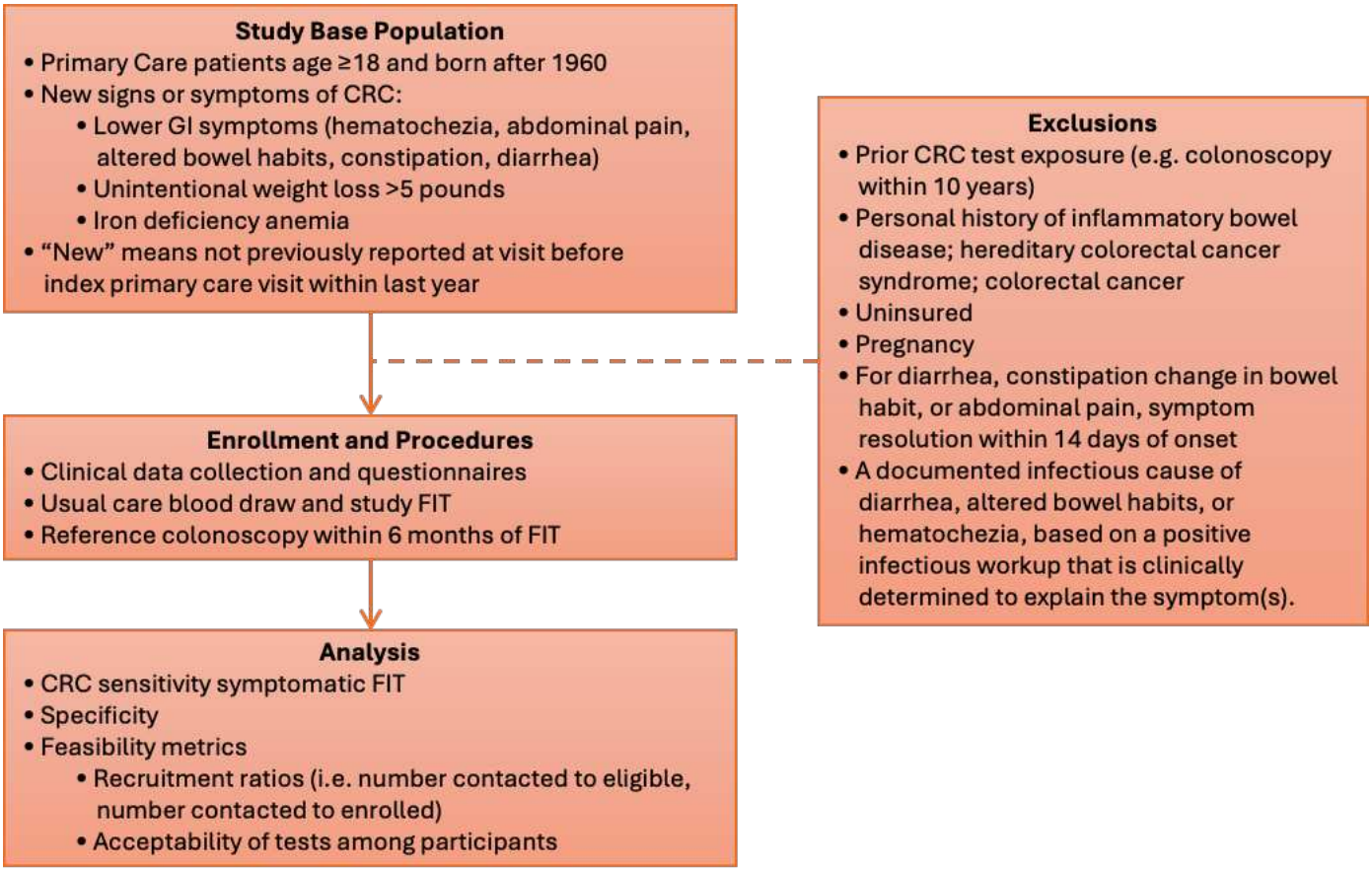


Figure 1. Objective Schematic of Pilot Cohort

Development of Data Algorithm and Data Model for Identifying Eligible Patients with Potential Signs/Symptoms of CRC

- In collaboration with Dr. Aaron Boussina, a specialist in bioinformatics at UCSD, we will access the UCSD Epic Clarity data base to identify adult patients born 1960 and later seen for outpatient primary care, or urgent care visits between 1/1/16 and 12/31/25. The data will be saved into a pipe delimited .csv format according to the data format requirements of the System.
- The EHR-based data for this study will be listed in the REDCap database elements (see Appendix E). Due to simplicity of input data/features, we use a standardized pipe delimited .csv file format. All extracted datasets will be stored in the UCSD Health's (UCSDH), HIPAA-compliant Amazon Web Services (AWS) environment.
- Data elements to be collected include patient demographic information, history of present gastrointestinal symptoms and usual care colonoscopy results. Please see Appendix E for a complete list of data elements.

- This pre-intervention data will be used to develop and validate an algorithm (using machine learning and other methods) for identifying individuals with potential signs and symptoms of CRC. The algorithm will then be utilized prospectively for identifying who are potentially eligible for prospective study inclusion.
- Predictive model results will be compared against random sample chart review of patients with and without symptoms of CRC. Additionally, the relationship of timing and pattern of signs and symptoms of CRC to 1) colonoscopy referral; 2) colonoscopy completion; 3) colonoscopy findings; 4) CRC diagnosis within 1 year of first documented symptom will be examined. These results will help to refine our algorithm for identifying individuals at risk for CRC.

Prospective Eligibility Screening

- The algorithm developed for identifying individuals with signs/symptoms of CRC will be utilized to generate a weekly query of individuals seen in outpatient primary care and urgent care settings with potential signs and symptoms of CRC. These patients and their primary care clinicians will be contacted to consider the study following the procedures documented below.

Contacting Eligible Patients

- We will implement a recruitment strategy, with study personnel located at UCSD, and patients providing review and informed consent virtually through phone and zoom.
- We will contact patients with any of the following signs/symptoms of CRC to offer study participation:
    - Hematochezia (blood in stool)
    - Persistent abdominal pain
    - Changes in bowel habits (constipation, diarrhea, narrower stools, or new irregularity)
    - Unexplained weight loss (>5 pounds without trying)
    - Iron deficiency anemia (low iron levels causing fatigue, shortness of breath, or dizziness)
- Appendix A includes the MyChart message approaching patients regarding the study
- Appendix B includes the call transcript to approach patients
- Appendix C includes the patient flyer about the study
- In addition to patient directed approaches, we will leverage our algorithm for identifying patients with potential signs/symptoms of CRC to generate alerts (via email or Epic message) to primary care clinicians requesting them to consider referring potential candidate patients to the study. An Epic referral order set will be developed to facilitate referral generation and orders for usual care tests (see below) associated with work up of signs and symptoms of CRC.
- Patients meeting the inclusion/exclusion criteria outlined below will be asked to provide informed consent for the study.
- Consent forms will be confirmed and sent to the patient's email or MyChart for the patient to read through and sign if they would like to join the study
- A completed and signed copy of the consent form will be saved in our secure UCSD web-based (OneDrive) study folder, and a copy will be sent to the patient for their own records.

Inclusion Criteria

1. Adults (>18 years-old) born in 1960 or later
2. Presenting to primary care with newly reported* potential signs or symptoms of CRC, including hematochezia, abdominal pain, altered bowel habits, unintentional weight loss over 5 pounds, constipation, diarrhea, or iron deficiency anemia.

   * "Newly identified" symptom is one not reported to a primary care clinician preceding the index primary care visit where the symptom/sign was documented.

Exclusion criteria

1. Acute presentations of abdominal pain, diarrhea, constipation, or change in bowel habit within 14 days of onset, where urgent work-up is more appropriate
2. Up-to-date CRC testing: colonoscopy within 10 years, sigmoidoscopy within 5 years, FIT within 1 year, or multi-target stool DNA/RNA or cfDNA testing within 3 years

3. Medical history: prior CRC, colorectal resection, hereditary CRC syndromes (e.g., Lynch syndrome or Familial Adenomatous Polyposis), or inflammatory bowel disease (Crohn's disease; ulcerative colitis)
4. A documented infectious cause of diarrhea, altered bowel habits, or hematochezia, based on a positive infectious workup that is clinically determined to explain the symptom(s). A negative infectious workup, or the absence of an infectious workup, does not exclude a patient from study participation.
5. Pregnancy
6. Coverage barriers: lack of health insurance, since protocolized procedures (e.g., colonoscopy; complete blood count) require health insurance

Participant activities include (Figure 1):

1. Screening/informed consent visit (in person or virtual)
2. Usual care blood draw
3. Stool sample collection with an at home FIT kit
4. Complete usual care colonoscopy

Blood draws will be performed in person at UC Health. FIT kits will be mailed to patients to be completed at home. Usual care blood draws for CBC and ferritin will be done at a UC clinical lab or lab of the patient's choice. Usual care colonoscopy will be done at any UC Health facility performing colonoscopies.

The currently approved procedures use the Polymedco OC-Light FIT, with testing performed by UCSD. Because Polymedco has discontinued this product, we plan to transition to Polymedco's research quantitative FIT, with testing performed directly by Polymedco, once the required institutional agreement is fully executed and IRB approval for the change has been obtained. Until then, testing will follow the currently approved procedures, subject to test availability. Under both arrangements, specimens and test results will be identified by study IDs only, with test results securely transmitted to and received by authorized UCSD study personnel. Once the Polymedco arrangement is activated, fecal specimens will be shipped to Polymedco for quantitative FIT testing. The key linking study IDs to participant identities will remain securely stored at UCSD and will not be shared with Polymedco. Polymedco will provide testing, supplies, and shipping at no charge to the study or participants.

Each participant's direct time commitment is approximately 6 hours. The patient's duration of involvement is estimated to be between a few weeks to six months, depending on usual care colonoscopy scheduling.

Study Activities

Table 2. Usual Care Test Procedures and Procedures Solely for Research Purposes

*Standard of Usual Care	Experimental Research Procedures
Diagnostic Colonoscopy	Symptomatic FIT
Complete Blood Count (CBC), Ferritin	

*Usual care orders will be coordinated with primary care clinicians and billed to insurance

We propose colonoscopy and CBC as usual care procedures because these are within standard of care clinical paradigms for work up of signs and symptoms potentially consistent with CRC.

Clinical Data Collection

- Demographic (e.g., age, sex, race/ethnicity, language, and insurance), clinical, laboratory, and usual care colonoscopy data from the EHR and patient questionnaires (See **Table 3**).
- Usual care colonoscopy abstraction will include exam extent, bowel prep, polyp characteristics, and pathology as part of usual care.
- Annual chart review and patient follow-up will capture new diagnoses.

- A questionnaire, adapted from the Sister Study, will assess medical history, medications, lifestyle, environmental exposures, three-generation family cancer history, which will be accessible via an embedded link in the EHR portal.
- Participants will receive compensation for each completed study activity: $25 for the study stool test, $25 for the study blood draw, $25 for the study questionnaire, and $75 for the colonoscopy, up to a total of $150 in gift cards for completing all study activities.

Table 3. Baseline Subject Data to Be Collected and Source

Data Element	Source
Demographics (i.e., age, date of birth, biologic sex, race, and ethnicity)	Self-report and EHR, with primacy given to self-report
Medical conditions	EHR and questionnaire*
Medications	EHR and questionnaire*
Health behaviors (e.g., physical activity; tobacco and alcohol use)	Questionnaire*
Residential history	Questionnaire*
Occupation	Questionnaire*
Personal and household product use	Questionnaire*
Diet	Questionnaire*
Three-generation family history of cancer	Questionnaire

Note. *The questionnaire will be adapted from the Sister Study[70] to account for exposures relevant to biologic males.

Fecal Sample Collection

- Participants will receive a FIT kit (Polymedco) with written multi-lingual (English and Spanish), pictorial instructions, a study label, and instructions for how to complete and return the samples in a prepaid mailer within 1-2 days of sample collected. Under both the current UCSD testing arrangement and the planned Polymedco testing arrangement, specimens and test results will be identified by study IDs only, without participant names, dates of birth, or MRNs. Before activation of the Polymedco arrangement, participants will be instructed to return specimens to the UCSD pathology laboratory. Once the required institutional agreement is fully executed and IRB approval for the change has been obtained, participants using the quantitative FIT kit will return specimens directly to Polymedco for testing. Under both arrangements, test results will be securely transmitted to and received by authorized UCSD study personnel. The key linking study IDs to participant identities will remain securely stored at UCSD and will not be shared with Polymedco.
- Collection will precede usual care colonoscopy and not occur during course of bowel preparation for colonoscopy.
- FIT has extensive U.S. clinical use, and the study team has extensive experience with utilizing FIT for practice-based research, which includes generating best practice guidelines for use of FIT.

FIT Processing

- Before activation of the Polymedco testing arrangement, samples will be returned by U.S. first-class mail to UCSD's lab to promote receipt within 1-2 days of sample collection, to be refrigerated and processed weekly per manufacturer guidance. Following execution of the required institutional agreement and IRB approval, coded specimens will be returned by U.S. first-class mail to Polymedco for quantitative FIT testing for research use. Specimen handling, shipping, and processing will follow the applicable manufacturer and testing laboratory requirements. Results will be identified by study ID and handled in accordance with the blinding and safety procedures below.
- If a FIT cannot be processed due to excessive or inadequate samples, the study team will provide the subject with an additional FIT collection kit for repeat sampling.

Usual Care Blood Collection

- Complete Blood Count (CBC) and ferritin obtained as usual care blood draws.

Blinding and Reference Colonoscopy

- Usual care colonoscopies will be performed blind to FIT results to avoid incorporation bias.
- Primary care clinicians, usual care colonoscopists, and study team members involved in colonoscopy outcome assessment will remain blinded to FIT results prior to usual care colonoscopy completion.
- Reference colonoscopies will be scheduled as soon as possible and considered "on protocol" if completed within 6 months of FIT as stage shift for CRC does not appear to occur before 9 months after an abnormal FIT[74].
- Quality metrics (e.g., bowel prep, cecal intubation, and documentation) will be abstracted.
- FIT testing is performed for research use and will not be routinely reported for clinical care. As a safety precaution, if usual care colonoscopy has not been completed within six months of a abnormal research FIT, designated study personnel will notify the participant's primary care provider and request that the provider advise the participant to obtain a usual care colonoscopy, as patients with abnormal tests are at increased risk for CRC. Otherwise, research FIT results will not be returned to the patient or primary care clinician.

Analysis Plan

- Feasibility metrics for completion will be calculated for each step. Some metrics include the feasibility of recruitment, and obtaining samples
- To determine the efficiency of recruitment, we will calculate several ratios including but not limited to:
    - Number of patients contacted to the number eligible
    - Number of patients contacted to number enrolled
    - Number of patients who completed the study to number enrolled
- Such feasibility metrics will be important for designing and completing the eventual larger study with a proposed target recruitment of thousands of participants. To finalize the larger study's protocol and logistics, this pilot study of 40 participants is crucial.
- We will also assess practicality in obtaining blood draws and shipping FIT kits, along with multisite logistics.
- We will determine the acceptability of these non-invasive tests among our patient population and gather preliminary data on FIT results compared to usual care colonoscopy results.
- We will identify any logistical challenges in patient recruitment and data collection prior to performing the full-scale trial, allowing us to refine the protocol before broader implementation.

Analytic Sample

- For assessment of feasibility outcomes of the pilot study, the analytic sample will include all individuals who were deemed eligible for enrollment based on electronic health record queries and chart review.
- For preliminary analysis of FIT test performance for neoplasia detection, the primary analytic sample will include all subjects with (1) a valid FIT result and (2) an adequate-quality reference usual care colonoscopy completed within 6 months of FIT.
- Usual care colonoscopy quality will be defined as complete to the cecum with adequate bowel preparation, unless incomplete exams were due to the presence of CRC or a mass lesion.
- Adequate bowel preparation will be defined by any of the following: Boston Bowel Preparation Scale 6 or greater, Aronchick scale rated fair/good/excellent, or notation of preparation sufficient to detect lesions >5 mm.
- Colonoscopies with incomplete extent or suboptimal preparation will be included when CRC is identified, consistent with prior diagnostic performance studies[34].
- Diagnostic performance metrics (i.e., sensitivity, specific, PPV, and NPV) will be estimated with 95% confidence intervals calculated. Subgroup analyses will evaluate heterogeneity in diagnostic performance, and exact methods will be applied for small sample sizes. ROC analysis and thresholds that optimize the sensitivity and specificity will be explored.

Data and Biospecimen Storage

- Any data will be stored in RedCap for up to five years. Dr. Samir Gupta will oversee the data for the length of time they will be in possession. This data will be deidentified and secured through a password-protected database in which only study personnel will have access. The linkage key connecting study IDs to participant identifiers will be stored separately and securely at UCSD and will not be accessible to Polymedco. Research FIT results will be coded by study ID and stored in a password-protected database with access restricted to authorized study personnel.
- There will be no storage of biospecimens.

7. RESEARCH PARTICIPANTS

The inclusion and exclusion criteria are described in detail above in section 6.

8. RECRUITMENT

Recruitment will occur through multiple channels in each health system:

1. Weekly EHR queries by site coordinators to identify symptomatic patients meeting inclusion and exclusion criteria.
2. Primary care physician engagement via meetings and emails to refer patients directly or activate a study-specific order set.
3. Patient self-referral from site-branded low literacy recruitment materials in primary care exam rooms. Site coordinators will conduct chart reviews to confirm eligibility and approach eligible patients for informed consent and enrollment.
4. MyChart messages to eligible patients (see Appendix A).

Study team members will describe the study procedures to ensure voluntary participation of these patients. Any involved PHI from EHR queries will be stored in a REDCap database that is password protected. Specimens shared with Polymedco and the corresponding FIT results will be coded by study ID; the linkage key will remain at UCSD and will not be shared with Polymedco. Publications will not include participant identifiers.Any identifiers will be anonymized and de-identified when sharing with other sites and future publications.

1. MyChart Message (Appendix A)
2. Phone Transcript (Appendix B)
3. Patient Study Flyer (Appendix C)

Participants will receive compensation for each completed study activity: $25 for the FIT sample, $25 for the blood draw, $25 for the questionnaire, and $75 for the colonoscopy, up to a total of $150 in gift cards for completing all protocol activities.

9. INFORMED CONSENT

1. Site coordinators who are fully trained will fully describe the study procedures to eligible participants to ensure voluntary participation and obtain informed consent.
2. The eligible patient will receive the consent form and be given a waiting period and sufficient time to read over the consent form and decide whether to participate in the study. They may give informed consent in person in clinic or virtually through REDCap and only accessible by designated study personnel. The patient will be given as much time as they need to consider the study, ask questions, and autonomously decide whether to participate without coercion.
3. Language used by those obtaining consent will be understood at a sixth-grade literacy level.
4. Spanish-version of the consent form will be available as well.

5. Methods of documenting consent will be through a password-protected REDCap database and that consent will be obtained before any study procedures are performed.
6. The information communicated to the participant or legally authorized representative during the consent process will not include exculpatory language through which the participant or legally authorized representative is made to waive or appear to waive any of the participant's legal rights or release or appear to release the Researcher, Sponsor, the University or its agents from liability for negligence.

If participants who cannot read or speak English may be enrolled, we will use a document translated into the participant's primary language, use of an official, appropriate translator, and provide continued, qualified interpretive services to the participant.

10. BANKING OF INFORMATION/BIOSPECIMENS FOR FUTURE USES

- This pilot study will not involve banking of information or biospecimens for future use.

11. MINIMIZATION OF RISK

This study will minimize risks through the following:

1. Collecting the minimum data necessary for the research, including the minimum number of identifiers, and performing only procedures that are necessary for the study objectives.
2. Minimizing the risk of the procedures and including only necessary study activities, coding data, and samples to conceal identifiers.
3. Combining research procedures with clinical care such as the timing of FIT sample collection, blood draws, and other procedures to occur at the same time as clinical procedures, including colonoscopies and related usual care orders.
4. Incorporating adequate safeguards into the research design, such as an appropriate data safety monitoring plan, the presence of trained study personnel who can respond to emergencies, procedures to protect the confidentiality of the data and collection (e.g., encryption, study codes, and passwords), and safeguards to protect results and information from blood draw.

Overall Impact

- The knowledge gained from this study is incredibly valuable. This pilot will enable the successful implementation of a full-scale cohort study to evaluate FIT as rule-out strategies for CRC detection.

12. PRIVILEGES/CERTIFICATIONS/LICENSES AND RESEARCH TEAM RESPONSIBILITIES

Study Personnel

- PI Samir Gupta, MD has experience with not only conducting extramurally funded health-system based research on strategies for detection and prevention of CRC *and* leading recruitment and biospecimen collection for large studies, but also the clinical and technical aspects of FIT. Dr. Gupta has published numerous papers, serves as MPI for a VA Merit Study, and has previously recruited thousands of patients to practice based studies.
- Aaron Boussina, PhD, has experience in creating models using artificial intelligence to screen patients who may be eligible for the study based on red flag GI symptoms.
- Yi Le, MS will conduct the statistical analyses as the study biostatistician.
- Lin Liu, PhD will supervise statistical analyses.
- Study coordinators Leisa Sutton, MAS, Katheryn Rodriguez, and Isaac Cesena, BS, will be trained to screen and recruit patients, facilitate study procedures such as scheduling blood draws and mailing FIT kits, data collection and analysis, and conducting post-study follow up.

13. REFERENCES

Gupta S, May FP, Kupfer SS, Murphy CC. Birth Cohort Colorectal Cancer (CRC): Implications for Research and Practice. Clin Gastroenterol Hepatol. 2024;22(3):455-69 e7. Epub 20231209. doi: 10.1016/j.cgh.2023.11.040. PubMed PMID: 38081492; PMCID: PMC11304405.

Rosenberg PS, Miranda-Filho A. Cancer Incidence Trends in Successive Social Generations in the US. JAMA network open. 2024;7(6):e2415731. Epub 20240603. doi: 10.1001/jamanetworkopen.2024.15731. PubMed PMID: 38857048; PMCID: PMC11165384.

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Berry E, Miller S, Koch M, Balasubramanian B, Argenbright K, Gupta S. Lower Abnormal Fecal Immunochemical Test Cut-Off Values Improve Detection of Colorectal Cancer in System-Level Screens. Clin Gastroenterol Hepatol. 2020;18(3):647-53. Epub 20190511. doi: 10.1016/j.cgh.2019.04.077. PubMed PMID: 31085338; PMCID: PMC7731666.

Goshgarian G, Sorourdi C, May FP, Vangala S, Meshkat S, Roh L, Han MA, Croymans DM. Effect of Patient Portal Messaging Before Mailing Fecal Immunochemical Test Kit on Colorectal Cancer Screening Rates: A Randomized Clinical Trial. JAMA Netw Open. 2022;5(2):e2146863. Epub 20220201. doi: 10.1001/jamanetworkopen.2021.46863. PubMed PMID: 35119462; PMCID: PMC8817202.

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14. BIBLIOGRAPHY

List up to **five relevant articles** that the IRB can use to provide necessary background for the protocol. Do not append an extensive NIH-grant-style bibliography.

1. Gupta S, May FP, Kupfer SS, Murphy CC. Birth Cohort Colorectal Cancer (CRC): Implications for Research and Practice. *Clinical Gastroenterology and Hepatology*. 2024;22(3):455-469.e7. doi:10.1016/j.cgh.2023.11.040

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Statistical Analysis Plan for Symptomatic FIT for Colon Cancer Detection
UCSD IRB 814209 | 4 November 2026, v2

This plan specifies the descriptive analyses for the pilot cohort of approximately 40 participants.

Study sample: The numbers screened, pre-selected as eligible, approached, contacted, confirmed eligible, excluded before informed consent, enrolled, excluded after enrollment, and included in the FIT performance sample will be reported. Reasons for exclusion before and after enrollment will be enumerated. Patients will be counted once at each stage; exclusion reasons may overlap and need not sum to the total. A negative infectious workup, or the absence of one, will not constitute an exclusion.

Table 1. Participant flow

Stage	**Overall n = ___**
Screened	
Pre-selected as eligible	
Approached	
Contacted	
Excluded before informed consent, total	
Acute abdominal pain, diarrhea, constipation, or bowel-habit change within 14 days of onset requiring urgent work-up	
Up-to-date CRC testing	
Prior CRC, colorectal resection, hereditary CRC syndrome (Lynch/FAP), or inflammatory bowel disease (Crohn's/UC)	
Positive infectious workup with a documented cause clinically explaining diarrhea, altered bowel habits, or hematochezia	
Pregnancy	
No health insurance	
Other pre-consent exclusion (specify)	
Confirmed eligible after assessment	
Declined participation	
Consented and enrolled	
Completed all required study procedures (as applicable)	
Excluded after enrollment, total	
No valid FIT result	
No colonoscopy within six months of FIT	
Colonoscopy inadequate for performance analysis	
Withdrawal or lost to follow-up	
Other post-enrollment reason (specify)	
Included in FIT performance sample	

Analytic samples: The feasibility sample includes all individuals deemed eligible for enrollment through EHR queries and chart review. Procedure completion outcomes will use the enrolled participants specified in Table 3. The FIT performance sample includes enrolled participants with a valid FIT result and an adequate-quality usual-care colonoscopy completed within six months of FIT. Demographic characteristics and baseline symptoms of the FIT performance sample will be summarized using counts and percentages for categorical variables and medians with interquartile ranges or means with standard deviations for continuous variables, as appropriate. Baseline symptoms will come from the eligibility assessment; more than one symptom may be reported.

Table 2. FIT performance sample characteristics

Characteristic	**Overall n = ___**
Age	
Sex	
Race and ethnicity	
Insurance type	
Language	
Baseline symptoms	
Hematochezia	
Persistent abdominal pain	
Altered bowel habits	
Diarrhea	
Constipation	
Unintentional weight loss (>5 pounds)	
Low iron or iron-deficiency anemia (self-report)	

Outcomes: For each outcome, the numerator, denominator, proportion, and associated 95% confidence interval will be reported. No formal statistical comparisons are planned. FIT results will be obtained from UCSD laboratory or Polymedco reports; colonoscopy and pathology results will be obtained from EHR records or an EHR query. Six-month colonoscopy completion will be measured from the FIT date; overall completion includes colonoscopy recorded through the study data cutoff. Missing or unavailable values will be reported, and outcome denominators will include only participants with the information required to assess that outcome unless Table 3 specifies otherwise.

Protocol definitions: FIT specimens will be collected before usual-care colonoscopy and not during bowel preparation. If a specimen cannot be processed because of an excessive or inadequate sample, an additional collection kit will be provided. The currently approved test is the Polymedco OC-Light FIT, tested at UCSD; a transition to Polymedco quantitative FIT testing is planned after the required agreement is executed. A reference colonoscopy is on protocol if completed within six months of FIT. An adequate-quality examination reaches the cecum and has adequate bowel preparation, defined as BBPS ≥6, Aronchick fair/good/excellent, or documentation that preparation was sufficient to detect lesions >5 mm. Incomplete examinations due to CRC or a mass lesion are included; examinations with incomplete extent or suboptimal preparation are also included when CRC is identified.

Table 3 Outcome proportions

Outcome	n / N	Proportion (%)	95% CI
Confirmed eligible among contacted			
Enrolled among contacted			
Questionnaire completed among enrolled			
FIT specimen returned among enrolled			
Valid FIT result among enrolled			
Blood draw completed among enrolled			
All required study procedures completed among enrolled (as applicable)			
Colonoscopy completed within six months of FIT among enrolled with a FIT date			
Colonoscopy completed at any time during observed follow-up among enrolled			
Positive FIT among participants with valid FIT result			
Colorectal cancer confirmed by colonoscopy/pathology among participants with qualifying reference colonoscopy			

Exploratory analyses: Where estimable, FIT sensitivity, specificity, positive predictive value, and negative predictive value for neoplasia will be calculated in the FIT performance sample, with 95% confidence intervals. Descriptive subgroup and ROC/threshold analyses may be explored if sample size and assay data permit. The target condition for neoplasia and any subgroup definitions will be specified before analysis.