Study Title: Engaging Patients in Colon Cancer Screening Decisions During COVID-19

Document Title: Design and Analysis plan for the randomized controlled trial in the PRIMED COVID Supplement Study

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Background: Thousands of colonoscopies were cancelled during the initial surge of the COVID-19 pandemic. As facilities resumed elective health care services, many faced additional challenges such as longer wait times due to backlogs, limits on volume due to new requirements for infection control, and some patients were hesitant to reschedule. Informing patients about their CRC screening options, including home-based stool tests and colonoscopy, and eliciting and addressing their concerns about testing may improve decisions and help increase overall screening rates**.** However, studies suggest clinicians tend to recommend one screening test with little discussion of other options, falling short of the shared decision making (SDM) ideal. Whether a SDM approach would work with patients who may be hesitant to seek care during the pandemic is not clear. The purpose of this study was to determine whether a decision aid plus telephone coaching would increase colorectal cancer (CRC) screening and improve patient reports of shared decision making (SDM).

Design: Randomized controlled trial where patient participants were randomized 1:1 into either intervention or control arms.

On June 2, 2020, the co-investigators from the Massachusetts General Hospital Gastroenterology Department extracted a list of patients aged 45-75, with preferred language of English or Spanish, who had a screening or surveillance colonoscopy that was cancelled, who had a referral for a screening colonoscopy that had not been processed, or who should have been contacted by the GI department to schedule a screening colonoscopy but had not been due to COVID-19 restrictions since March 15, 2020.

The intervention mailings went out in four waves, about two weeks apart, between September 10, 2020 and October 22, 2020. Participants in the intervention arm received a decision worksheet in the mail followed by a call from a decision coach. A subset of participants across both arms were selected to receive a survey. Staff mailed a survey to the selected subset of control and intervention participants about 8 weeks after the intervention packet was mailed to their wave. The survey packet included a cover letter, an information sheet, an incentive ($10 gift card), the survey and a return envelope. Patients were able to complete the survey by mail, online via REDCap, or over the phone with study staff. Staff made up to three reminder phone calls and sent a reminder mailing to non-responders with 3 additional reminder calls. Spanish-speaking research staff conducted reminder calls for Spanish-speaking participants. Staff conducted chart review to collect screening tests completed within 6 months.

Randomization and blinding: The study statistician used a computer random number generator to randomly select 800 eligible patients, assign each to intervention or control arm, and to one of 4 waves. All 800 patients were followed to track colon cancer screening tests completed and a subset in each wave were randomly selected to receive a survey to measure patient-reported outcomes. The staff who entered the data from the paper surveys and who conducted chart review to collect screening were blinded to the assignment. The statistician analyzing the results was not blinded to the assignment.

Outcomes:

Screening uptake: study staff examined medical records to determine receipt of any colorectal cancer screening test for all subjects within 6 months.

The following measures were collected in the patient survey:

SDM Process Scale: 4-item survey asks about discussion of stool test, pros and cons of colonoscopy and patient's screening preference. Total scores range from 0-4 with higher scores indicating higher shared decision making. Patients who indicated that they did not talk with anyone about CRC screening received a SDM Process score of 0.

SURE scale: the brief 4-item version of the decisional conflict scale. A point is given for each "yes" response for total scores 0-4 and we report the percentage receiving the top score of 4, which indicates no decisional conflict.

Screening preference: One item asked patient's preferred approach to screening (with responses: colonoscopy, stool-based test, delay screening, not sure).

Additional measures were collected to describe the sample and used as covariates including whether or not the patient had a CRC discussion with health care provider in the past two months, PROMIS Scale v1.2-Global Health Physical 2a, Single Item Literacy Screener, CRC screening and history, COVID-19 worry, decision worksheet use and decision coaching exposure. Basic demographics for the full sample were collected via chart review.

Sample Size: The sample size of 800 was determined based on the screening uptake, with 800 participants, the study had 81% power to detect a difference of 10% in rates. For the survey, we assumed a 60% response rate and as a result, planned to invite about 500 patients (250 in each arm) to obtain 300 responses. With 300 survey responses, the study had 80% power to detect a difference of 0.32 standard deviation (SD) for the SDM Process score. Studies have found effect sizes ranging from 0.39SD – 0.88SD for SDM Process when comparing sites that used formal

decision support (coaching or decision aids) and those that did not. For dichotomized survey outcomes (% SURE top score and % prefer screening), with 300 responses, we had 80% power to detect a 13% difference, from 70% to 83%.

Statistical methods: Sample demographics and characteristics were compiled and compared to evaluate the balance between the two arms. Responders and non-responders to the survey were compared between arms to evaluate potential non-response bias.

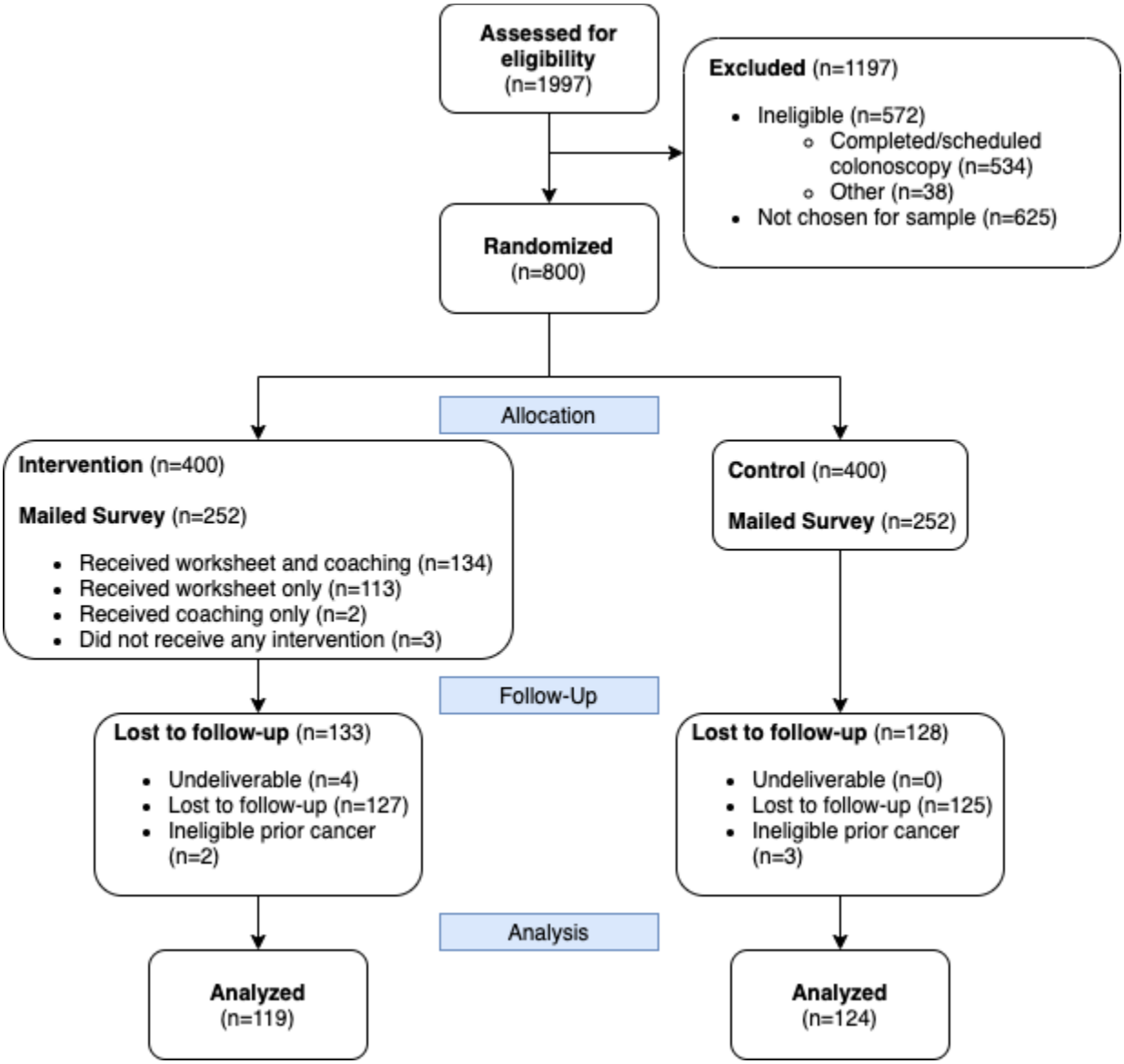
The following hypotheses were evaluated using an intention to treat approach, and patients were analyzed based on their assigned arm.

1. Compared to the control group, patients in the intervention arm will be more likely to have a screening test within 6 months (the percentage of patients who had either stool test or colonoscopy in each arm compared using a Fisher Exact test). We also used cumulative incidence function to compare time to screening completion.
2. Compared to the control group, patients in intervention arm will report higher SDM scores (compared mean scores using a two sample t-test).
3. Compared to the control group, patients in the intervention arm will (3a) be more likely to have a clear preference for colon cancer screening (either colonoscopy or stool-based test) and (3b) have less decisional conflict (i.e. higher percentage of SURE top scores). We compared the percentage of patients with these outcomes between arms using Chi-square analyses.

In a pre-specified analysis, we explored the heterogeneity of treatment effects (HTE) to identify differential treatment effects among subgroups of patients stratified by sex as a biological

variable, age, race/ethnicity, education, overall health, prior screening history, COVID worry and interaction with decision coach. We used linear or logistic regression models to test the interaction between study arms and these factors. We highlighted the subgroups that presented differential effects regardless the significance of p values for the intervention and subgroup interaction. These results are exploratory in nature as the study was not powered for any of the subgroup analyses, and there was no attempt to control for potential biases.

CONSORT:


Assessed for eligibility (n=1997)
Excluded (n=1197)
Ineligible (n=572)
Completed/scheduled colonoscopy (n=534)
Other (n=38)
Not chosen for sample (n=625)
Randomized (n=800)
Allocation
Intervention (n=400)
Mailed Survey (n=252)
Received worksheet and coaching (n=134)
Received worksheet only (n=113)
Received coaching only (n=2)
Did not receive any intervention (n=3)
Control (n=400)
Mailed Survey (n=252)
Follow-Up
Lost to follow-up (n=133)
Undeliverable (n=4)
Lost to follow-up (n=127)
Ineligible prior cancer (n=2)
Lost to follow-up (n=128)
Undeliverable (n=0)
Lost to follow-up (n=125)
Ineligible prior cancer (n=3)
Analysis
Analyzed (n=119)
Analyzed (n=124)