Colonoscopy Outreach for Rural Communities (CORC) Aim 2

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Principal Investigator: Allison Cole, MD, MPH
University of Washington
Department of Family Medicine
acole2@uw.edu

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CORC
COLONOSCOPY OUTREACH FOR RURAL COMMUNITIES

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Statistical Analysis Plan

1. Randomization

Participants are randomized by research staff via REDCap with random allocation sequence generated by the study biostatistician. Randomization is done with a 1:1 ratio to the intervention and comparison arms. Anticipated sample sizes are 240 participants per arm. Randomization is stratified on primary care organization and insurance coverage (insured, uninsured, unknown). For purposes of randomization, two clinics within one primary care organization were treated as two separate strata due to their unique patient populations and colonoscopy referral workflows. Within each stratum randomized assignments are generated in random blocks with random sizes of 4 or 8 to ensure approximately balanced arms throughout enrollment.

2. Sample Size

The sample size of 480 participants was chosen to provide at least 80% power to detect an absolute difference between arms of 15% (e.g., 75% versus 60%) in rates for the primary outcome (colonoscopy completion within 12 months). The power calculation is based on a chi-squared test with a type I error rate of 0.05 and assumed missing outcome data in 20% of participants.

3. Endpoints

3.1. Primary endpoint

The primary endpoint is completion of colonoscopy within 12 months of referral (colonoscopy procedure $\leq$ 365 days from referral date)

3.2. Secondary endpoints

1) Completion of colonoscopy within 6 months of referral to colonoscopy (colonoscopy procedure $\leq$ 183 days from referral date)
2) Completion of colonoscopy within 9 months of referral to colonoscopy (colonoscopy procedure occurred $\leq$ 274 days from referral date)
3) Time from referral to completion of colonoscopy (days)

3.3. Other endpoints

1) Completion of colonoscopy within 12 months of referral, with adequate bowel preparation
2) Completion of colonoscopy within 12 months of referral, with cecal intubation
3) Completion of any colorectal cancer screening within 12 months of referral to colonoscopy

4. General considerations

Except where noted below, all analyses for comparison of treatment arms will use the intent-to-treat approach in which participants are included in the arm to which they were randomized regardless of the treatment received. Outcomes will be obtained using electronic health records and by self-report if participants deny access to health records. Differences between treatment arms on dichotomous outcomes will be expressed as odds-ratios with 95% confidence intervals based on logistic regression or conditional logistic regression. A single hypothesis test will be used to test the null hypothesis associated with the primary endpoint. All other analyses will be considered exploratory and no adjustment for multiple hypothesis testing will be used. Descriptive statistics will be used to characterize participants in the two treatment arms. All analyses will be conducted with the participant as the unit of analysis except where noted below. All analyses will be completed using Stata or R by a Research Scientist or the CORC biostatistician, blinded to treatment allocation.

5. Descriptive Statistics

Descriptive statistics (mean and SD for continuous variables, proportions for categorical variables) will be used to summarize all endpoints and pre-randomization variables to be used in analyses overall, by randomization stratum, and by treatment arm.

Pre-randomization variables

1. **Clinical organization** (Orgs 1-7): Primary care organization where participant is a patient
2. **Insured** (Yes, No, Don't know): Whether or not participant has insurance
3. **Insurance type** (Private, Medicare, Medicaid, Uninsured): Type of health insurance
4. **Rurality** (Rural, Not Rural): FORHP definition of rurality based on participant zipcode
5. **Age** (45-49, 50-64, 65-76): Age at date of referral to colonoscopy
6. **Gender** (Male, Female): Self-reported gender
7. **Ethnicity** (Hispanic or Latino, Not Hispanic or Latino): Self-reported ethnicity
8. **Language** (English, Spanish): Self-reported preferred language for study communications
9. **Education** (Less than HS degree or GED, HS degree or GED, Some college or Associates degree, Bachelors degree or higher): Self-reported educational attainment
10. **Prior colonoscopy** (Yes, No): Self-report of having previously had a colonoscopy
11. **Family history of colorectal cancer** (Yes, No): Self-reported family history of CRC
12. **General health** (Excellent or Very Good, Good, Fair or Poor): Self-reported health status
13. **Social and Emotional support** (Always or Usually, Sometimes or Rarely or Never): Self-reported strength of social or emotional support they receive
14. **Employment** (Employed, Retired, Not working): Self-reported employment status

6. Primary Analysis

Rates for the primary endpoint will be compared between treatment arms using conditional logistic regression to account for the stratification variables (primary care organization and insured). The outcome variable will be a binary indicator of completion of colonoscopy within 12 months of referral. Any cases with unknown completion status will be coded as not completed. The treatment variable will be the randomized treatment arm. Parameter estimates and 95% confidence intervals will be obtained using maximum-likelihood method based on the conditional likelihood.

7. Analysis of Secondary Endpoints and Other Endpoints

7.1. Secondary Endpoints

Analyses for the secondary endpoints that are represented by binary variables will be conducted using the same methods as above for the primary endpoint. Analyses of time to colonoscopy completion will be conducted using the Cox proportional hazards model and the difference between treatment arms expressed as a hazard ratio with 95% confidence interval.

7.2. Other Endpoints

Rates for other endpoints will be compared descriptively between treatment arms.

8. Sub-group Analyses

The analyses for primary and secondary endpoints will be conducted separately within sub-groups of participants based on the following variables:

1) **Had prior colonoscopy** (Yes, No)
2) **Insurance status** (Private, Medicare, Medicaid)
3) **Participant gender** (Male, Female)
4) **Education** (High school graduate or below, Above high school graduate)
5) **Organization with colonoscopy backlog** (Yes, No)
6) **Clinical organization** (1-7)

7) **Participant language** (English, Spanish)

For the primary and secondary endpoints, descriptive estimates of treatment effects will be obtained for each sub-group. For the primary endpoint, tests for interactions between treatment arm and sub-group variables will be conducted using likelihood-ratio tests based on conditional logistic regression.

9. Sensitivity Analyses

9.1. Adjusted Analyses

The analyses of the primary and secondary endpoints will be repeated with adjustment for variables known to be related to colonoscopy completion. Cox proportional hazards analysis of time to colonoscopy completion will also be repeated with adjustment for these variables.

9.2. As-Treated Analyses

The analyses of primary and secondary endpoints will be repeated including only the subset of participants in the intervention arm who received the intervention, defined as receiving at least Topic 1 of the CORC Patient Navigation program, using navigation variables. All participants assigned to the usual care control group will be included in this analysis. If warranted by findings, adjusted analyses will be conducted as described in section 9.1.

9.3 Excluding Missing Completion Status Analyses

The analyses of the primary and secondary endpoints will be repeated excluding participants with unknown completion status.

9.4 Referral for Primary Screening Analyses

The analyses of the primary and secondary endpoints will be repeated including only the subset of participants referred to colonoscopy for primary CRC screening, i.e., excluding participants referred for follow-up after an abnormal stool test result. If warranted by findings, adjusted analyses will be conducted as described in section 9.1.

10. Other Considerations

10.1. Missing Data Analyses

For adjusting and reporting on pre-randomization variables, missing cases will be excluded. For primary, secondary, and other endpoints examining colonoscopy completion, cases with unknown colonoscopy completion status will be coded as not completed, as described in Section 6. For other endpoints examining cases with completed colonoscopy, cases with missing data will be excluded from analysis.