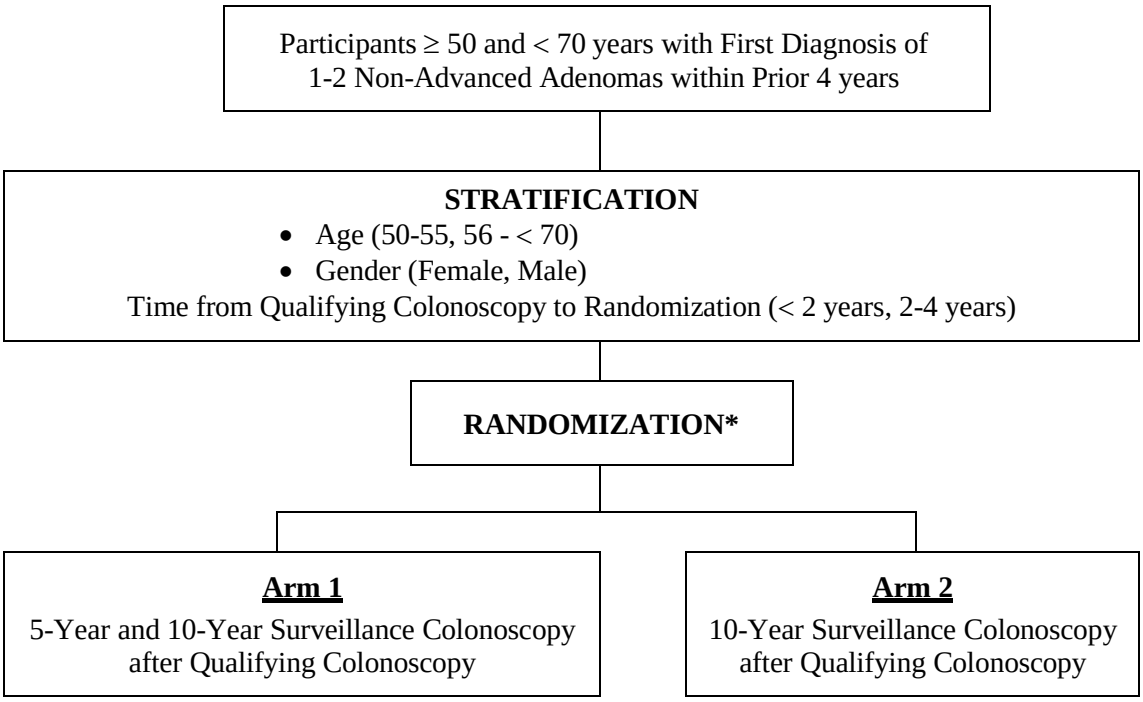
Figure 1.
NRG-CC005 SCHEMA



* Randomization is 1:1.

3.1 PARTICIPANT SELECTION, ELIGIBILITY, AND INELIGIBILITY CRITERIA

Note: Per NCI guidelines, exceptions to inclusion and exclusion criteria are not permitted. For questions concerning eligibility, please contact the Clinical Coordinating Department (CCD [see protocol cover page]).

3.2 Participant Selection Guidelines

Although the guidelines provided below are not inclusion/exclusion criteria, investigators should consider these factors when selecting participants for this trial. Investigators also should consider all other relevant factors (medical and non-medical), as well as the risks and benefits of the study, when deciding if an individual participant is an appropriate candidate for this trial.

3.2.1 "Qualifying colonoscopy" refers to the colonoscopy performed within 4 years prior to randomization that is used to determine eligibility.

Note: The use of retrospective chart review is permitted for identifying potential NRG-CC005 participants. Natural Language Processing (NLP) programs may be used, as allowed by local regulatory guidelines, to facilitate the identification of participants who may be eligible for the study.

3.2.2 Certain hereditary cancer syndromes may predispose patients to colorectal cancer and should be considered when deciding if a patient is appropriate for this study.

3.2.3 Participants must have the psychological ability and general health that permits completion of the study requirements and required follow up.

3.3 Eligibility Criteria

A participant cannot be considered eligible for this study unless ALL of the following conditions are met.

3.3.1 The participant must have signed and dated an IRB-approved consent form that conforms to federal and institutional guidelines.

3.3.2 Participants ≥ 50 and < 70 years of age at the time of randomization.

3.3.3 Participants with a first-time diagnosis of 1-2 non-advanced tubular adenomas (< 10 mm without tubulovillous or villous changes or high grade or severe dysplasia) ***from the qualifying colonoscopy*** within 4 years prior to randomization.

- Sessile serrated polyps/adenomas, as long as they do not meet the criteria for advanced adenomas, will be considered as non-advanced adenomas.

3.3.4 Qualifying colonoscopy must be a complete colonoscopy with visualization of the cecum and with adequate cleansing within 4 years prior to randomization.

3.3.5 Complete excision of all observed polyps in qualifying colonoscopy (see Section 3.3.7).

3.3.6 Participants must be able to read or understand English or Spanish.

3.4 Ineligibility Criteria

Participants with one or more of the following conditions are NOT eligible for this study.

3.4.1 Prior history of colorectal cancer or colorectal adenomas including sessile serrated polyps/adenomas excluding those found on the qualifying colonoscopy.

3.4.2 Prior history of a hyperplastic polyp measuring ≥ 1 cm in size.

3.4.3 Traditional serrated adenomas found on the qualifying colonoscopy.

3.4.4 Hyperplastic polyp measuring ≥ 1 cm in size found on the qualifying colonoscopy.

3.4.5 Previous malignancies unless the patient has been disease-free for 5 or more years prior to randomization and is deemed by the physician to be at low risk for recurrence. Patients with the following cancers are eligible if diagnosed and treated within the past 5 years: all in situ cancers and basal cell and squamous cell carcinoma of the skin.

3.4.6 Colonoscopy performed ***after*** the qualifying colonoscopy but prior to randomization.

3.4.7 Incomplete qualifying colonoscopy (e.g., cecum not visualized).

3.4.8 Incomplete endoscopic excision of adenomatous polyps based on colonoscopist impression at qualifying colonoscopy. (Excision of all hyperplastic rectosigmoid polyps is not required.)

3.4.9 Sub-total colectomy or total proctocolectomy. (Segmental resections are allowed.)

3.4.10 Family history of CRC diagnosed at ≤ 60 years of age in a first degree relative (mother, father, child, sibling) or in two first degree relatives with CRC at any age.

3.4.11 Participants with a clinical diagnosis of a significant heritable risk for colorectal cancer (Familial Adenomatous Polyposis, Hereditary Nonpolyposis Colorectal Cancer [Lynch Syndrome]).

3.4.12 Participants tested positive for a Familial Adenomatous Polyposis, Hereditary Nonpolyposis Colorectal Cancer [Lynch Syndrome] genetic mutation that increases risk of colorectal cancer.

3.4.13 Inflammatory bowel disease (e.g., Crohn's Disease, ulcerative colitis).

3.4.14 Life expectancy less than 10 years due to comorbid conditions in the opinion of the investigator.

3.4.15 Other comorbid conditions that would prevent the participant from having colonoscopies or would prevent required follow-up.