Colonoscopy versus FIT in Reducing Mortality from CRC (CONFIRM)

Update 2018
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Primary Aim

To determine if a strategy of screening colonoscopy decreases CRC mortality over 10 years in average risk adults as compared to annual FIT screening.
Secondary Aims

1. To determine if a screening colonoscopy decreases 10 year CRC incidence as compared to annual FIT screening

2. To evaluate the safety of screening colonoscopy

3. To evaluate the association between colonoscopists’ characteristics and the initial detection of colorectal neoplasia, complications and post-colonoscopy CRC
Colonoscopy vs. Fecal Immunochemical Test in Reducing Mortality From Colorectal Cancer (CONFIRM): Rationale for Study Design

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and for the CONFIRM Study Group

“CONFIRM is a large, pragmatic, randomized, controlled, superiority trial designed to compare the effectiveness of screening colonoscopy and annual FIT screening…”

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Population

- Those considered suitable for colorectal cancer screening
  - Veterans age 50-75
  - Able to provide informed consent (pre randomization consent)

- Key Exclusions
  - Those at high risk for colorectal cancer
    - Personal history of polyps or inflammatory bowel disease
    - Family history of colorectal cancer (any 1st degree relative)
    - Symptoms of colorectal cancer (e.g. bleeding; weight loss)
  - Those at low risk for colorectal cancer
    - Recently screened
      - e.g. FOBT (last year), colonoscopy (last 10 years)
Baseline Evaluation

- Demographics
- Prior CRC Screening
- BMI
- NSAID, ASA, Statins
- Habits (e.g. Tobacco, Alcohol, Exercise)
- Hormone exposure (women only)
- Health Services (e.g. %VA use, distance to care)
- Alternate Contacts and Release of Information
Recruit 50,000 ‘screen eligible’ Veterans (Age 50-75)

Randomize

Screening Colonoscopy

Annual FIT Test

FIT Test Positive?

Yes

Evaluation by Site PI for further Follow-up

No

10th Year of Follow-Up?

No

Yes

Follow-up for outcomes over 10 years
- CRC Mortality (Primary Outcome)
- CRC Incidence (Secondary Outcome)
Sample Size

- Target = **50,000** participants (25,000 per treatment arm)
  - Study duration of ~15 years
  - ~5 years accrual period
  - Minimum follow-up of 10 years
Current Status of Trial

- Recruitment milestones
  - First randomization May 22, 2012
  - 5,000\(^{th}\) recruitment in June 2013
  - 15,000\(^{th}\) recruitment in April 2014
  - 25,000\(^{th}\) recruitment in March 2015
  - 35,000\(^{th}\) recruitment in February 2016
  - 45,000\(^{th}\) recruitment in February 2017
  - 50,000\(^{th}\) recruitment in November 2017
Study Participants—Age Distribution Through December 1, 2017 (N=50128)

Mean age = 59.1

Number of Participants

Age Group
50-55
55-<60
60-<65
65-<70
70-75

Percentage
34.1%
18.3%
20.6%
19.8%
7.2%
Study Participants - Gender Through December 1, 2017 (N=50128)

- Male: 93.1%
- Female: 6.9%
Study Participants—Race Through December 1, 2017 (N=50128)

- White: 71.1%
- Black: 25.0%
- Amer Indian: 2.6%

Legend:
- White
- Black
- Amer Indian
## FIT Intervention

<table>
<thead>
<tr>
<th>Pragmatic</th>
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<tbody>
<tr>
<td>OC–Sensor FIT using manufacturer cut-off</td>
</tr>
<tr>
<td>Reported as positive or negative</td>
</tr>
<tr>
<td>2 FIT per annual cycle</td>
</tr>
<tr>
<td>Letter sent prior to FIT</td>
</tr>
<tr>
<td>Central Processing in Albuquerque, NM</td>
</tr>
<tr>
<td>using Diana® high throughput processor</td>
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<tr>
<td>When FIT is positive</td>
</tr>
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<td>Letter informing participant</td>
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<tr>
<td>Letter informing Local Site PI &amp; orders colo using standard process</td>
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<td>Lab result placed in lab package</td>
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# FIT Intervention

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<tr>
<td>OC–Sensor FIT using manufacturer cut–off</td>
<td>Storing data on quantitative values</td>
</tr>
<tr>
<td>Reported as positive or negative</td>
<td></td>
</tr>
<tr>
<td>2 FIT per annual cycle</td>
<td>Letter preceding FIT also contains a survey</td>
</tr>
<tr>
<td>Letter sent prior to FIT</td>
<td></td>
</tr>
<tr>
<td>Central Processing in Albuquerque, NM using Diana® high throughput processor</td>
<td>Using priority mail</td>
</tr>
<tr>
<td>When FIT is positive</td>
<td>Dedicated case report form to follow-up on all FIT +</td>
</tr>
<tr>
<td>Letter informing participant</td>
<td>Participant reminders if colonoscopy not complete</td>
</tr>
<tr>
<td>Letter informing Local Site PI &amp; orders colo using standard process</td>
<td></td>
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<tr>
<td>Lab result placed in lab package</td>
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Median time to colonoscopy = 45 days

N = 1686
Facility-Level Variation in Timely Completion of Colonoscopy by Region

Percent of Timely Colonoscopy

Region ID

North East
South
Central
West

Percent of Timely Colonoscopy

Region ID

North East
South
Central
West
## Colonoscopy Intervention

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<td>Scheduled through ‘standard processes’</td>
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<tr>
<td>Exams are also ‘standard’ for that VA</td>
</tr>
<tr>
<td>Any credentialed physician endoscopist</td>
</tr>
<tr>
<td>Fellow involvement OK</td>
</tr>
<tr>
<td>No specific requirement for preparation</td>
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<td>Quality tracked, but interventions generally limited to feedback</td>
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<td>Scheduled through ‘standard processes’</td>
<td>Coordinator can work with scheduler</td>
</tr>
<tr>
<td>Exams are also ‘standard’ for that VA</td>
<td>NP or PA endoscopists not allowed</td>
</tr>
<tr>
<td>Any credentialed physician endoscopist</td>
<td>Fellow must have real-time supervision</td>
</tr>
<tr>
<td>Fellow involvement OK</td>
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Colonoscopy Measures
N=16794

- High Definition Colonoscopes: 97.1%
- Cecal Intubation Rate: 97.0%
  - Terminal Ileum Intubation Rate: 23.4%
- Average Withdrawal Time: 11.2 minutes
Bowel Prep Quality
N=16794

- Adequate: 92.4%
- Not Adequate: 5.1%
- Missing: 5.1%
Summary

- Recruitment is finished!
- Study participants are very diverse
- We are meeting colonoscopy quality benchmarks
- FIT to colonoscopy—reasonable study wide
  - Further work to understand regional variation being considered
- Trial design favors pragmatism (large simple trial)
CONFIRM Study Team

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