National Colonoscopy Study (NCS) Screening Colonoscopy versus Annual Fecal Occult Blood Test
NCT 00102011

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June 1, 2018
WEO Colorectal Cancer Screening Committee
Major Outcomes for NCS

• Adherence for one time colonoscopy versus adherence for annual FOBT
  – All eligible accrued for at least 4 rounds of FOBT
  – Subset (early registrants) eligible for up to 7 rounds

• Clinical findings for Colonoscopy vs program of annual FOBT
  – Percent with adenomas and with advanced neoplasia

• Third aim- microsimulation modeling of long term incidence and mortality reduction
  (Reinier Meester)
Study Population and Recruitment

• Ages 50-75 (40-75 at LSUHS)
• Recruitment at three clinical sites
  – Un of Minnesota and Minnesota Gastroenterology
    • General population registered to be in RCT
  – Kaiser-Washington (formerly Group Health Cooperative)
    • Age and screening eligible from GHC electronic records
  – Louisiana University Health Sciences (Shreveport, LA)
    (health wellness clinic)
    • Clinic records
• Exclusions
  – Recent screenings or high comorbidity levels
    • Ascertained by patient report or electronic records
Strengths

• Representative of different health care delivery practices in the United States
• Designed with best clinical practices to optimize CRC screening (non-pragmatic)
  – Patient navigator to facilitate scheduling of colonoscopy, prep for colonoscopy, and to encourage FOBT compliance
• Informed consent prior to randomization
• Representative of US population with 56% unscreened
• Included serrated polyp pathway
National Colonoscopy Study
Flow Chart of Colonoscopy versus Annual FOBT

Group Health Cooperative & University of Minnesota
- Men and Women age 50-69 from integrated health plan list or mailing lists
  - Recruitment letters sent
  - Ineligibility Criteria
    - FAP history
    - Prior CRC
    - Prior Colonoscopy
    - On Cancer Treatment
    - Comorbidity
  - Determination of eligibility
  - 3526 Randomized eligible persons ages 40-69
  - Baseline and family history questionnaires

Louisiana State University Health Sciences Center
- Men & Women age 40-69 from Partners in Wellness Clinic or general outreach

1761 Screening Colonoscopy
- Participate Screening Colonoscopy and Blood Draw
- Refuse Screening Colonoscopy

1762 Annual FOBT
- (-) Result: Reapproach Annually
- Participate in FOBT
- Refuse FOBT
- (+) Result: Refer for Colonoscopy

Annual Follow Up
Interventions

• **Screening Colonoscopy (n=1761)**
  – With appropriate surveillance for those with adenomas

• **Program of annual F0BT (n=1762)**
  – Screening exposure
    • 100% adherence to multiple FOBTs (per protocol)
      – Positive FOBT referred to colonoscopy
    • Any FOBT (intention to screen)
      – Positive FOBT referred to colonoscopy
    • Cross over from FOBT to colonoscopy (intention to screen)
      – Negative FOBT or no FOBT

• Randomized by permuted block design at coordinating center (MSK)
FOBT Adherence

FOBT Adherence by Round (R1-R7)

Round 1: 73%
Round 2: 66%
Round 3: 64%
Round 4: 60%
Round 5: 54%
Round 6: 56%
Round 7: 54%

Total FOBT:

FOBT Adherent: 78%
No FOBT: 22%
Adherence by Arm over 4 rounds

**Per Intention to Screen**

- **Col**: 86%
- **Fobt, round 4**: 27%

**Per Protocol**

- **Col**: 86%
- **Per-protocol**: 33%
Clinical findings
Per intention to screen up to 7 rounds

- Advanced Neoplasia
- Colonoscopy  FOBT
- 6%  5%

- Any neoplasia* (adenomas or CRC)
- Colonoscopy  FOBT
- 23%  12%

*139 FOBT positive (21%) and 513 cross over colonoscopy (79%) of all those with colonoscopy
Quality Assurance and Oversight

• Patient navigator to facilitate prep and scheduling for colonoscopy and reminders for FOBT
• Endoscopist review committee to assure high quality exams with experienced physicians
• Withdrawal time and reach cecum
• Central distribution of FOBT kits (similar lots)
• Central processing (MSK) of FOBTs
• Annual meetings of sites
• Site visits by MSK IRB
• Data safety monitoring committee (annually)
Conclusions

• 100% adherence is not feasible even with those motivated to join RCT of screening with patient navigation
  – High adherence (86%) for colonoscopy screening
  – 44% adherent to 4 of 4 FOBTs, 84% with any screening exposure
  – Expect crossover to colonoscopy (~30% here)
• Advanced neoplasia comparable for two arms
  Adenomas not comparable by arms
• Microsimulation modeling to assimilate adherence patterns and project long term results