


## Colonoscopy versus FIT in Reducing Mortality from CRC (CONFIRM)

### Impact of Mailing Time and Season on FIT Positivity




## CONFIRM Study Team

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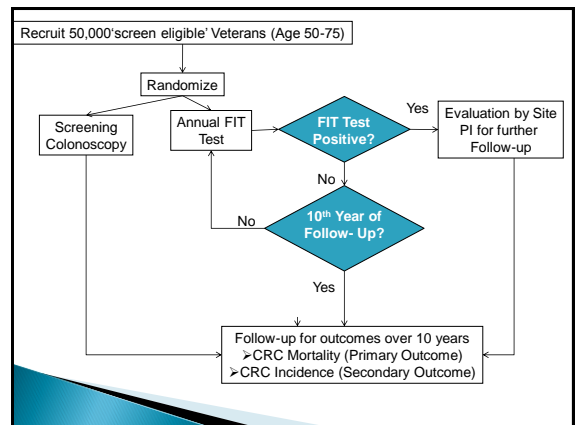
## CONFIRM Investigators

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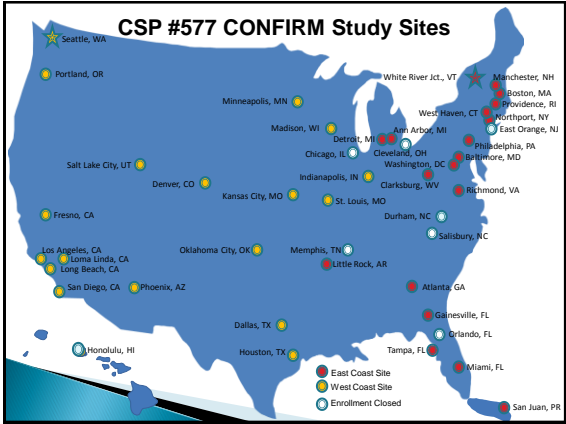
## Aim of CONFIRM

**To determine if a strategy of screening colonoscopy decreases CRC mortality and incidence over 10 years in average risk adults as compared to annual FIT screening**


### Current Status of Trial

- ▶ ~36 centers enrolling participants
- ▶ Recruitment milestones
  - First randomization May 22, 2012
  - 5,000<sup>th</sup> recruitment in June 2013
  - 15,000<sup>th</sup> recruitment in April 2014
  - 25,000<sup>th</sup> recruitment in March 2015
  - 35,000<sup>th</sup> recruitment in February 2016

### Interventions: FIT

- ▶ One sample
  - OC-FIT CHEK analyzed with the Diana®
    - Polymedco, Inc., Cortland Manor, NY
- ▶ Positivity:  $\geq 20 \mu\text{g hgb/g stool}$
- ▶ Centralized processing (Albuquerque, NM)
- ▶ Only samples arriving within 15 days of collection are processed
- ▶ If no collection date, specimen is processed
- ▶ Samples are refrigerated upon arrival in lab



### Mean Hgb Concentration by Season

| Study                  | Spring     | Summer     | Fall       | Winter     | p      |
|------------------------|------------|------------|------------|------------|--------|
| Grazzini et al         | 27.6 ng/mL | 25.2 ng/mL | 29.2 ng/mL | 29.5 ng/mL | <0.001 |
| Cha et al <sup>†</sup> | 0.45 ng/mL | 0.25 ng/mL | 0.20 ng/mL | 0.32 ng/mL | <0.001 |

<sup>†</sup>log transformed

*Gut* 2010; 59:1511-1515  
*Dig Dis Sci* 2012; 57:2178-2183

### FIT Positivity by Season

| Study          | Test                          | Spring | Summer | Fall | Winter | p            |
|----------------|-------------------------------|--------|--------|------|--------|--------------|
| Grazzini et al | OC Sensor (20 $\mu\text{g}$ ) | 3.7%   | 3.5%   | 3.7% | 4.2%   | Not reported |
| Chausserie     | OC Sensor (30 $\mu\text{g}$ ) | 2.9%   | 2.3%   | 3.0% | 3.0%   | 0.159        |
| Van Roon       | OC Sensor (20 $\mu\text{g}$ ) |        | 8.0%   |      | 9.7%   | 0.006        |

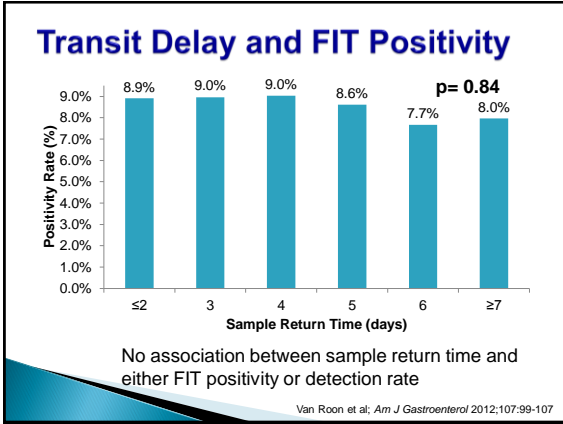
*Gut* 2010; 59:1511-1515  
*Int J. Cancer* 2015;136:1827-1834  
*Am J Gastroenterol* 2012;107:99-107

### Transit Delay and FIT Positivity

- ▶ Population: Netherlands
- ▶ FIT: OC Sensor (10  $\mu\text{g hgb/g stool}$ )
- ▶ Of the 6157 who returned a kit, 3767 reported the date of collection

| Transit Time  | N    | Positivity |
|---------------|------|------------|
| 1-4 days      | 3067 | 8.7%       |
| $\geq 5$ days | 705  | 6.0%       |
| $\geq 7$ days | 195  | 4.1%       |

van Rossum et al; *Int J Cancer* 2009;125:746-750

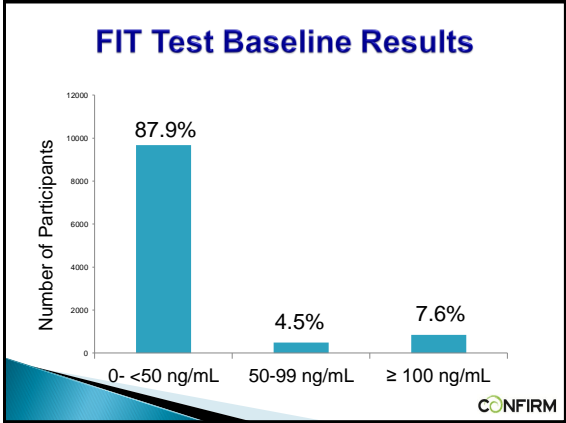


### Aim of Sub-Study

- ▶ To determine the impact of season and time between specimen collection and receipt in the laboratory (shipping time) upon the FIT positivity rate.

### Methods

- ▶ Initially, FIT mailed using first class mail
- ▶ Switched to US Priority Mail after discovery of some unacceptable shipping delays in some areas
- ▶ Chi-square test was used to compare positivity rate by season and the association between FIT positivity and shipping time



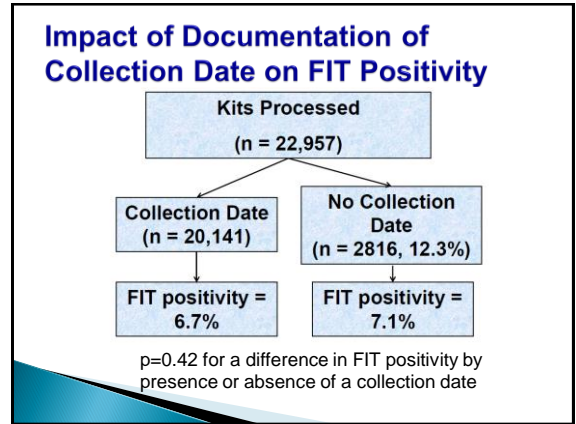
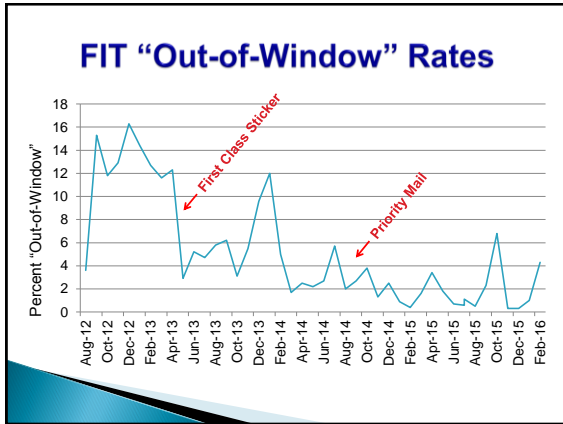
### “Out-of-Window FIT Kits”

- ▶ FIT Kits Returned 27,507
- ▶ Unusable Kits 5%
- ▶ Out-of-Window 3%

### Results: Shipping Time (Days)

| Method                         | Mean | Std Dev | Median | 25 <sup>th</sup> -75 <sup>th</sup> Percentile | 90 <sup>th</sup> Percentile | 95 <sup>th</sup> Percentile |
|--------------------------------|------|---------|--------|---|-----------------------------|-----------------------------|
| 1 <sup>st</sup> Class (n=8020) | 8.5  | 9.4     | 7      | 4-12  | 14                          | 17                          |
| Priority Mail (N=16,141)       | 6.5  | 4.2     | 5      | 3-8   | 13                          | 14                          |

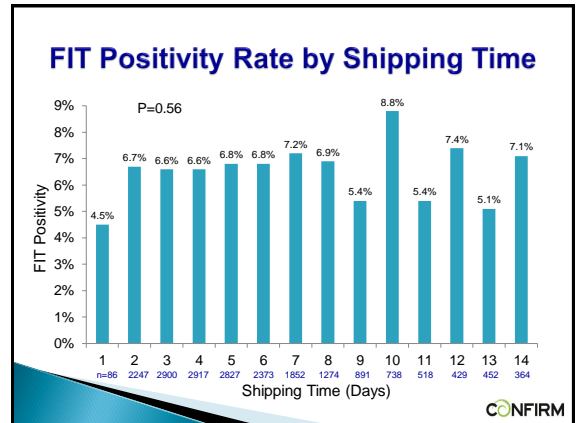
p<0.0001



### Association Between Season and FIT Positivity

| Meteorological Season  | Kits Processed (N) | Positivity (%) |
|------------------------|--------------------|----------------|
| Winter (Dec 1- Feb 28) | 3754               | 7.3            |
| Spring (Mar 1- May 31) | 5290               | 6.9            |
| Summer (June 1-Aug 31) | 5712               | 5.8            |
| Fall (Sep 1- Nov 30)   | 5391               | 7.2            |

p=0.007



- ### Summary
- ▶ Overall FIT positivity rate was 6.8%
  - ▶ Positivity rates varied significantly by season, being lowest in the summer
  - ▶ Shipping times of up to 14 days did not appear to affect FIT positivity rates
  - ▶ The presence or absence of a sample collection date did not affect positivity rates
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- ### Limitations
- ▶ We did not assess impact of variation in positivity rate on endoscopic findings, such as adenoma or advanced neoplasia detection
  - ▶ Generalizability to FIT-based programs that are not nationally-based (with presumably smaller distances between participant and processing center) is not clear
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## Conclusions

- ▶ Our findings support the clinical use of specimens returned without a collection date
- ▶ Seasonal variation in positivity rates is a potential threat to FIT-based screening programs
- ▶ Potential solutions, including improved buffers and/or avoiding mailing during the warmest seasons, might be explored
- ▶ Further work to understand the impact on sensitivity and specificity is needed



## Sample Return Time & Season with New Buffer

| Factor             | n    | Positivity |
|--------------------|------|------------|
| Sample Return Time |      |            |
| ≤ 3 days           | 6130 | 4.1%       |
| 4-5 days           | 8643 | 4.1%       |
| 6-7 days           | 5598 | 4.6%       |
| Season             |      |            |
| Winter             | 4797 | 4.3%       |
| Spring             | 8488 | 4.1%       |
| Summer             | 4818 | 4.5%       |
| Autumn             | 2268 | 3.9%       |

Dancourt et al; *European J of Cancer Prevention* 2016;25: 109-114

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