Predictors of Timely Colonoscopy After a Positive Fecal Immunochemical Test (FIT) in the CONFIRM Study

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Possible conflicts of interest

- None relevant to the presentation
Stool Based Colorectal Cancer Screening

• Reduces colorectal cancer mortality in RCT’s
  – Fecal immunochemical test (FIT) increasingly replacing conventional FOBT

• Stool based screening programs rely on **timely completion** of colonoscopy in those with a positive screening test
Delayed Colonoscopy after FIT + Impacts Screening Effectiveness

- Microsimulation modeling in a screening population
- Examined impact of delay relative to colonoscopy at 2 weeks after a positive test
- Results:
  - CRC incidence $\uparrow 0.3\% /\text{month}$
  - CRC mortality $\uparrow 1.4\% /\text{month}$
**Timely Colonoscopy after FOBT + Varies By Site**

<table>
<thead>
<tr>
<th>System</th>
<th>1 months</th>
<th>3 months</th>
<th>6 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kaiser Northern CA</td>
<td>28.3%</td>
<td>73.4%</td>
<td>80.9%</td>
</tr>
<tr>
<td>Kaiser Southern CA</td>
<td>39.3%</td>
<td>69.6%</td>
<td>74.4%</td>
</tr>
<tr>
<td>Group Health, WA</td>
<td>14.9%</td>
<td>51.3%</td>
<td>62.8%</td>
</tr>
<tr>
<td>Parkland Health, TX</td>
<td>2.4%</td>
<td>34.7%</td>
<td>50.2%</td>
</tr>
</tbody>
</table>

N=62384

*Cancer Epidemiol Biomarkers Prev. 2016;25:344-50*
AIM

To determine factors associated with timely colonoscopy completion (< 60 days) of a positive FIT
CONFIRM Trial Overview
Recruit 50,000 ‘screen eligible’ Veterans (Age 50-75)

Randomize (1:1)

Screening Colonoscopy

Annual FIT Test

FIT Test Positive?

Yes

Colonoscopy (as appropriate)

No

10th Year of Follow-Up?

No

Yes

Follow-up for outcomes over 10 years

- CRC Mortality (Primary Outcome)
- CRC Incidence (Secondary Outcome)
Recruit 50,000 ‘screen eligible’ Veterans (Age 50-75)

Randomize (1:1)

Screening Colonoscopy

Annual FIT Test

FIT Test Positive?

Yes

Colonoscopy Complete ≤ 1 year

No

10th Year of Follow-Up?

No

Follow-up for outcomes over 10 years

- CRC Mortality (Primary Outcome)
- CRC Incidence (Secondary Outcome)

Yes

Focus of Current Analysis
Methods - Details of FIT intervention

• Initial FIT given by local coordinator; all others sent out centrally to participant through US mail
  – OC-Auto FIT (20 ug hgb/gm stool)

• Participants send completed kit back to central lab (Albuquerque, NM) via Priority Mail

• Results released to both participant and local study investigator (LSI)
  – LSI arranges follow up for those FIT positive via “usual care”
Methods- Main Outcome

• “Timely Colonoscopy” defined as colonoscopy < 60 days of a positive FIT
• Date of positive test available from high throughput Polymedco Diana FIT processor
  – Automated result notification to participant and LSI
• Colonoscopy date determined from dedicated case report form that track all positive FIT
  – Include colonoscopy completed ≤ 1 year of FIT +
Methods - Co-variante Measurement

• Baseline data obtained at enrollment
  – Race/ethnicity
  – Education
  – Habits (Alcohol use, Tobacco use)
  – Prior endoscopy
  – Distance/Time to VA/Insurance information

• Geographic Region
  – 4 regions based on US census categorization
Methods-Statistical Analysis

• Exploratory Analysis examining continuous and categorical covariates with colonoscopy completion < 60 days
  – Two sided t-test (continuous)
  – Pearson's Chi-Square (categorical)

• Predictors of Timely Colonoscopy were modelled using
  – Univariate logistic regression
    • A significance level of p<0.2 was used as a threshold for inclusion of variables in a multivariable logistic regression
  – Multivariable logistic regression
    • Estimate the odds of completing timely colonoscopy adjusted for all significant covariates
Results

• 1686 FIT positive Veterans with colonoscopy
  – 95% male
  – 77% white
  – 8.5% Hispanic

• Median time to colonoscopy 45 days
  (interquartile range 31-67 days)
Number of Days from Positive FIT to Colonoscopy

Count of Participants

Time to Colonoscopy [Days]

N=1686
### Exploratory Analysis (continuous)

<table>
<thead>
<tr>
<th></th>
<th>Colonoscopy Done</th>
<th></th>
<th></th>
<th>T-test</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>less than 60 days</td>
<td>60 days or more</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age [years]</td>
<td>60.4 (6.7)</td>
<td>60.4 (6.5)</td>
<td>0.70</td>
<td></td>
</tr>
<tr>
<td>Travel distance [miles]</td>
<td>25.6 (31.6)</td>
<td>24.9 (27.1)</td>
<td>0.65</td>
<td></td>
</tr>
<tr>
<td>Travel Time [minutes]</td>
<td>39.4 (34.9)</td>
<td>38.5 (29.7)</td>
<td>0.64</td>
<td></td>
</tr>
</tbody>
</table>
## Exploratory Analysis (Categorical)

<table>
<thead>
<tr>
<th>Factor</th>
<th>% Timely Colonoscopy</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Race</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>70.5%</td>
<td>0.0008</td>
</tr>
<tr>
<td>Non White</td>
<td>63.3%</td>
<td></td>
</tr>
<tr>
<td><strong>Ethnicity</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>76.4%</td>
<td>0.04</td>
</tr>
<tr>
<td>Non-Hispanic</td>
<td>68.3%</td>
<td></td>
</tr>
<tr>
<td><strong>Prior Colonoscopy</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>67.2%</td>
<td>0.01</td>
</tr>
<tr>
<td>Yes</td>
<td>73.7%</td>
<td></td>
</tr>
<tr>
<td><strong>Region</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>West</td>
<td>65.1%</td>
<td>0.03</td>
</tr>
<tr>
<td>South</td>
<td>69.9%</td>
<td></td>
</tr>
<tr>
<td>Central</td>
<td>70.9%</td>
<td></td>
</tr>
<tr>
<td>North East</td>
<td>74.9%</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>North East</td>
<td>74.9%</td>
<td></td>
</tr>
<tr>
<td><strong>Education</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High School or Less</td>
<td>71.1%</td>
<td>0.12</td>
</tr>
<tr>
<td>Some College</td>
<td>65.9%</td>
<td></td>
</tr>
<tr>
<td>College or Above</td>
<td>70.1%</td>
<td></td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>64.1%</td>
<td>0.35</td>
</tr>
<tr>
<td>Male</td>
<td>69.1%</td>
<td></td>
</tr>
<tr>
<td><strong>Alcohol</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>69.9%</td>
<td>0.52</td>
</tr>
<tr>
<td>No</td>
<td>68.3%</td>
<td></td>
</tr>
<tr>
<td><strong>Tobacco</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>68.2%</td>
<td>0.78</td>
</tr>
<tr>
<td>No</td>
<td>69.2%</td>
<td></td>
</tr>
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</table>
Predictors of Timely (< 60 days) Colonoscopy After FIT Positive Univariate Analysis

<table>
<thead>
<tr>
<th>Factor</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>1.00</td>
<td>0.98, 1.01</td>
</tr>
<tr>
<td>Race (Non-white vs White)</td>
<td>0.72</td>
<td>0.57, 0.92</td>
</tr>
<tr>
<td>Ethnicity (Hispanic vs Non Hispanic)</td>
<td>1.50</td>
<td>1.00, 2.24</td>
</tr>
<tr>
<td>Gender (Female vs Male)</td>
<td>0.80</td>
<td>0.50, 1.28</td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High school or less vs college or more</td>
<td>0.78</td>
<td>0.61, 1.00</td>
</tr>
<tr>
<td>Some College credit but no degree vs College graduate</td>
<td>0.95</td>
<td>0.73, 1.24</td>
</tr>
<tr>
<td>Alcohol (Drinker vs non drinker)</td>
<td>0.93</td>
<td>0.75, 1.16</td>
</tr>
<tr>
<td>Tobacco (Smoker vs non smoker)</td>
<td>1.05</td>
<td>0.83, 1.31</td>
</tr>
<tr>
<td>Prior colonoscopy (Yes vs No)</td>
<td>1.37</td>
<td>1.07, 1.74</td>
</tr>
<tr>
<td>Region</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Central vs West</td>
<td>1.42</td>
<td>1.08, 1.88</td>
</tr>
<tr>
<td>East vs West</td>
<td>1.63</td>
<td>1.14, 2.34</td>
</tr>
<tr>
<td>South vs West</td>
<td>1.19</td>
<td>0.92, 1.53</td>
</tr>
</tbody>
</table>

Age, gender, alcohol and tobacco use insignificant and removed for the model.
### Predictors of Timely (< 60 days) Colonoscopy After FIT Positive Multivariable Analysis

<table>
<thead>
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<td>0.57, 0.92</td>
<td>0.73</td>
<td>0.57, 0.94</td>
</tr>
<tr>
<td><strong>Ethnicity (Hispanic vs Non Hispanic)</strong></td>
<td>1.50</td>
<td>1.00, 2.24</td>
<td>1.59</td>
<td>1.06, 2.38</td>
</tr>
<tr>
<td><strong>Gender (Female vs Male)</strong></td>
<td>0.80</td>
<td>0.50, 1.28</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Education</strong></td>
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<td></td>
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<td>0.78</td>
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<td>0.70, 1.17</td>
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<td>1.14, 2.34</td>
<td>1.68</td>
<td>1.16, 2.44</td>
</tr>
<tr>
<td>South vs West</td>
<td>1.19</td>
<td>0.92, 1.53</td>
<td>1.31</td>
<td>1.01, 1.70</td>
</tr>
</tbody>
</table>
Facility-Level Variation in Proportion With Timely Colonoscopy

Percent of Timely Colonoscopy

Region ID

North East
South
Central
West
Summary

• Non-white participants and those enrolled in West Coast sites less likely to get colonoscopy within 60 days

• Hispanic participants and those with a prior colonoscopy history more likely to get colonoscopy within 60 days
Limitations

• Analysis performed within the framework of a clinical trial only involving US Veterans (generalizability)

• Did not examine all potential factors that could influence timely colonoscopy completion
  – Significant other/availability of a driver

• Cannot examine FIT positive with NO colonoscopy completion

• Importance of the 60 day definition of ‘timely colonoscopy’
Colonoscopy Delay After FIT positive & Colorectal Cancer

N=70124

- 8-30 days: 1 [Reference]
- 2 months: 0.92 [0.83, 1.02]
- 3 months: 0.95 [0.82, 1.10]
- 4-6 months: 0.98 [0.82, 1.16]
- 7-12 months: 1.37 [1.09, 1.70]
- >12 months: 2.25 [1.89, 2.68]

JAMA. 2017;317:1631-1641
Conclusions

• Time to colonoscopy is associated with patient and facility characteristics

• Patient navigation might be explored for persons less likely to complete colonoscopy within 60 days
  – no previous colonoscopy
  – Non-white race

• Regional variation is likely accounted by facility and organizational level factors
  – Site-specific investigation of contributing factors needed
Local Site Investigators - Present

- Aasma Shaukat, MD, MPH
- Adnan Said, MD, MS
- Amelia (Beth) Underwood, MD
- Andrew J. Gawron, MD
- Andrew M. Kaz, MD
- Charles H. Beymer, MD, MPH
- Charles Kahi, MD
- Christian S. Jackson, MD
- Christopher Lenza, DO
- Claudio Tombazzi, MD
- Curt H. Hagedorn, MD
- David Lieberman, MD
- Deborah A. Fisher, MD, MHS
- Devang Prajapati, MD
- Dipendra Parajuli, MD
- Doris H. Toro, MD
- Douglas J. Nguyen, MD
- E. Carter Paulson, MD
- Edward Sun, MD
- Endashaw Omer, MD, MPH
- Eric K. Taylor, NP
- Erik C. von Rosenvinge, MD
- Fadi Antaki, MD
- Frank S. Pancotto, MD
- Gyorgy Baffy, MD, PhD
- Heather Hockman, MD
- Heiko Pohl, MD
- Heiko Pohl, MD
- Helen W. Wong, MD
- Ildiko Halasz, MD
- Isabelita Cordoba Rellosa, MD
- Jed E. Olson, MD
- Jeffrey A. Gill, MD
- Jill E. Elwing, MD
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- Joseph Manlolo, MD
- Joseph R. Pisegna, MD
- Katarina B. Greer, MD, MS
- Kittichai Promrat, MD
- Lyn Sue Kahng, MD
- Margaret F. Kinnard, MD
- Michael Yao, MD
- Michele Young, MD
- Mitchell Schubert, MD
- Mohammad Madhoun, MD
- Nancy C. Ho, MD
- Paul A. Feldman, MD, MSC
- Petr Protiva, MD
- Prateek Sharma, MD
- Priscilla Magno, MD
- Rebecca J. Beyth, MD, MSc
- Rhonda A. Cole, MD

- Riaz Cassim, MD
- Ronald Fernando, MD
- Sameer Saini, MD, MS
- Samir Gupta, MD, MSCS
- Samuel B. Ho, MD
- Stacy Menees, MD
- Stephan Goebel, MD
- Swati G. Patel, MD
- Tarun Rai, MD
- Thomas F. Imperiale, MD
- William M. Tierney, MD
- William V. Harford, Jr. MD
Local Site Investigators - Past

- Christopher Lopez, MD
- Dennis J. Ahnen, MD
- Farrukh H. Merchant, MD
- Fernando V. Ona, MD
- J. Andy Mengshol, MD, PhD
- Juan Diego Baltodano, MD
- Kenneth H. Berman, MD
- Lubna Maruf, MD
- M. Mazen Jamal, MD, MPH
- Mae F. Go, MD

- Marcos C. Pedrosa, MD, MPH
- Martin Tobi, MB, ChB
- Mohammad Wehbi, MD
- Phillip Schoenfeld, MD, MSEd, MSc
- Ranjan C.V. Mascarenhas, MD
- Robert D. Shaw, MD
- Shahnaz Sultan, MD, MHSc
- Steven R. Warlick, MD
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- Toan D. Nguyen, MD
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