

# Delay to Diagnostic Colonoscopy after Abnormal FIT/FOBT Screening Results is Associated with Colorectal Cancer Incidence and Mortality in a Large United States Cohort

Yazmin San Miguel<sup>1,2</sup>; Joshua Demb<sup>1,3</sup>; Maria Elena Martinez<sup>2,4</sup>; SamirGupta<sup>1,2,3</sup>; Folasade (Fola) P. May<sup>5,6</sup>

<sup>1</sup>Division of Gastroenterology, Department of Medicine, Veterans Affairs San Diego Healthcare System; <sup>2</sup>Moore's Cancer Center, University of California San Diego; <sup>3</sup>Division of Gastroenterology, Department of Internal Medicine, University of California San Diego.

<sup>4</sup>Department of Family Medicine and Public Health, University of California San Diego; <sup>5</sup>Division of Gastroenterology, Department of Medicine, Veterans Affairs Greater Los Angeles Healthcare System;

<sup>6</sup>The Vatche and Tamar Manoukian Division of Digestive Diseases, Department of Medicine, David Geffen School of Medicine, University of California Los Angeles

UC San Diego  
MOORES CANCER CENTER



## BACKGROUND

- Colorectal cancer (CRC) is the second most common cause of cancer-related mortality in the United States but largely preventable by screening.
- The fecal occult blood test (FOBT) and fecal immunochemical test (FIT) are common screening methods that must be followed by diagnostic colonoscopy when abnormal (i.e. positive).
- The literature varies on the optimal time interval for diagnostic colonoscopy after an abnormal FIT/FOBT.
- Understanding the relative importance of time to colonoscopy on outcomes allows for concrete care guidelines for diagnostic follow-up after an abnormal FIT/FOBT.

## PURPOSE

To examine the association between incident and fatal colorectal cancer (CRC) and time to colonoscopy among individuals who underwent diagnostic colonoscopy after an abnormal FIT/FOBT in a cohort of United States Veterans.

## METHODS

### Study Population:

- Veteran Health Administration (VA) patients age 50 to 75
- Abnormal FOBT/FIT result between 1999 and 2010 in national electronic health record data
- Colonoscopy receipt after abnormal FIT/FOBT result.

### Exclusions:

- Colonoscopy prior to abnormal FIT/FOBT result.
- < 2 clinic visits in the 2 years before abnormal FIT/FOBT date.

### Approach:

- Patients were followed through CRC-related death, other death, or until December 31, 2015.
- Colonoscopy receipt was ascertained using current procedural terminology codes.
- Incident colorectal cancer was identified from the Oncology Domain (Corporate data Warehouse).
- CRC death was defined through the National Death Index.

### Analysis:

Multivariable Cox proportional hazards regression models to estimate hazard ratio (HR) and 95% confidence interval (CI) for 3-month colonoscopy intervals, with 3-6 months as the reference group.

## RESULTS

**Table 1: Risk for incident CRC based on timing of colonoscopy receipt after abnormal FIT, 1999-2015; N=228194**

Time to Colonoscopy after abnormal FIT/FOBT	No. of Patients	No. cases due to CRC	Unadjusted HR (95% CI)	Adjusted HR (95% CI)
<3 months	82,989	3037	<b>1.18 (1.11-1.26)*</b>	<b>1.21 (1.13-1.29)*</b>
4-6 months	40,486	1353	REF	REF
7-9 months	18,451	614	0.97 (0.88-1.07)	0.97 (0.88-1.06)
10-12 months	10,241	365	1.03 (0.92-1.16)	1.03 (0.92-1.15)
13-15 months	7,608	320	<b>1.24 (1.10-1.41)*</b>	<b>1.24 (1.10-1.40)*</b>
16-18 months	5,573	256	<b>1.35 (1.18-1.55)*</b>	<b>1.34 (1.18-1.54)*</b>
19-21 months	4,356	203	<b>1.37 (1.19-1.59)*</b>	<b>1.38 (1.19-1.60)*</b>
22-24 months	3,623	166	<b>1.34 (1.14-1.57)*</b>	<b>1.35 (1.15-1.58)*</b>
> 24 months	54,867	1756	<b>0.88 (0.82-0.95)*</b>	0.96 (0.90-1.04)

\* Denotes significance in findings

HR: Hazard Ratio; CI: Confidence Interval; No.: Number

Adjusted for age, race/ethnicity, smoking, Charlson Comorbidity Index, and BMI

**Table 2: Risk for CRC-specific death based on timing of colonoscopy receipt after abnormal FIT, 1999-2015; N=228194**

Variable	No. of Patients	No. deaths due to CRC	Unadjusted HR (95% CI)	Adjusted HR (95% CI)
Time to Colonoscopy after abnormal FIT/FOBT				
<3 months	82,989	756	<b>1.23 (1.08-1.40)*</b>	<b>1.29 (1.14-1.47)*</b>
4-6 months	40,486	346	REF	REF
7-9 months	18,451	172	1.05 (0.87-1.26)	1.04 (0.87-1.25)
10-12 months	10,241	92	1.02 (0.81-1.27)	0.99 (0.79-1.26)
13-15 months	7,608	69	1.01 (0.79-1.32)	1.03 (0.79-1.31)
16-18 months	5,573	65	<b>1.32 (1.01-1.72)*</b>	1.29 (0.99-1.69)
19-21 months	4,356	59	<b>1.54 (1.17-2.03)*</b>	<b>1.56 (1.19-2.06)*</b>
22-24 months	3,623	47	<b>1.42 (1.06-1.93)*</b>	<b>1.46 (1.07-1.96)*</b>
> 24 months	54,867	443	<b>0.82 (0.71-0.94)*</b>	0.94 (0.81-1.08)

\* Denotes significance in findings

HR: Hazard Ratio; CI: Confidence Interval; No.: Number

Adjusted for age, race/ethnicity, smoking, Charlson Comorbidity Index, and BMI

## SUMMARY OF RESULTS

### Characteristics of Study Population:

- Mean study follow-up time: 8.3 years, s.d. ± 4.1
- Mean age: 61.4 years, s.d. ± 6.9
- Non-Hispanic White (NHW), 72%; NH Black, 20%; Hispanic, 1.7%; Asian/Pacific Islander (API), 1.1%
- Colonoscopy completed ≤ 1 year: 69%
- CRC Rate: 4%
- CRC-related death rate: 1%

### Association between abnormal FIT and CRC Incidence:

- Compared to patients with colonoscopy at 3-6 months (standard of care), there was an increased risk for CRC Incidence for the following groups: 0-3 months, 12-15 months, 15-18 months, 18-21 months, and 21-24 months. (Table 1)

### Association between abnormal FIT and CRC Death:

- Compared to patients with colonoscopy at 3-6 months (standard of care), there was an increased risk for CRC Death for the following groups : 0-3 months, 15-18 months, 18-21 months, and 21-24 months. (Table 2)

## CONCLUSIONS

- Time to colonoscopy plays a significant role in CRC incidence and CRC-related death after abnormal FIT/FOBT.
- Compared to a patient with a colonoscopy performed within 3 to 6 months of an abnormal FIT/FOBT, a patient with colonoscopy performed after 12 months had a higher risk for incident CRC.
- Compared to a patient with a colonoscopy performed within 3 to 6 months of an abnormal FIT/FOBT, those with a colonoscopy performed after 15 months had a higher risk for fatal CRC.
- Interventions to increase timely diagnostic follow-up after abnormal FIT/FOBT are essential to improve overall CRC outcomes and should focus on achieving diagnostic follow-up within 12 months of the abnormal result.
- We speculate increased risk for incident and fatal CRC observed among Veterans with colonoscopy 0-3 months after abnormal FIT/FOBT is due to urgent work up of patients with signs/symptoms of CRC concurrent to the abnormal FIT/FOBT (e.g. abnormal FIT/FOBT with iron deficiency and weight loss).

## ACKNOWLEDGMENTS

Work supported by SDSU/UCSD Comprehensive Cancer Center Partnership (U54CA132384 & U54CA132379); Greater Los Angeles Veterans Affairs Healthcare System; Vatche and Tamar Manoukian Division of Digestive Diseases; UCLA Jonsson Comprehensive Cancer Center; 1101HX001574-01A1 (PI: Gupta) from VA Health Services Research and Development; 1R37CA 222866-01 (PI: Gupta) from National Cancer Institute/National Institute of Health.

