

Family Physicians & Cancer Control Workshop - 2017

FIT Update

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Dr. Wong Disclosure(s)

Organization	Domain	Speaker's Bureau / Honoraria	Consulting Fees	Research Support / Grants
Alberta Health Services	Employee			
Medtronic/Covidien Boston Scientific			Yes	
Allergan, Ferring, Takeda, Pendopharm	Advisory Board			
Allergan, Takeda, Pendopharm		Yes		



Dr. Wong's Potential Conflict(s) of Interest

Organization	Product(s) Discussed	Type of Support	Description of Support	Latest Engagement		
	None relevant to this talk					



Dr. Wong's Mitigation of Potential Bias

Organization	Mitigation of Potential Bias
	Will identify if any products disclosed would influence the talk (none will be relevant)



Objectives

- At the end of this session, the attendee will have an increased understanding of:
 - Burden of CRC and Screening Rate
 - Results of FIT implementation
 - When to Order and Not to Order FIT

Colon Cancer Burden



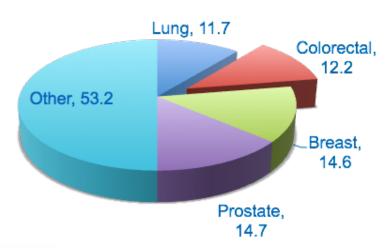


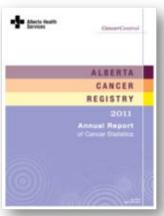


CRC Burden in Alberta

2011

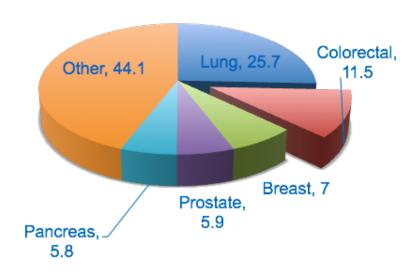








Deaths





Risk of CRC

Men 1 in 13 Women 1 in 16

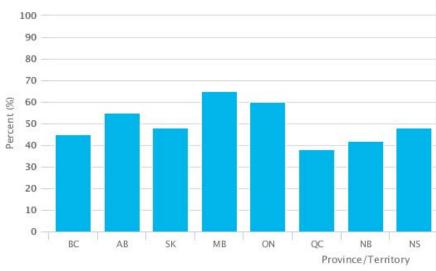
Age Group (Years)	Males	Females	
Lifetime Risk (all ages)	1 in 13	1 in 16	
0-20	Less than 1 in 10,000	Less than 1 in 10,000	
20-30	1 in 5,428	1 in 4,506	
30-40	1 in 1,613	1 in 1,355 1 in 410	
40-50	1 in 450		
50-60	1 in 161	1 in 158	
60-70	1 in 77	1 in 77	
70-80	1 in 45	1 in 46	
80+	1 in 28	1 in 25	



Are we Screening for CRC?

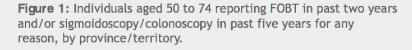
CCHS 2008-2012 - CRC screening data

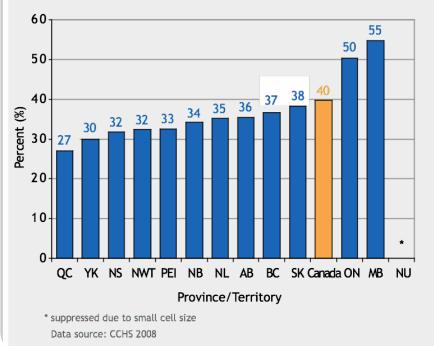
Percentage of population (aged 50-74) who reported having h two years and/or a sigmoidoscopy/colonoscopy in the past by province/territory — 2012 reporting year



† Any reason includes family history of colorectal cancer, regular check-up/routine screen follow-up of colorectal cancer treatment or other.

Data source: Statistics Canada, Canadian Community Health Survey.







E Interpret with caution owing to large variability in the estimate.

[&]quot;Target" indicates screening participation target

The Fecal Immunochemical Test





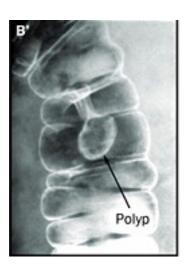
How to "best" screen for CRC?











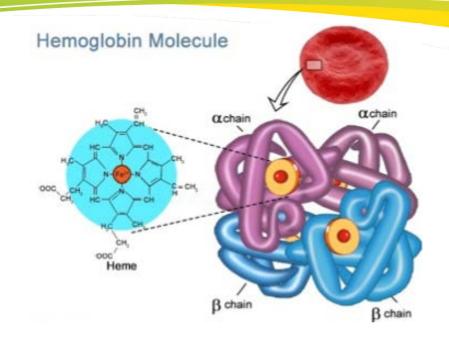




FIT for CRC screening

- ELISA based-to globalNo Diet interference
- Mass testing
- Qualitative and quantitativeAdjustable cutoff
- •FIT for Alberta:
 - ∘Polymedco (Eiken) OC FIT-CHEK







FIT...Evidence Based Practice





FIT Accuracy

Annals of Internal Medicine

Review

Accuracy of Fecal Immunochemical Tests for Colorectal Cancer

Systematic Review and Meta-analysis

Jeffrey K. Lee, MD, MAS; Elizabeth G. Liles, MD, MCR; Stephen Bent, MD; Theodore R. Levin, MD; and Douglas A. Corley, MD, PhD

Background: Performance characteristics of fecal immunochemical tests (FITs) to screen for colorectal cancer (CRC) have been inconsistent.

Purpose: To synthesize data about the diagnostic accuracy of FITs for CRC and identify factors affecting its performance characteristics.

Data Sources: Online databases, including MEDLINE and EMBASE, and bibliographies of included studies from 1996 to 2013.

Study Selection: All studies evaluating the diagnostic accuracy of FITs for CRC in asymptomatic, average-risk adults.

Data Extraction: Two reviewers independently extracted data and critiqued study quality.

Data Synthesis: Nineteen eligible studies were included and metaanalyzed. The pooled sensitivity, specificity, positive likelihood ratio, and negative likelihood ratio of FITs for CRC were 0.79 (95% CI, 0.69 to 0.86), 0.94 (CI, 0.92 to 0.95), 13.10 (CI, 10.49 to 16.35), 0.23 (CI, 0.15 to 0.33), respectively, with an overall diagnostic accuracy of 95% (CI, 93% to 97%). There was substantial heterogeneity between studies in both the pooled sensitivity and specificity estimates. Stratifying by cutoff value for a positive test result or removal of discontinued FIT brands resulted in homogeneous sensitivity estimates. Sensitivity for CRC improved with lower assay cutoff values for a positive test result (for example, 0.89 [CI, 0.80 to 0.95] at a cutoff value less than 20 μ g/g vs. 0.70 [CI, 0.55 to 0.81] at cutoff values of 20 to 50 μ g/g) but with a corresponding decrease in specificity. A single-sample FIT had similar sensitivity and specificity as several samples, independent of FIT brand.

Limitations: Only English-language articles were included. Lack of data prevented complete subgroup analyses by FIT brand.

Conclusion: Fecal immunochemical tests are moderately sensitive, are highly specific, and have high overall diagnostic accuracy for detecting CRC. Diagnostic performance of FITs depends on the cutoff value for a positive test result.

Primary Funding Source: National Institute of Diabetes and Digestive and Kidney Diseases and National Cancer Institute.

Ann Intern Med. 2014;160:171-181. For author affiliations, see end of text. www.annals.org

Bottom Line

Lee et al., AIM 2014

- Pooled Sensitivity 0.79
- Pooled Specificity 0.94
- Accuracy 95%

Single Use FIT Sensitivity:

80%

FIT vs Colonoscopy

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Colonoscopy versus Fecal Immunochemical Testing in Colorectal-Cancer Screening

Enrique Quintero, M.D., Ph.D., Antoni Castells, M.D., Ph.D., Luis Bujanda, M.D., Ph.D., Joaquín Cubiella, M.D., Ph.D., Dolores Salas, M.D., Angel Lanas, M.D., Ph.D., Montserrat Andreu, M.D., Ph.D., Fernando Carballo, M.D., Ph.D., Juan Diego Morillas, M.D., Ph.D., Cristina Hernández, B.Sc., Rodrigo Jover, M.D., Ph.D., Isabel Montalvo, M.D., Ph.D., Juan Arenas, M.D., Ph.D., Eva Laredo, R.N., Vicent Hernández, M.D., Ph.D., Felipe Iglesias, R.N., Estela Cid, R.N., Raquel Zubizarreta, M.D., Teresa Sala, M.D., Marta Ponce, M.D., Mercedes Andrés, M.D., Gloria Teruel, M.D., Antonio Peris, M.D., María-Pilar Roncales, R.N., Mónica Polo-Tomás, M.D., Ph.D., Xavier Bessa, M.D., Ph.D., Olga Ferrer-Armengou, R.N., Jaume Grau, M.D., Anna Serradesanferm, R.N., Akiko Ono, M.D., José Cruzado, M.D., Francisco Pérez-Riquelme, M.D., Inmaculada Alonso-Abreu, M.D., Mariola de la Vega-Prieto, M.D., Juana Maria Reyes-Melian, M.D., Guillermo Cacho, M.D., José Díaz-Tasende, M.D., Alberto Herreros-de-Tejada, M.D., Carmen Poves, M.D., Cecilio Santander, M.D., and Andrés González-Navarro, M.D., for the COLONPREV Study Investigators*

57,404 subjects randomly assigned to COL or FIT

	Colonoscopy 26,703	FIT 26,599
NNScope for 1 Cancer	191	18
Complications (%)	0.5	0.1
Overall Screened	5059	10,611
Rate of participation (%)	24.6	34.2



FIT Cutoffs & Results



British Journal of Cancer (2009) 101, 1274-1281

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www.bjcancer.com

Cutoff value determines the performance of a semi-quantitative immunochemical faecal occult blood test in a colorectal cancer screening programme

LGM van Rossum*, AF van Rijn², RJF Laheij¹, MGH van Oijen¹, P Fockens², JBMJ Jansen¹, ALM Verbeek³ and E Dekker²

Department of Gastroenterology and Hepatology, Radboud University Nijmegen Medical Center, P.O.Box 9101, 6500 HB, Nijmegen, The Netherlands, Department of Gastroenterology and Hepatology, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands; Department of Epidemiology and Biostatistics and MTA, Radboud University Nijmegen Medical Center, Nijmegen, The Netherlands

BACKGROUND The cutoff of semi-quantitative immunochemical foecol occult blood tests (iFOBTs) influences colonoscopy referrals and detection rates. We studied the performance of an iFOBT (OC-Sensor) in colorectal cancer (CRC) screening at different cutoffs. METHOOS: Dutch screening participants, 50−75 years of age, with average CRC risk and an iFOBT value ≥50 ngml⁻¹ were offered colonoscopy. The detection rate was the percentage of participants with CRC or advanced adenomas (≥10 mm, ≥20% villous, high-grade dysplasia). The number needed to scope (INNTScope) was the number of colonoscopies to be carried out to find one person with CRC or advanced adenomas.

RESULTS: iFOBT values \geqslant 50 ng ml $^{-1}$ were detected in 526 of 6157 participants (8.5%) and 428 (81%) underwent colonoscopy. The detection rate for advanced lesions (28 CRC and 161 with advanced adenomas) was 3.1% (95% confidence interval: 2.6-3.5%) and the NNTScope was 2.3. At 75 ng ml $^{-1}$, the detection rate was 2.7%, the NNTScope was 2.0 and the CRC miss rate compared with 50 ng ml $^{-1}$ was <5% (N = 1). At 100 ng ml $^{-1}$, the detection rate was 2.4% and the NNTScope was <2. Compared with 50 ng ml $^{-1}$, up to 200 ng ml $^{-1}$ CRC miss rates remained at 16% (N = 4).

CONCLUSIONS Cutoffs below the standard 100 ng ml⁻¹ resulted in not only higher detection rates of advanced lesions but also more colonoscopies. With sufficient capacity, 75 ng ml⁻¹ might be advised; if not, up to 200 ng ml⁻¹ CRC miss rates are acceptable compared with the decrease in performed colonoscopies.

British Journal of Cancer (2009) 101, 1274-1281. doi:10.1038/sj.bjc.6605326 www.bjcancer.com

Published online 15 September 2009

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Keywords: colorectal cancer; faecal occult blood test; screening; epidemiology; colonoscopy

•In Average Risk group 50-74, first time test, at a cutoff of 75 ng/mL:



AMA TOP Guidelines

- Simplified algorithm
- 2013



Colorectal Cancer Screening

Summary of the Clinical Practice Guideline | November 2013

Colorectal cancer screening (CRC) is:

- . IMPORTANT: CRC is the 2nd leading cause of cancer deaths
- . EFFECTIVE: Screening has the potential to reduce CRC deaths up to 1/2
- SIMPLE: Screen average risk men and women age 50-74 with FIT every 1-2 years

RISK ASSESSMENT

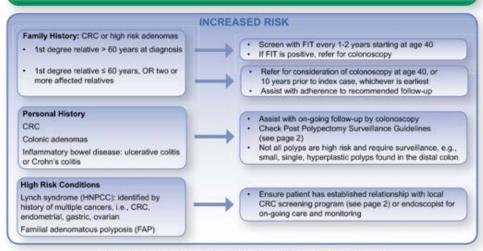
Assess CRC risk for all men and women. Do not wait for patient to turn 50 to assess.

AVERAGE RISK

Men and Women age 50 - 74

75+ years: consider co-morbidities, risk of screening, general health and life expectancy

- · Screen with Fecal Immunochemical Test (FIT) every 1-2 years
- If FIT result is positive refer for colonoscopy
- For colonoscopy services use local CRC screening program (see page 2) or endoscopist
- Wait 10 years after a normal colonoscopy to start or re-start FIT
- If quality of colonoscopy was uncertain, start or re-start FIT 5 years after colonoscopy



For the complete guideline refer to the TOP website: www.topalbertadoctors.org

These recommendations are systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances. They should be used as an adjunct to sound clinical decision making.

Page 1 of 2

ZUIU GII FIIG GIVG Guiueillies



Early release, published at www.cmaj.ca on February 22, 2016. Subject to revision.

CMAJ

GUIDELINES

Recommendations on screening for colorectal cancer in primary care

Canadian Task Force on Preventive Health Care*

"We recommend screening adults aged 50 to 74 years for colorectal cancer with FOBT (either gFOBT or FIT) every two years..."

"We recommend not using colonoscopy as a screening test for colorectal cancer."

FIT so Far...Results







CRC screening program availability in Canada, July 2016

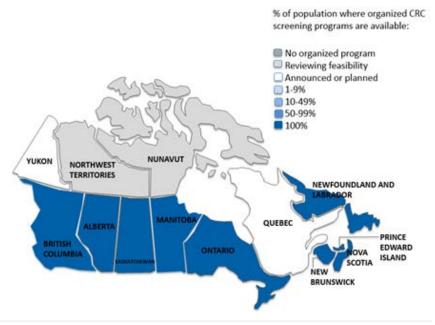
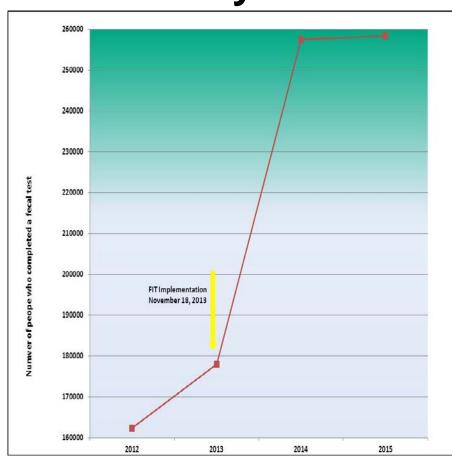
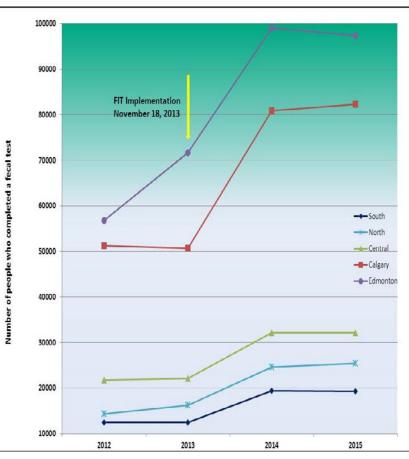


Table 2 Overview of Colorectal Cancer Screening Across Provinces and Territories in 2013-14

Province Territory	Program Start Date	Target Population	Screening Interval	Primary Screening Test	Primary Screening Test Brand	FTi Cut-off Value for an Abnormal Screening Result
АВ	March 2007	50-75	Annual or biennial	FTi replaced FTg in November 2013	Polymedco	>74ng/ml
ВС	2009 pilot; November 2013 province-wide	50-74	Biennial	FTi	Alere	>49ng/ml
МВ	April 2007	50-75	Biennial	FTg	Hemoccult II SENSA	
NB	November 2014	50-74	Biennial	ETI		≥100ng/ml
NL	March 2010	50-74	Biennial	FTi	Alere	≥ 100ng/ml
NT	No organized screening program	50-74	Annual or biennial	<u>FTi</u>	Hemoccult ICT	75ng/ml
NS	April 2009	50-74	Biennial	ETI	Hemoccult ICT	0.3 mg <u>Hb</u> /g
NU	No organized screening program	50-74		ETI		
ON	March 2008	50-74	Biennial	FTg	Hema- screen	
PE	2009; province- wide May 2011	50-74	Biennial	FTi	Alere	≥ 100ng/ml
QC	No organized screening program	50-74	Biennial	ETi		≥175 ng/ml
SK	January 2009	50-75	Biennial	ETI	Polymedco >100ng/ml	
YT	No organized screening program	50-74	N/A	ETI		

How Many Fecal Tests ordered since 2013?







What is the FIT Screening Rate?

Table Percentage of survey population 50-74 who are up to date for colorectal cancer screening

Time of Survey	Alberta Screening Rate (%)	Data Source			
2008 (baseline)	36	Canadian Community Health Survey (CCHS)			
2012	53	Canadian Community Health Survey (CCHS)			

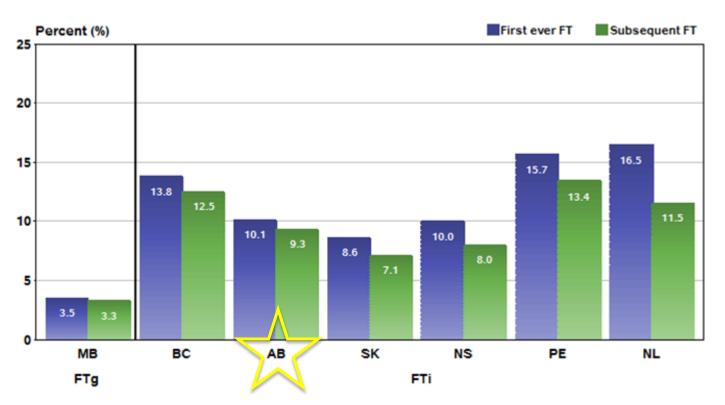
Percentage of individuals 50-74 who have a FIT test at least Biennially

Time Period / Health Zone	Target Population	Number of People had FIT	Screening Rate (%)						
2014-2015									
South	83,361	33,355	40.0						
Calgary	412,907	139,563	33.8						
Central	136,641	54,759	40.1						
Edmonton	350,655	159,764	45.6						
North	120,628	43,506	36.1						
Alberta	1,104,223	432,728	39.2						
015-2016									
South	85,162	32,767	38.5						
Calgary	429,071	139,009	32.4						
Central	139,909	54,617	39.0						
Edmonton	362,037	160,356	44.3						
North	124,493	44,002	35.3						
Alberta	1,140,693	433,902	38.0						

Notes:

- 1 The total numbers from 5 Health Zones do not add up to the total numbers for Alberta due to missing values in the data for defining individual zones
- 2 The FIT (Fecal Immunochemical Test) has been in use as a colorectal cancer screening tool in Alberta since November 18, 2013
- 3 Data Sources: a. Alberta Colorectal Cancer Screening Program (ACRCSP) database as of Feb 13, 2017
 - DIMR Alberta Health Care Insurance Plan Registry (AHCIP) data

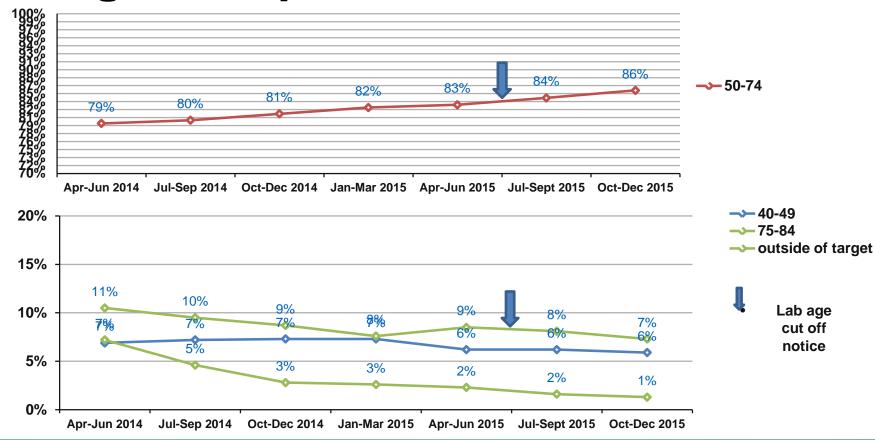
How many FITs are Positive?



By province and screening sequence, 2013 and 2014 screening years combined.

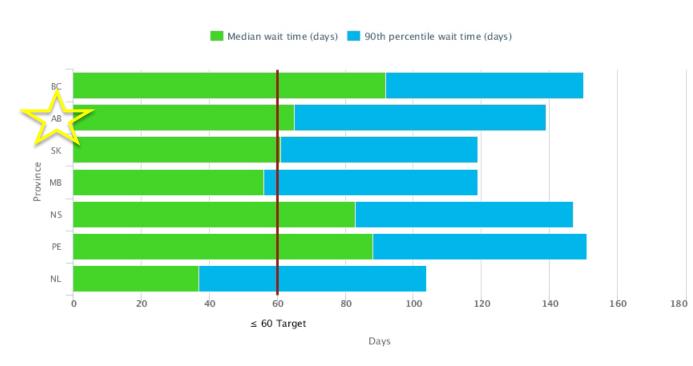


How Many FITs are in the Target Age Group?





What is the Wait Time for FIT+ to Colonoscopy?



Among those who have had a follow up colonoscopy within 180 days, by province, 2013 and 2014 screening years combined.

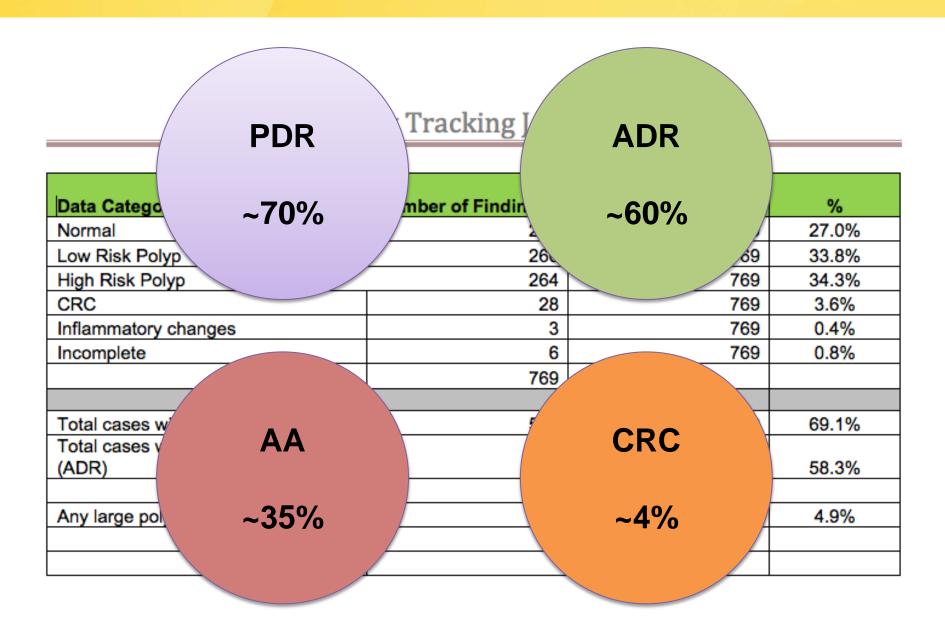
Data include colonoscopies performed within 180 days of abnormal fecal test results.

Target: The Canadian Association of Gastroenterology recommends that colonoscopy be completed within 60 days of an abnormal fecal test.

Data source: National Colorectal Cancer Screening Network.



UNIVERSITY OF ALBERTA FACULTY OF MEDICINE & DENTISTRY What are we Finding for FIT+?



To FIT...Practice TIPS





Who to FIT?

Age 50-74

Asymptomatic

Never Screened

Age 40-49

Asymptomatic

Never Screened

FHx: FDR age >60

Previous FIT or Colonoscopy

Asymptomatic

Average Risk

Follow Intervals

Most Common Areas of FIT Mis-Use

Age

Interval

Diagnostic

Why Not >80

- Risk of Colonoscopy
 - Significant increase in risk of morbidity and mortality in >80 group

ORIGINAL RESEARCH | 3 JANUARY 2017

Effectiveness of Screening Colonoscopy to Prevent Colorectal Cancer Among Medicare Beneficiaries Aged 70 to 79 Years: A Prospective Observational Study

Xabier García-Albéniz, MD, PhD; John Hsu, MD, MBA, MSCE; Michael Bretthauer, MD, PhD; Miguel A. Hernán, MD, DrPH Article, Author, and Disclosure Information

70-74 vs 75-79:

8 year risk CRC 2.19 vs 2.84 30 day AE: 5.6 vs 10.3

- <40 no screening (only if genetic high risk)</p>
- •40-49 only if FDR over age 60 has CRC or HRA
- •50-74 if no personal/family history, YES, FIT group!
- 75-84 carefully weight quality of life, comorbidities and life expectancy. Individualize screening and work with local endoscopists
- •<85 screening not recommended. In rare exceptions, consider referral to endoscopist</p>

Why Not in Shorter Interval

- Additional pickup is small
 - In FOBT studies, < 1%
- Increase exposure to endoscopy risk
- Longer wait times
- Cost to system and patients

Why Not as a Diagnostic?

- Does not change management
- Delay of care

Narula et al., Can J Gastro 2014 28:421 Van Rijn et al., Eur J GastroHep 2012 24:1266



Referrals to Medical Oncology FIT + and CRC Delays

- November 2015 to April 2016
- Patients who had FIT+
- Northern Alberta

- •5 Medical Oncologists new CRC referrals
- ●N=61

FIT+, CRC and Wait Time

Symptoms	Yes	No	Unsure
N	36 (59%)	22 (36%)	3 (5%)
Wait Time to colonoscopy (mean)	158 days	214 days	310 days



FIT+, CRC Stage and Symptoms

Stage	1			IV	
N	3 (5%)	14 (23%)	29 (47.5%)	15 (24.5%)	
Wait Time (days)	196.6	215.7	182.8	161.7	
Had Symptoms	33%	50%	58.6	92.3%	



What's New?

Coming Soon...
FIT Positive Central Referral Centre - Including
Non-eligible for SCOPE

Coming Soon...

PICCS - Dashboard

Partnership to Integrate Colon Cancer Screening





SCREENING ACTION PLAN: SUMMARY REPORT

COLORECTAL CANCER (CRC) SCREENING INFORMATION AVAILABLE FOR YOUR PANEL

The Partnership to Integrate Colorectal Cancer Screening in the Calgary Zone (PICCS-CZ) project will support you in CRC screening. Your panel information is linked to CRC screening data to provide CRC screening status for each patient.

These results are intended for improvement and not judgement. Your clinical judgement may supersede clinical guidelines. We look forward to your feedback on the value of the information provided in this report.

What will you get?

- This summary report of colorectal cancer screening rates in your panel
- Actionable List of colorectal screening status for each patient aged 40 to 84 showing who is due for screening
- Resources to support quality improvement for colorectal cancer screening for your patients

Date of Panel Pull

Day Month Year

Screening Status as of: Day Month Year

Summary	50-74
	N
Due for Screening	n,%
Positive FIT with no record of colonoscopy	n,%
Due for surveillance	n,%
Guideline Adherent	What do we want to highlight?
Up to Date Rate	
Goal	

What does Screening Status mean?

- Due for Screening: Patients who have been screened but are overdue for their next screen according to routine screening
 intervals or patients for whom there is no record of testing. This can include patients who have never initiated screening
 and patients for whom there is no up-to-date information due to:
 - delays in receiving information about tests
 - patient tested in another province
 - patient not considered eligible for screening based on their PHN (mismatches and discrepancies)
- Positive FIT with no record of colonoscopy: Patients with a positive FIT/FOBT result but has no record of a follow up colonoscopy
- Due for Surveillance: Overdue for their next test based on surveillance intervals for patients with polyps detected at
- Up-to-Date: Most recent test within recommended interval

Actionable Lists (Excel spreadsheet)

DRAFT

Sample Actionable List fields provided to each physician about patients in their panel

Date linked to data sources: 14 July 2016

Colorectal Cancer Screening (FIT/FOBT)

								Recommended				
					Date of last	Results of last	Date of last	surveillance	Next test	Date next test		
PHN	Last Name	First Name	Gender	Age	FIT/FOBT	FIT/FOBT	colonoscopy	interval	recommended	recommended	Screening Status	Qualifier
												FIT every 1-2 years recommended for
3456789	Smith	John	Male	63	28-Jan-2015	Negative	None	None	FIT	28-Jan-17	Up to date	average risk with no prior colonoscopy.
												FIT every 1-2 years recommended for
4567890	Doe	Jane	Female	59	3-Jul-2014	Negative	None	None	FIT	3-Jul-16	Due for screening	average risk with no prior colonoscopy.
												FIT every 1-2 years recommended for
												average risk with no prior colonoscopy. See
												CPG for recommendations for patients with
1234569	Lee	Josephine	Female	64	None	None	None	None	FIT	14-Jul-16	No record of FIT/FOBT	prior colonoscopy and/or polyps.
1234568	Johnson	Anna	Female	36	None	None	None	None	None	None	Outside Guideline	
1234567	Williams	Joe	Male	52	6-Feb-2015	Positive	None	None	Colonoscopy		In need of follow-up	Refer for colonoscopy.
												Normal colonoscopy, can return to FIT
8765432	Smith	Abbie	Female	60	21-Apr-2015	Positive	31-May-15	10 yrs	FIT	31-May-25	Follow-up Completed	screening after 10 years
												Post polypectomy surveillance guidelines
2345678	Miller	James	Male	58	None	None	3-Jul-15	3 yrs	Colonoscopy	3-Jul-18	Surveillance	suggest repeat colonoscopy within 3 years.

Summary

- CRC is a major cause of cancer and cancer deaths but screening rates are not at target
- FIT is the preferred strategy for asymptomatic CRC screening
- FIT has made an impact in detecting advanced polyps and cancers
- The most common mis use of FIT is in wrong age, within an interval and as a diagnostic tool

Average risk: Age 50-74

No personal or family history of polyps or colorectal cancer (crc)

ACRCSP advises your patient is screened with FIT every 1-2 years

If FIT positive refer for colonoscopy

Please wait 10 years after a normal colonoscopy (i.e., no polyps), or follow surveillance recommendation by endoscopist, to screen with FIT

If your patient has been screened prior to this recommended interval and is now FIT positive please refer the patient to the endoscopist who performed the previous colonoscopy for consultation

If the quality of the colonoscopy was uncertain, screen with FIT 5 years after colonoscopy

Screening is not recommended for patients aged 75 and older

Increased risk

Family History: cRC and/or high risk adenomas

High risk colonic adenoma is defined as having one or more of the following: size greater or equal to 1 cm; villous elements; high grade dysplasia; more than three adenomas found at one colonoscopy

1st degree relative >60 years at diagnosis

ACRCSP advises your patient is screened with FIT every 1-2 years starting at age 40

If FIT positive refer for colonoscopy 1st degree relative ≤60 years at diagnosis or two or more affected relatives

ACRCSP advises your patient is referred for a colonoscopy at age 40, or 10 years prior to the index case, whichever is earliest



As a diagnostic test for CRC in symptomatic patients (e.g., reported bloody stools or recent change in bowel habit)

As a diagnostic test to investigate patients' reporting gastrointestinal symptoms at any age (e.g., abdominal pain)

To determine or exclude a cause for anemia and/or rectal bleeding

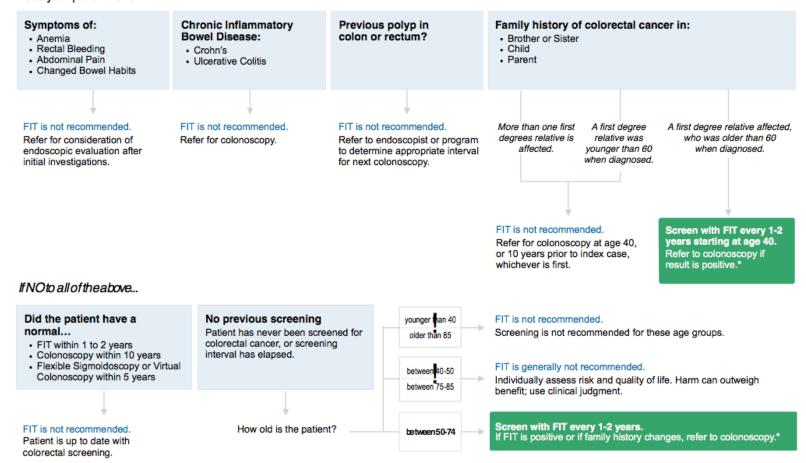
As a CRC screening test when the patient has inflammatory bowel disease, acute gastroenteritis or C. difficile colitis, actively bleeding hemorrhoids or anal fissure or similar acute gastrointestinal condition Using FIT for non-CRC screening purposes can lead to delays in proper diagnostic workup.

Recommend

the patient is referred for gastroenterology consultation

Does my Patient Need a Fecal Immunochemical Test (FIT)?

Does your patient have...



*If the colonoscopy is not 'adequate quality', it may be repeated at a shorter interval (endoscopist to decide).

For additional information and details visit: screeningforlifeca or topalbertadoctors.org



