

ADDs 2014: Plenary 2

# FIT Update

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Provincial Medical Lead, Alberta Colorectal Cancer Screening Program

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Saturday, June 7, 2014  
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## Objectives

- After this session, the attendee will have increased knowledge regarding fecal immunochemical testing (FIT) in regards to:
- Evidence for CRC and AA detection
- Test characteristics and effectiveness
- FIT results in Alberta since implementation

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## FIT Overview

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## Why FIT?

- Long GI referral wait times
- Improved sensitivity over FOBT
- Population strategy
- ?Trust by family physicians/patients

Figure 1: Individuals aged 50 to 74 reporting FOBT in past two years and/or sigmoidoscopy/colonoscopy in past five years for any reason, by province/territory.

Province/Territory	Percent (%)
QC	27
YK	30
NS	32
NB	32
NWT	33
PEI	34
ND	35
NL	36
AB	37
BC	38
SK	40
Canada	50
ON	55
MB	55
NU	4

\*suppressed due to small cell size  
Data source: CCHS 2008

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## ACRCSP FIT Launch Nov 18, 2013

EDMONTON JOURNAL

Alberta hopes to save lives with new colorectal cancer screening kit

FIT test helps to detect colorectal cancer sooner

January 13, 2014

Colorectal cancer is the second leading cause of cancer deaths in Alberta. The new faecal immunochemical test (FIT) is a home stool test with no dietary restrictions. It is the primary screening test for average-risk individuals between the ages of 50 to 74. FIT is the most sensitive test available in the province.

FIT is available in two provinces, screening-related colorectal services across Alberta? says Dr. Chandra Singh, medical head of colorectal cancer at the University of Alberta. FIT is available in two provinces, screening-related colorectal services across Alberta? says Dr. Chandra Singh, medical head of colorectal cancer at the University of Alberta. FIT is available in two provinces, screening-related colorectal services across Alberta? says Dr. Chandra Singh, medical head of colorectal cancer at the University of Alberta.

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## Fecal immunochemical test (FIT)

- Immunochemical based test for globin in the stool
- FIT for Alberta:
  - Polymedco OC FIT-CHEK

Hemoglobin Molecule

Polymedco OC FIT-CHEK

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## FIT Advantages

- No dietary change
  - FIT only detects human globin
  - No peroxidase reaction
- More specific for lower GI bleeding
- Single collection from one sample annually
- Easier to use
  - Better completion rate in studies
- Quantifiable

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## FIT Indications in Alberta

- Average Risk 50-74
- Moderate Risk 40-49 (FDR >60)
- 75-84 - carefully weight quality of life, commodities and life expectancy. Individualize screening and work with local endoscopists



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## When NOT to use FIT

- Symptomatic patients
- Acute care settings
- Interval FIT
- Out of age range patients
- If quality of life is poor or life expectancy is less than 10 yrs



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# FIT Evidence

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## FIT Accuracy

Annals of Internal Medicine REVIEW

### Accuracy of Fecal Immunochemical Tests for Colorectal Cancer

Systematic Review and Meta-analysis

Jeffrey A. Lee, MD, MSc; Elizabeth C. Lee, MD, MCR; Stephen Best, MD; Theodore R. Levin, MD; 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 meta-analyzed. The pooled sensitivity, specificity, positive likelihood ratio, and negative likelihood ratio of FITs for CRC were 0.79 (95% CI, 0.69 to 0.88), 0.94 (CI, 0.92 to 0.95), 13.10 (CI, 10.49 to 16.30), 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 µg/g vs 0.79 [CI, 0.59 to 0.81] at cutoff values of 20 to 50 µg/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 Sources:** National Institute of Diabetes and Digestive and Kidney Diseases and National Cancer Institute.

Ann Intern Med 2014;160:173-181.  
For author affiliations, see end of text.

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## Lee et al., AIM 2014

- 1383 records screened
- 19 studies/data sets included in meta-analysis

Figure 2. Pooled sensitivity and specificity for fecal immunochemical tests for the detection of colorectal cancer for all included studies.

Author, Year, Reference	Sensitivity (95% CI)	Specificity (95% CI)
Lee et al. 2014 (14)	0.79 (0.69-0.88)	0.94 (0.92-0.95)
Lee et al. 2013 (15)	0.80 (0.69-0.88)	0.94 (0.92-0.95)
Allen et al. 1998 (16)	0.80 (0.69-0.88)	0.94 (0.92-0.95)
Johnson et al. 2007 (17)	0.80 (0.69-0.88)	0.94 (0.92-0.95)
Lee et al. 2007 (18)	0.80 (0.69-0.88)	0.94 (0.92-0.95)
Cheng et al. 2002 (19)	0.80 (0.69-0.88)	0.94 (0.92-0.95)
Anderson et al. 2005 (20)	0.80 (0.69-0.88)	0.94 (0.92-0.95)
Nakamura et al. 1999 (21)	0.80 (0.69-0.88)	0.94 (0.92-0.95)
Hsieh et al. 1998 (22)	0.80 (0.69-0.88)	0.94 (0.92-0.95)
Looney et al. 2005 (23)	0.80 (0.69-0.88)	0.94 (0.92-0.95)
Lee et al. 2006 (24)	0.80 (0.69-0.88)	0.94 (0.92-0.95)
Hsieh et al. 2008 (25)	0.80 (0.69-0.88)	0.94 (0.92-0.95)
Patel et al. 2011 (26)	0.79 (0.69-0.88)	0.94 (0.92-0.95)
de Witte et al. 2013 (27)	0.79 (0.69-0.88)	0.94 (0.92-0.95)
Park-Wilson et al. 2010 (28)	0.79 (0.69-0.88)	0.94 (0.92-0.95)
Cheng et al. 2012 (29)	0.79 (0.69-0.88)	0.94 (0.92-0.95)
Cheng et al. 2011 (30)	0.79 (0.69-0.88)	0.94 (0.92-0.95)
Brayton et al. 2011 (31)	0.79 (0.69-0.88)	0.94 (0.92-0.95)
Brayton et al. 2012 (32)	0.79 (0.69-0.88)	0.94 (0.92-0.95)
Overall	0.79 (0.69-0.88)	0.94 (0.92-0.95)

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## Bottom Line

Lee et al, AIM 2014

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

- Overall, a moderately sensitive and highly specific test for CRC

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## FIT Cutoffs & Findings

British Journal of Cancer (2009) 101, 1211-1216  
© 2009 Cancer Research UK. doi:10.1038/sj.bjc.6605326 www.bjpcancer.com

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

**LGH van Rossum<sup>1,2</sup>, AF van Rijn<sup>1</sup>, RJP Lahai<sup>1</sup>, MGH van Oijen<sup>1</sup>, P Fockens<sup>3,4</sup>, Jansen<sup>5</sup>, ALM Verbeek<sup>6</sup> and E Dekker<sup>1</sup>**

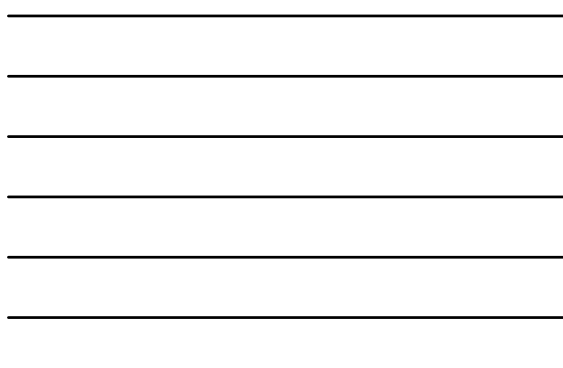
<sup>1</sup>Department of Gastroenterology and Hepatology, Radboud University Nijmegen Medical Centre, PO Box 9101, 6500 HB, Nijmegen, The Netherlands; <sup>2</sup>Department of Gastroenterology and Hepatology, Academic Medical Centre, University of Amsterdam, Amsterdam, The Netherlands; <sup>3</sup>Department of Endoscopy and Biotechnology and <sup>4</sup>IRCA, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands

**Abstract** The cutoff of semi-quantitative immunochemical faecal 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 (n=103). Dutch screening participants 50-75 years of age, with average CRC risk and an iFOBT value ≥20 ng ml<sup>-1</sup> were offered colonoscopy. The detection rate was the percentage of participants with CRC or advanced adenomas (≥a Cohen, ≥20% adenoma, high-grade dysplasia). The number needed to scope (NNT<sub>scope</sub>) was the number of colonoscopies to be carried out to find one patient with CRC or advanced adenomas. iFOBT values ≥20 ng ml<sup>-1</sup> were detected in 326 of 617 participants (53%) and 428 (69%) underwent colonoscopy. The detection rate for advanced lesions (CRC and  $\geq$  a Cohen) was 3.3% (95% confidence interval 2.6-3.9%) and the NNT<sub>scope</sub> was 2.3. At 75 ng ml<sup>-1</sup> the detection rate was 2.7% (the NNT<sub>scope</sub> was 3.6) and the CRC was not compared with 20 ng ml<sup>-1</sup> was 4.3% (95% CI 3.6-5.0%) (the detection rate was 3.2% and the NNT<sub>scope</sub> was 4.5). Compared with 20 ng ml<sup>-1</sup> up to 200 ng ml<sup>-1</sup> CRC was not detected at 18% (N=6). Conclusions: Cutoffs below the standard (20 ng ml<sup>-1</sup>) resulted in not only higher detection rates of advanced lesions but also more colonoscopies. With sufficient cascade, 75 ng ml<sup>-1</sup> might be advised. If not, up to 200 ng ml<sup>-1</sup> CRC miss rates are acceptable. *British Journal of Cancer* (2009) 101, 1211-1216. doi:10.1038/sj.bjc.6605326 www.bjpcancer.com © 2009 Cancer Research UK

**Keywords:** colorectal cancer; faecal occult blood test; screening; colonoscopy; adenoma

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## Van Rossum, BJC 2009

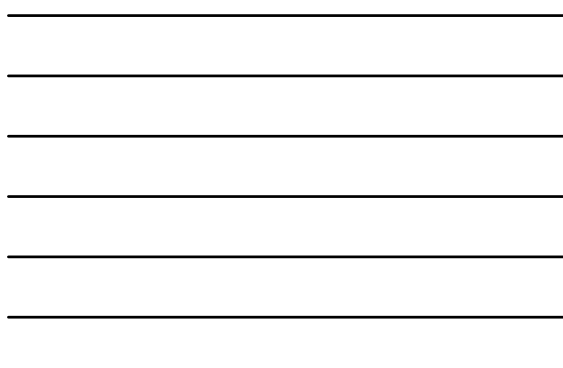
**Table 3** The performance characteristics of the iFOBT, OC Sensor, at different cutoff levels

	Cutoff values (ng ml <sup>-1</sup> )									
	50	75	100	125	150	175	200	225	250	275
Positive adherent to colonoscopy (%)	428	336	280	248	234	215	198	187		
Colonoscopy rate (%)	70%	53%	45%	40%	38%	33%	32%	30%		
Number of lesions (n)										
Colorectal cancer	28	27	24	24	24	24	24	23		
CRC advanced adenoma	189	163	145	136	131	121	113	109		
Detection rate (%)										
Colorectal cancer	0.45%	0.44%	0.39%	0.39%	0.39%	0.39%	0.39%	0.37%		
CRC advanced adenoma	3.1%	2.6%	2.4%	2.2%	2.1%	2.0%	1.8%	1.8%		
Confidence interval (95% CI)	2.6-3.5%	2.3-3.1%	2-2.7%	1.8-2.6%	1.8-2.3%	1.6-2.3%	1.5-2.2%	1.4-2.1%		
Number needed to scope (NNT <sub>scope</sub> ) (%)										
Colorectal cancer	15.3	12.4	11.7	10.3	9.8	9.0	8.3	8.1		
CRC advanced adenoma	11.3-21.8	9.1-19.5	8.4-18.9	7.5-16.7	7.1-15.7	6.5-14.4	6-13.2	5.9-13.2		
Confidence interval (95% CI)	2.1	2.1	1.9	1.8	1.8	1.8	1.8	1.7		
Confidence interval (95% CI)	2.6-2.5	1.9-2.3	1.7-2.2	1.6-2.1	1.6-2	1.6-2	1.6-2	1.5-2		
Specificity (%)										
CRC advanced adenoma	96.0%	97.3%	97.8%	98.1	98.3	98.4	98.6	98.7		
Confidence interval (95% CI)	95.3-96.3%	96.3-97.3%	96.7-98.1%	97.0-98.3%	96.9-98.6%	96.1-98.8%	96.3-99.0%	96.4-99.0%		
OC miss rate (%)	N/A	3.0%	4.3%	4.3%	4.3%	4.3%	4.3%	4.3%		
Confidence interval (95% CI)	N/A	3.3-3.0%	4.3-2.7%	4.3-2.7%	4.3-2.7%	4.3-2.7%	4.3-2.7%	4.3-2.7%		

**Abbreviations:** CI, confidence interval; CRC, colorectal cancer; iFOBT, immunochemical faecal occult blood test. Patients adherent to colonoscopy = patients with a positive iFOBT who underwent a colonoscopy. Colonoscopy rate = percentage of participants with a positive iFOBT who underwent a colonoscopy. Detection rate = percentage of participants with lesions of reference. Number needed to scope = the number of patients to find one extra patient with lesions of reference. Specificity was calculated under the test disease assumption (Smet and Breen, 1997). CRC miss rate = the percentage of colorectal cancer patients at that cutoff who were not colonoscoped.

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## Bottom Line van Rossum BJC 2009

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

FIT +

1 in 13 CRC

FIT +

1 in 2 AA or  
CRC

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## FIT vs Colonoscopy Strategy

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 Cubellá, M.D., Ph.D., Dolores Salas, M.D., Ángel 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 Gid, R.N., Raquel Zubizarreta, M.D., Teresa Sala, M.D., Marta Porco, M.D., Mercedes Andrés, M.D., Gloria Teruel, M.D., Antonio Peris, M.D., María Pilar Roxcales, R.N., Mónica Polo-Tomé, M.D., Ph.D., Xavier Bessa, M.D., Ph.D., Olga Ferrer-Amtergou, R.N., Jaume Grau, M.D., Anna Serradeianform, R.N., Alkio Oro, M.D., José Cruzado, M.D., Francisco Pérez-Riquelme, M.D., Inmaculada Alonso-Abrue, M.D., Mariola de la Vega-Prieto, M.D., Juana María Reyes-Melán, M.D., Guillermo Cacho, M.D., José Díaz-Tasende, M.D., Alberto Herreros-de-Tejada, M.D., Carmen Poves, M.D., Cecilia Santander, M.D., and Andrés González-Navarro, M.D., for the COLONPREV Study Investigators\*

57,404 subjects randomly assigned to COL or FIT

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## Quintero et al., NEJM 2012

Table 1. Diagnostic Yield of Colonoscopy and Fecal Immunochemical Testing (FIT), According to the Intention-to-Screen Analysis.\*

Colorectal Lesion	Colonoscopy (N=26,705)		FIT (N=26,599)		Odds Ratio (95% CI)†	P Value
	Subjects	Rate	Subjects	Rate		
	no.	%	no.	%		
Cancer	30	0.1	33	0.1	0.99 (0.61-1.64)	0.99
Advanced adenoma‡	514	1.9	231	0.9	2.30 (1.97-2.69)	<0.001
Advanced neoplasia§	544	2.0	264	1.0	2.14 (1.85-2.49)	<0.001
Nonadvanced adenoma	1109	4.2	119	0.4	9.80 (8.10-11.85)	<0.001
Any neoplasia	1653	6.2	383	1.4	4.67 (4.17-5.24)	<0.001

\* The diagnostic yield was calculated as the number of subjects with true positive results divided by the number of subjects who were eligible to undergo testing. Subjects were classified according to the most advanced lesion.  
 † Odds ratios were adjusted for age, sex, and participating center. CI denotes confidence interval.  
 ‡ Advanced adenoma was defined as an adenoma measuring 10 mm or more in diameter, with villous architecture (>25%), high grade dysplasia, or intramucosal carcinoma.  
 § Advanced neoplasia was defined as advanced adenoma or cancer.

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### Quintero et al

	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

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### Bottom Line Quintero NEJM 2012

- Using a FIT population strategy:
- Increased overall participation
- Detected the same number of CRC
- Reduced the number of colonoscopies need to detect 1 CRC

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- **Factors Influencing Fecal Immunochemical Test Positivity Rate: Demographic, Pathological, Behavioral and Environmental Effects**  
Erin L. Symond, Graeme P. Young et al.
- **The Comparative Cost-Effectiveness of Faecal Immunochemical Tests vs. Screening Colonoscopy in the Detection of Neoplastic Lesions**  
Martin C. Wong, Joseph J. Y. Sung et al.

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DDW2014  
Digestive Disease Week

### Effect of temperature on FIT

Max temperature	OR	95% CI
17-25 °C	0.95	0.83-1.10
26-34 °C	0.81	0.68-0.95
>34 °C	0.69	0.53-0.91

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### Cost Effectiveness of FIT

	Annual FIT (5,863)		Colonoscopy (4,869)	
	N	Cost per finding (US\$)	N	Cost per finding (US\$)
Findings	Projection 1,004,618		Projection 834,298	
Adenoma	15,935	16,085	197,466	4,719
Adv Neoplasia	9,596	26,712	32,227	28,913
CRC	1,713	149,590	2,400	388,268

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DDW2014  
Digestive Disease Week

- **Impact on Colorectal Cancer Mortality of Screening Programmes Based on Immunochemical Fecal Occult Blood Test in the Veneto Region (Italy)**
- Zorzi et al
- Aim: Impact of FIT screening on CRC mortality
- Methods
  - Comparison of Early Screening Area (ESA) 2002-2004 vs Late Screening Area (LSA) 2008-2009
  - Analysis of CRC mortality in 50-74

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DDW2014  
Digestive Disease Week

### Zorzi et al

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# FIT in Alberta

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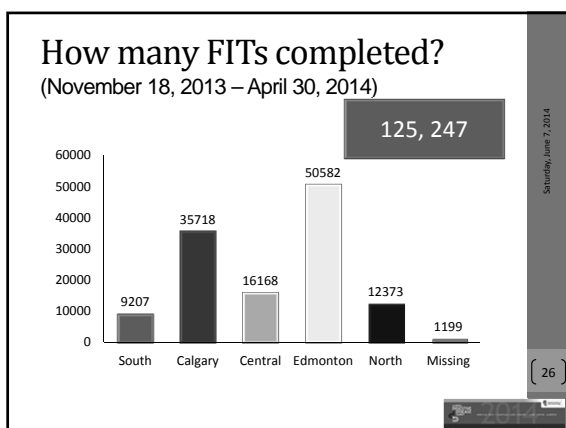
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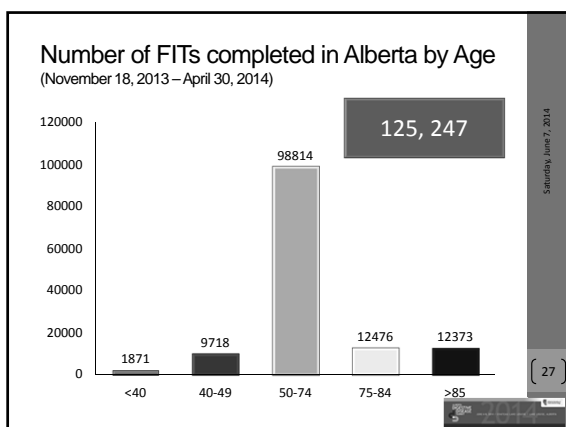
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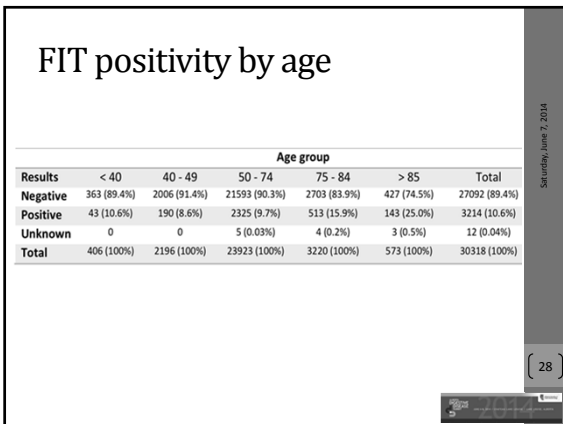
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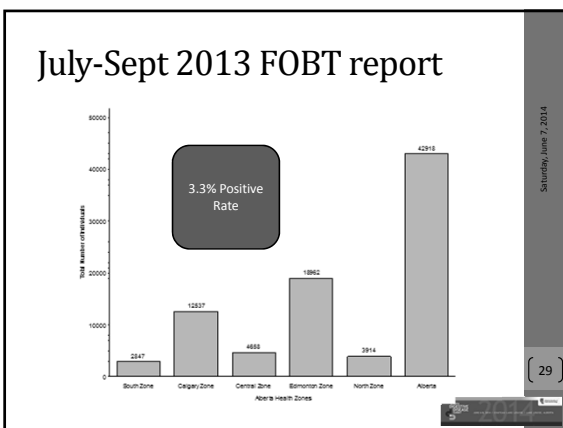
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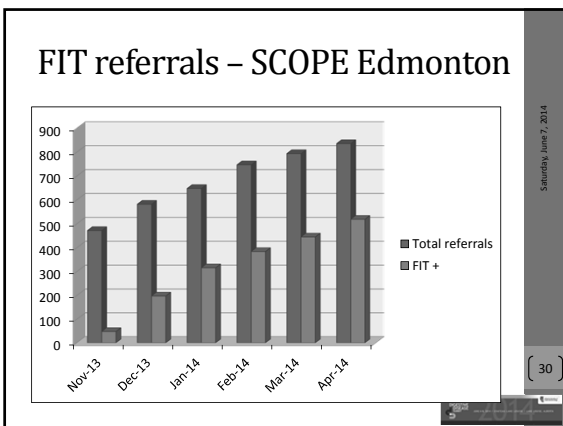
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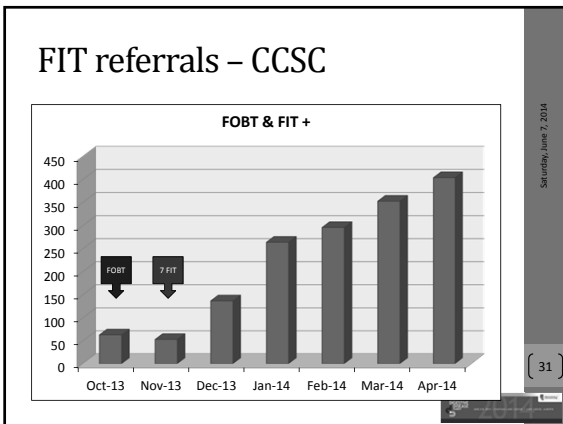
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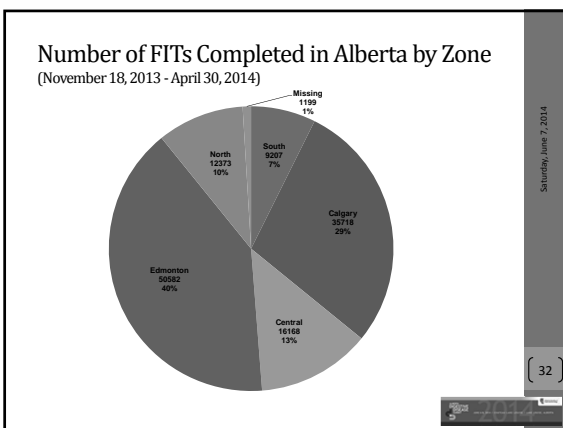
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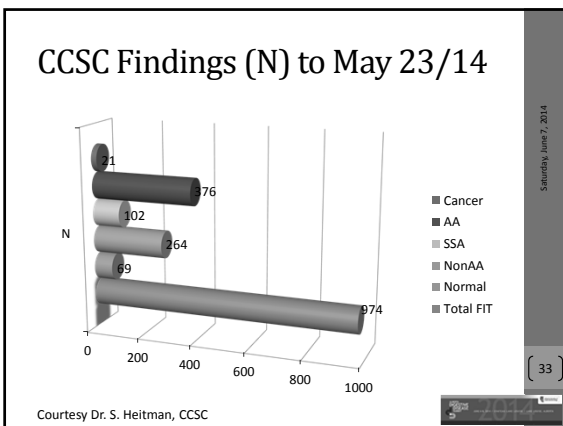
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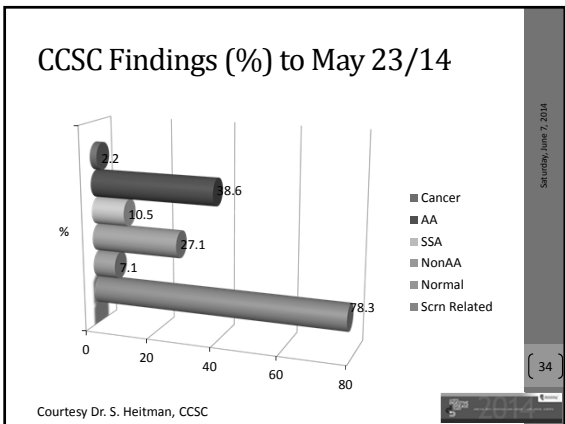
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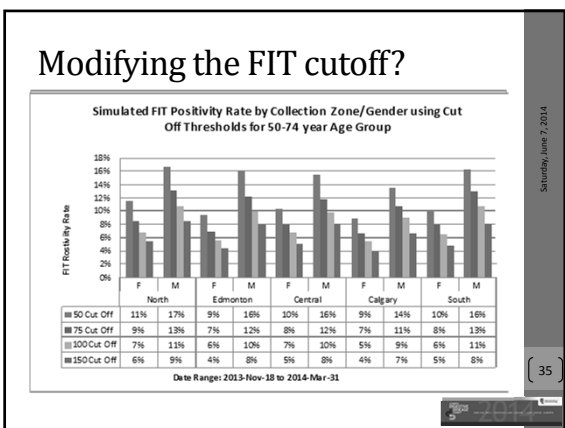
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### Summary

- FIT is an immunochemical test with moderate sensitivity and high specificity for CRC
- It has higher acceptance among patients
- FIT detects advanced adenomas
- FIT reduces the number needed to scope to find CRC
- In Alberta, FIT has been implemented since November 2013
  - Initial results show high acceptance
  - Positive rate ~10%
  - High number of significant findings

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