
2021 SCSG
GI SYMPOSIUM

Best of DDW Colorectal Cancer Abstracts: Screening & Surveillance

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Financial Disclosures

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- National Institutes of Health/National Cancer Institute

Consultant

- Colorectal Cancer Alliance

Objectives

- Review colorectal cancer (CRC) screening tests and current recommendations on test use
- Discuss DDW abstracts on non-invasive CRC screening test use
- Review the 2020 USMSTF polypectomy surveillance guidelines
- Discuss emerging topics on surveillance from DDW

Colorectal cancer is preventable but…

2nd leading cause of cancer deaths in the U.S.

150,000 diagnoses in 2021

53,000 deaths in 2021

35% adults 50-75 years never screened

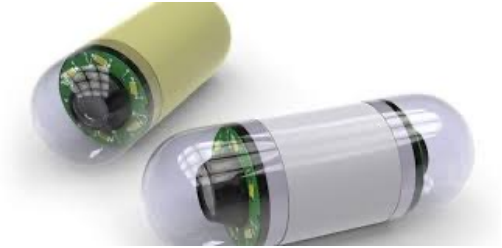
Siegel RL, Miller KD, Fuchs HE, Jemel A. Cancer Statistics, 2021. CA Cancer J Clin.

Overview of colorectal cancer screening tests

gFOBT

Fecal Immunochemical Test (FIT)

Mt-sDNA



Capsule Endoscopy

CT Colonography

Colonoscopy
Flexible Sigmoidoscopy

What is the best colorectal cancer screening test?

U.S. Multi-Society Task Force

Tier 1

- Colonoscopy every 10 years
- Annual Fecal Immunochemical Test (FIT)

Tier 2

- CT Colonography every 5 years
- FIT-DNA every 3 years
- Flexible Sigmoidoscopy every 5-10 years

Tier 3

- Capsule endoscopy every 5 years

Not Recommended

- Septin9

What is the best colorectal cancer screening test?

U.S. Preventive Services Task Force

"The risks and benefits of different screening tests vary. Because of limited evidence, the USPSTF recommendation does not include serum tests, urine tests or capsule endoscopy for colorectal cancer screening."

What is the best colorectal cancer screening test?

U.S. Preventive Services Task Force

- HSgFOBT or FIT – every 1 year
- Stool DNA-FIT – every 1 to 3 years
- CT colonography – every 5 years
- Flex Sig – every 5 years
- Flex Sig – every 5 years + annual FIT
- Colonoscopy – every 10 years

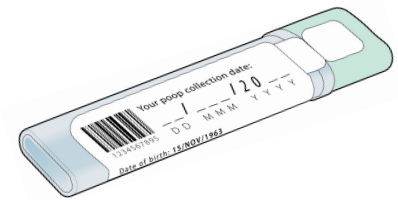
Fecal immunochemical test (FIT)

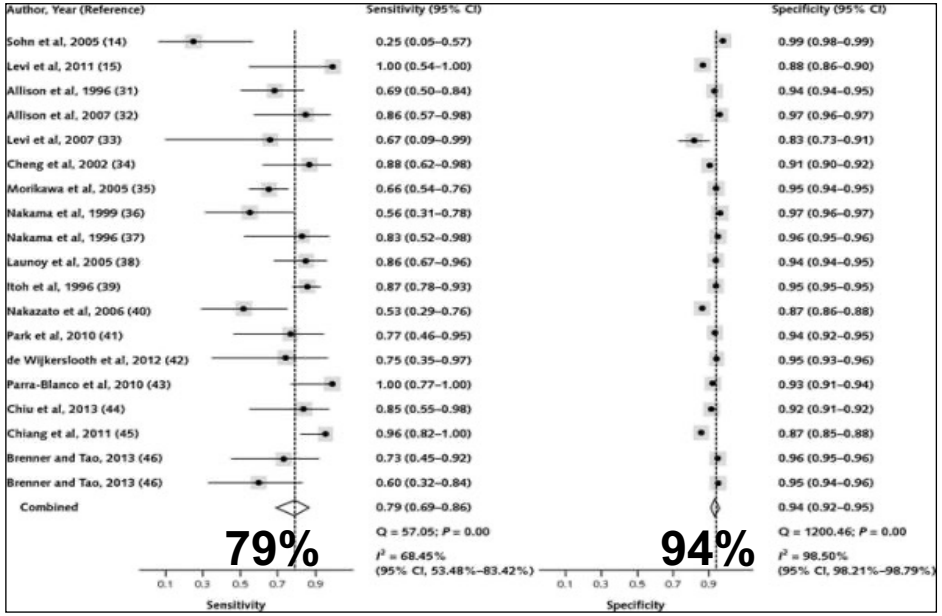
STOOL-BASED TESTS

FOBT

FIT

FIT-DNA





**20µg/g stool

Compared to colonoscopy:

- FIT correctly detected **79%** of colorectal cancer cases
- FIT was normal **94%** of the time when cancer was not present

Impact of the COVID-19 Pandemic on a Large Organized Colorectal Cancer Screening Program Based on Fecal Immunochemical Testing and Opportunistic Colonoscopy

Theodore R. Levin, Christopher D. Jensen, Amy R. Marks, Wei K. Zhao, Kevin T. Kao, Dan Li, Jeffrey K. Lee, Joanne E. Schottinger, Nirupa R. Ghai, Richard Contreras, Yi-Fen Chen, Smita Rouillard, Jessica Badalov, Evan Layefsky, Cheryl M. Carlson, Ngoc J. Ho, Douglas A. Corley.

Kaiser Permanente Research

BACKGROUND AND AIMS:

- Kaiser Permanente Northern California (KPNC) has a well-established organized colorectal cancer (CRC) screening program based on annual mailed fecal immunochemical test (FIT) outreach and opportunistic colonoscopy.
- Public health guidance related to the COVID-19 pandemic led to a pause in KPNC mailed FIT outreach and elective colonoscopies starting in March 2020.
- This study evaluated the impact of the pandemic on 2020 CRC screening measures compared to the two prior years (2018 and 2019).

METHODS:

- For 2018, 2019, and 2020, we evaluated the following screening measures:
  - Screening eligible population based on 51-75 years of age, enrolled in current and previous year, and no history of total colectomy
  - Up-to-date with screening due to colonoscopy within past 9 years or sigmoidoscopy within past 4 years
  - Remainder of population eligible for screening as of January 1 for each measurement year
  - FIT kit distributed
  - Completed a FIT
  - Completed a follow-up colonoscopy after a positive FIT
  - Completed a colonoscopy unrelated to a positive FIT
  - Up to date with screening by year end

RESULTS:

Table 1. CRC Screening Measures by Year

	2018 n	(%)	2019 n	(%)	2020 n	(%)
Screening eligible population	1,092,464		1,130,055		1,158,923	
Up-to-date with screening due to prior endoscopy	337,952	(30.9)	347,892	(30.8)	357,919	(30.9)
Remainder of population eligible for screening	754,512	(69.1)	782,163	(69.2)	801,004	(69.1)
Colonoscopy or flex sig instead of FIT	18,114	(2.4)	20,105	(2.6)	14,541	(1.8)
FIT kit distributed	637,082	(84.4)	692,804	(88.6)	712,578	(89.0)
FIT completed by end of year	503,824	(79.1)	515,952	(74.5)	459,372	(64.5)
FIT positive	17,750	(3.5)	17,880	(3.5)	15,575	(3.4)
FIT+ colonoscopy by end of year	13,604	(76.6)	13,604	(76.1)	10,484	(67.3)
FIT+ colonoscopy by end of following March	14,630	(82.4)	14,645	(81.9)	12,388	(79.5)
Total up-to-date with screening by end of year	859,890	(78.7)	883,949	(78.2)	831,832	(71.8)

Figure 1. Eligible Members Mailed a FIT Kit, by Month

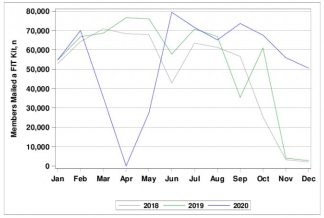


Figure 2. FITs Completed, by Month

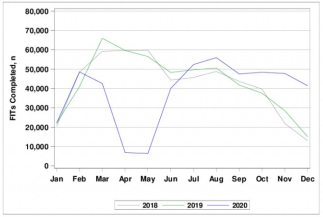


Figure 3. Colonoscopy After a Positive FIT, by Month

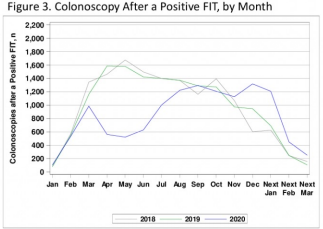


Figure 4. Colonoscopies, All Indications, by Month

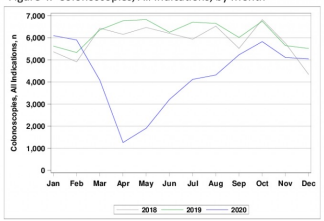


Figure 5. CRC Screening Eligible Population, by Age (Years)

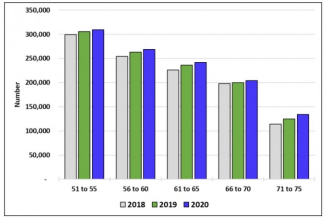


Figure 6. CRC Screening Up-to-Date by Year End, by Age (Years)

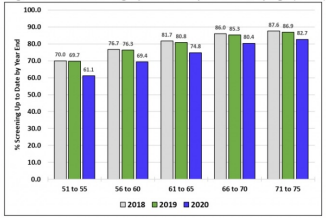


Figure 7. CRC Screening Eligible Population, by Race/Ethnicity

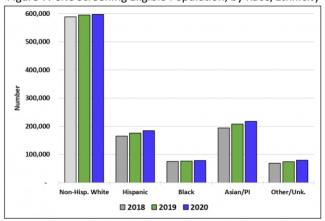
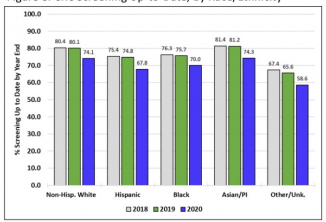


Figure 8. CRC Screening Up-to-Date, by Race/Ethnicity



CONCLUSIONS:

- The COVID-19 pandemic in 2020 resulted in temporary delays in the mailing and return of FITs, colonoscopy follow-up after a positive FIT, and colonoscopies for all indications compared to prior years.
- The KPNC organized CRC screening program allowed for the rapid resumption of mailed FIT and colonoscopy starting in April/May 2020.
- FIT completions lagged resumption of FIT kit distributions, likely in part due to patient reluctance to complete screening during the pandemic; completions were ~10% lower in 2020 compared to prior years.
- The completion of FIT-positive colonoscopies was ~9% lower at year end 2020 compared to prior years but was nearly caught up by March 2021.
- Overall, the COVID-19 pandemic in 2020 resulted in a ~6% decrease in screening-up-to-date status by the end of 2020 compared to prior years. The impact of the pandemic on screening delays was similar across age and racial/ethnic groups.
- Our next step is to assess the impact of screening delays on CRC outcomes.

Multi target stool-DNA

STOOL-BASED TESTS

FOBT
FIT
FIT-DNA

	FIT*	FIT-DNA
Sensitivity	79%	92%
Specificity	94%	87%
Test Interval	1-year	3-years
Cost	$25	$595-$695

*cutoff at 20µg/g of stool

Multi target stool-DNA

	USPSTF 2021	ACG 2021	NCCN 2020	ACP 2019	ACS 2018	USMSTF 2017
Recommend for screening	Yes	Yes	Yes	No	Yes	Yes
Starting age	45	45	50	--	45	50 (45)
Testing interval	1 to 3 years	3 years	3 years	--	3 years	3 years
Caveats/ comments		If unwilling to complete colonoscopy				Tier 2

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Mt-sDNA (MsD) ordering patterns and detection of adenomatous polyps and adenocarcinoma within a large, single-specialty gastroenterology practice

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1 Texas Digestive Diseases Consultants within the GI Alliance
Southlake, Texas, USA

PURPOSE / OBJECTIVES

Stool DNA sampling has been extensively ordered by primary care providers, with FDA approval for patients 45 years or older, at average risk for colorectal cancer. This study focuses on Mt-sDNA (MsD) tests ordered by providers in a large, single-specialty gastroenterology group, including indications, appropriateness of use, and adenoma and adenocarcinoma rates with both positive and negative CG results.

MATERIAL & METHODS

We identified charts of 1266 patients, cared for by Texas Digestive Disease Consultants (TDDC) providers, for whom MsD was ordered by their TDDC gastroenterologists between 2015 and 2019. Indications for ordering MsD were identified, and results of follow-up colonoscopies for positive MsD tests were reviewed to calculate rates of adenomatous polyps and adenocarcinomas. Colonoscopies performed within three years of patients with negative MsD testing were also reviewed. Rates of appropriate MsD use were calculated, based on FDA-approved screening indications. Reasons for non-screening MsD were also calculated.

RESULTS

MsD was appropriately ordered by TDDC providers in 811 (64.1%) patients, and not appropriately in 455 (35.9%) of patients. Of the latter cohort, 73% were ordered because of physician discretion, including patients not yet due for screening, with past histories of colorectal adenoma or adenocarcinoma, with family history of colorectal cancer, for symptoms including weight loss, hematochezia, abdominal pain, for heme-positive stools, for IBD surveillance, and in patients older than 85 years. 27% of the inappropriate cohort had MsD ordered because of patient insistence, with similar indications as the physician-discretion group (Figure 1). 917 patients completed MsD testing, of whom 194 (21.2%) had positive results, with 151 patients having follow-up colonoscopy. Of these, 77 (51.0%) were diagnosed with adenomatous polyps, 4 (2.64%) with adenocarcinoma, and 70 (46.4%) with no adenoma or adenocarcinoma. 723 (78.8%) of patients had negative MsD testing, with 21 having colonoscopies within three years thereafter. 7 (33.3%) were diagnosed with adenomas, but none with adenocarcinoma (Table 1).

While Mt-sDNA can identify patients at risk for colorectal neoplasia and carcinoma, gastroenterologists need to remain cognizant of its appropriate use.

RESULTS

Figure 1

a. Appropriate in 811 (64.1%)
b. Not appropriate in 455 (35.9%)
   i. 73% with CG ordered by physician discretion
      1. 141 pts (42.5%) not yet due for screening
      2. 60 pts (18.1%) with PMH of adenoma or colorectal cancer
      3. 22 pts (6.63%) with FMH of colorectal cancer
      4. 90 pts (27.1%) with symptoms – weight loss, hematochezia, abdominal pain
      5. 31 pts (9.34%) with heme-positive stools or anemia
      6. 2 pts (0.60%) with long-term IBD
      7. 5 pts (1.50%) above age 85
      8. 23 pts (6.93%) with multiple reasons
   ii. 123 patients, (27.0%) ordered from patient insistence
      1. 11 (8.94%) not yet due for screening
      2. 80 (65.0%) with PMH of adenoma or colorectal cancer
      3. 13 (10.6%) with FMH of colorectal cancer
      4. 1 (0.81%) for symptoms
      5. 22 (17.9%) with heme-positive stools or anemia
      6. 4 (3.25%) with PMH of long-term IBD
      7. 3 (2.44%) above age 85
      8. 2 (1.62%) repeat CG after positive CG test
      9. 2 (1.62%) with multiple reasons

Table 1

Mt-sDNA result	No adenoma or carcinoma identified	Adenoma(s) identified	Carcinoma identified
Positive	46.4%	51.0%	2.64%
Negative	66.7%	33.3%	0.00%

SUMMARY / CONCLUSION

Only about two thirds Mt-sDNA testing ordered by gastroenterologists, within a large, single-specialty practice, was appropriate per FDA screening guidelines. In patients with positive results, 51% had adenomatous polyps, and 2.6% had newly diagnosed adenocarcinomas. In those with negative results but undergoing colonoscopy within three years, one-third had adenomatous polyps, but none were diagnosed with cancer. These findings are consistent with prior Mt-sDNA studies but highlight the need for education regarding appropriateness of use by both primary-care providers and gastroenterologists.

Blood Test Increases Colorectal Cancer Screening Uptake in Individuals Who Have Declined Colonoscopy and Fecal Immunochemical Testing: A Randomized Controlled Trial

Peter S. Liang[1,2], Anika Zaman[1,2], Anne Kaminsky[1], YongYan Cui[2], Gabriel Castillo[2], Craig T. Tenner[1,2], Scott E. Sherman[1,2], Jason A. Dominitz[3,4]

[1]VA New York Harbor Health Care System [2]NYU Langone Health [3]University of Washington [4]VA Puget Sound Health Care System

BACKGROUND

In 2018, only 69% of Americans aged 50-75 years were up-to-date with colorectal cancer (CRC) screening

Blood tests may increase screening uptake by offering an alternative to 1st line screening tests (e.g., colonoscopy & fecal immunochemical testing (FIT))

The only FDA-approved blood test for CRC screening is indicated for patients who have declined 1st line screening tests

Objective: Assess effect of offering blood test on CRC screening uptake in individuals who've previously declined colonoscopy & FIT (NCT03598166)

METHODS

Design
RCT comparing outreach re-offering colonoscopy/FIT (control) vs additionally offering blood test as secondary option (intervention)

Inclusion criteria
-Patient at single VA medical center
-Age 50-75
-Average risk for CRC
-Eligible for screening
-Declined colonoscopy & FIT in prior 6 months per medical record

Figure 1. Study Flowchart

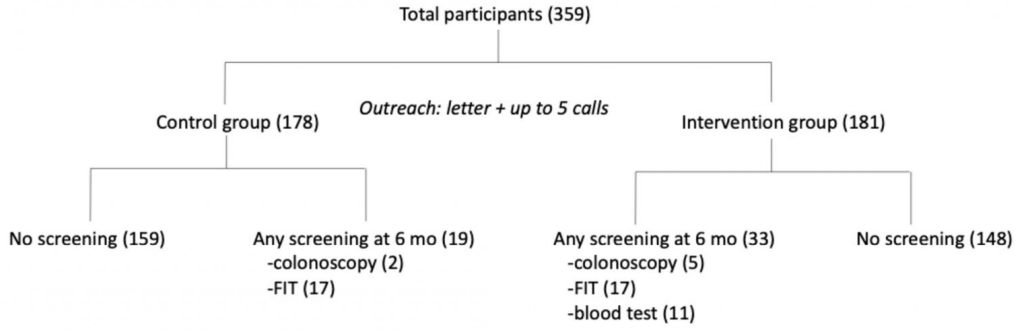
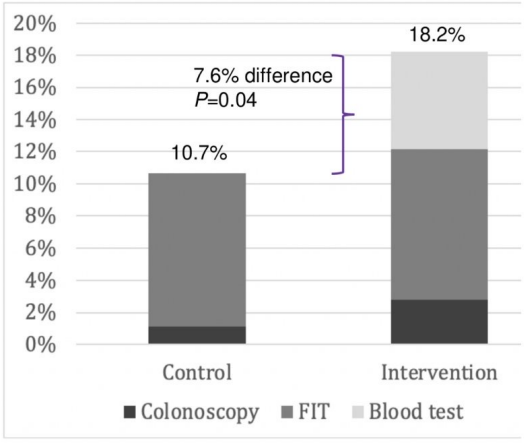


Table 1. Demographics

	Control (n=178)	Intervention (n=181)
Age Group		
50-59	38 (21.3%)	49 (27.1%)
60-69	78 (43.8%)	70 (38.7%)
70-75	62 (34.8%)	62 (34.3%)
Gender		
Male	171 (96.1%)	172 (95.0%)
Female	7 (3.9%)	9 (5.0%)
Race/Ethnicity		
Non-Hispanic White	68 (38.2%)	62 (34.3%)
Non-Hispanic Black	70 (39.3)	77 (42.5%)
Hispanic	26 (14.6%)	29 (16%)
Asian	3 (1.7%)	2 (1.1%)
Pacific Islander	1 (0.6%)	3 (1.7%)
Unknown	10 (5.6%)	8 (4.4%)

Figure 2. Screening at 6 months (primary outcome)



RESULTS

Individuals who **expressed interest in CRC screening**: 76/359 (21.3%)
19 (5.3%) for colonoscopy
33 (9.2%) for FIT
22 (12.2% of intervention group) for blood test

Test positivity rate
FIT: 8.8% vs blood test: 18.2%

Secondary outcome: Completed **full screening strategy** at 6 months (positive FIT/blood test followed by colonoscopy)
Intervention group: 15.5% vs. Control group: 10.1% (*P*=0.13)

Sensitivity analysis excluding participants whose 6 month follow up period overlapped with COVID-19 pandemic in NYC (n=318)
Intervention group: 19.9% vs. Control group: 9.6% (*P*=0.01)

CONCLUSIONS

Among individuals who've previously declined colonoscopy/FIT, offering blood test as secondary option increased screening by 8%

In those offered blood test, colonoscopy & FIT use did not decrease

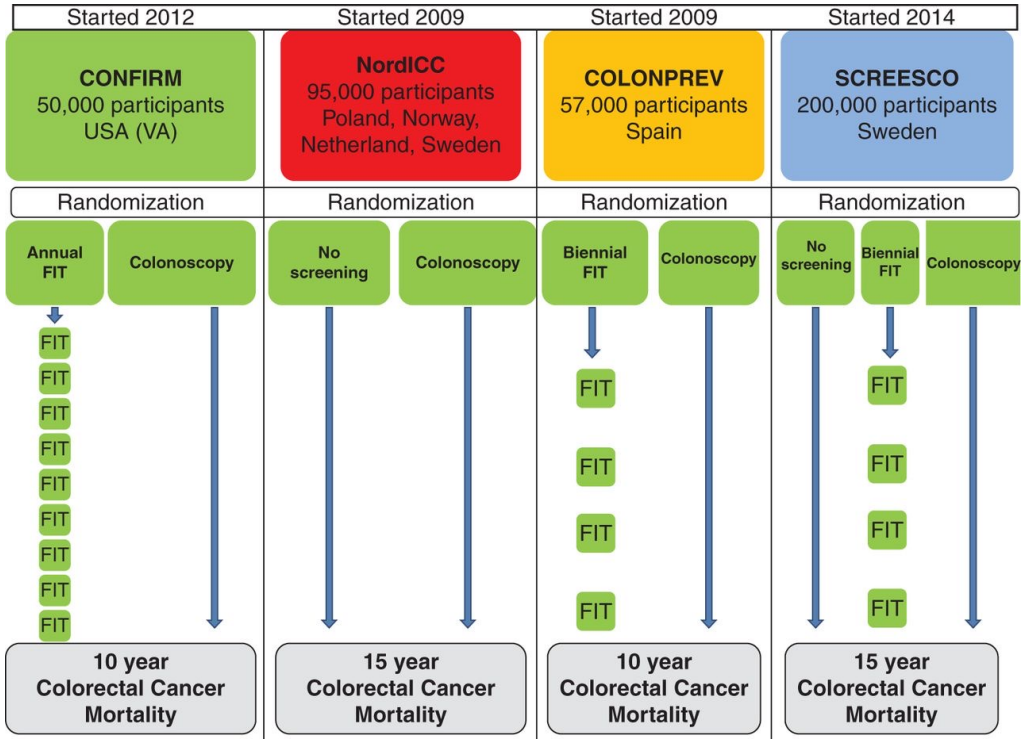
Funding: NYSGE/ASGE Florence Lefcourt Endoscopy Research Award, Epigenomics

Non-invasive screening tests require two steps

Abnormal screening result

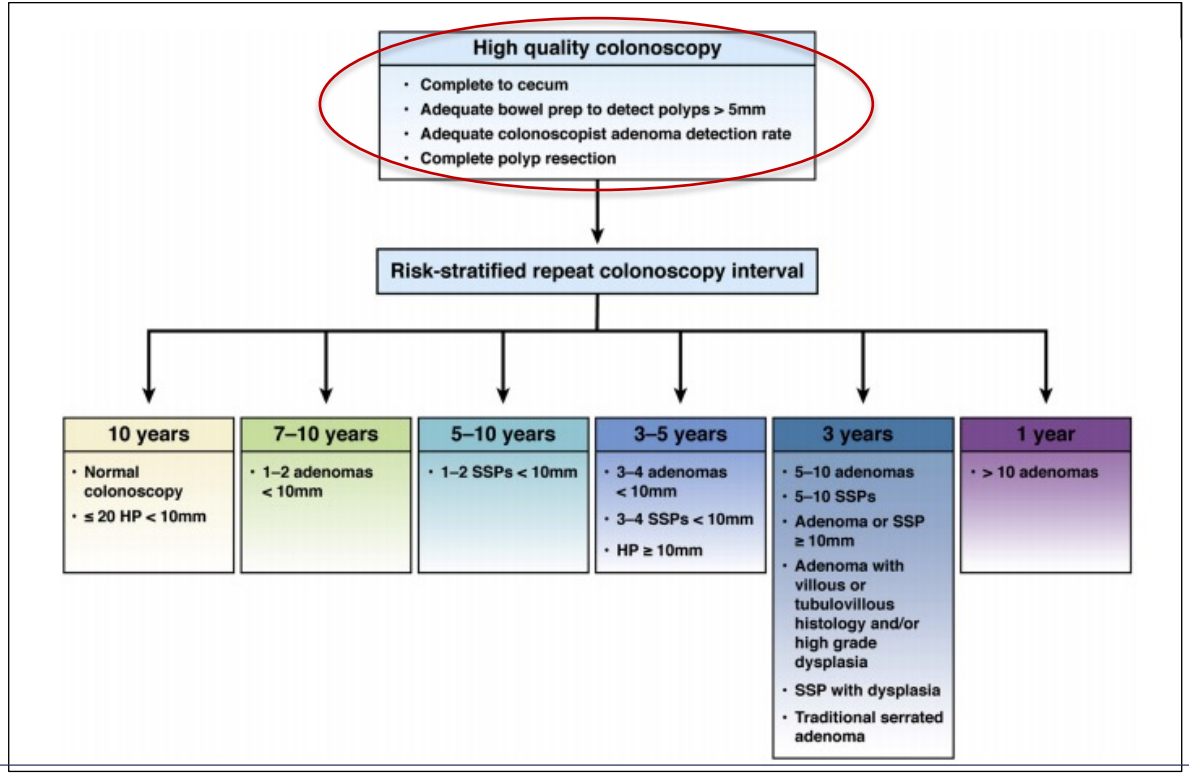
Colonoscopy to detect high-risk lesions or colorectal cancer

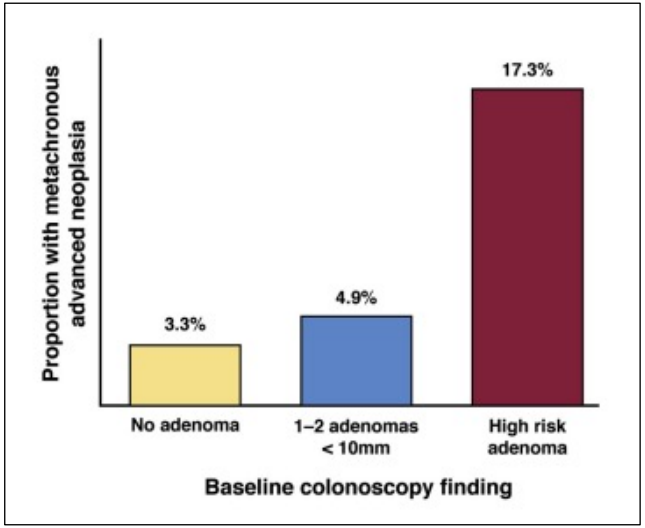
Ongoing randomized trials of colonoscopy



Best of DDW Colorectal Cancer Abstracts: Surveillance

2020 Polypectomy Surveillance Guidelines





Challenges with post-polypectomy surveillance

- Current guidelines for risk stratification for post-polypectomy surveillance are imprecise
  - Sensitivity 59-81%
  - Specificity 43-58%
- Leads to under-surveillance of low-risk individuals and over-surveillance of high-risk individuals
- Based only on number, size, and histology of polyps

Prediction model for metachronous advanced neoplasia after polypectomy

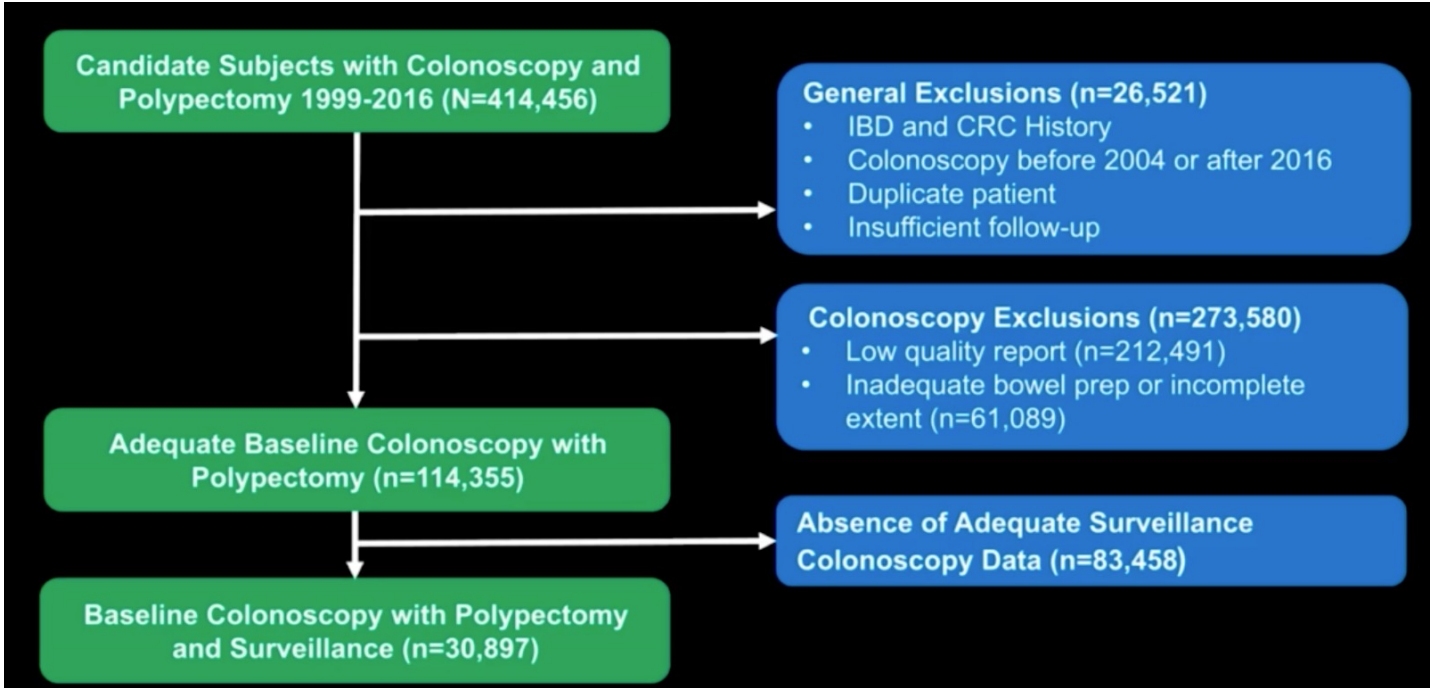
Design

- Retrospective national cohort study of US Veterans exposed to colonoscopy (VA Colonoscopy Cohort)
  - Curated structured data
    - Demographics, comorbidities, smoking exposure, medications incident and fatal colorectal cancer (CRC)
  - Extracted unstructured colonoscopy and pathology report data utilizing PaCRAT (Pathology and Colonoscopy Report Abstraction Tool):
    - System of natural language processing algorithms and data curation developed to extract exam extent, bowel preparation, number, size, histology, and location of polyps
- Inclusion Criteria:
  - Baseline polypectomy 2004-2016, defined by either adenoma or sessile serrated adenoma/polyp/lesion removal; and
  - >=1 surveillance colonoscopy
- Exclusion Criteria:
  - Baseline incomplete exam or inadequate bowel preparation
  - Baseline/prior CRC or inflammatory bowel disease

VACC
VA COLONOSCOPY COLLABORATIVE

PACRAT

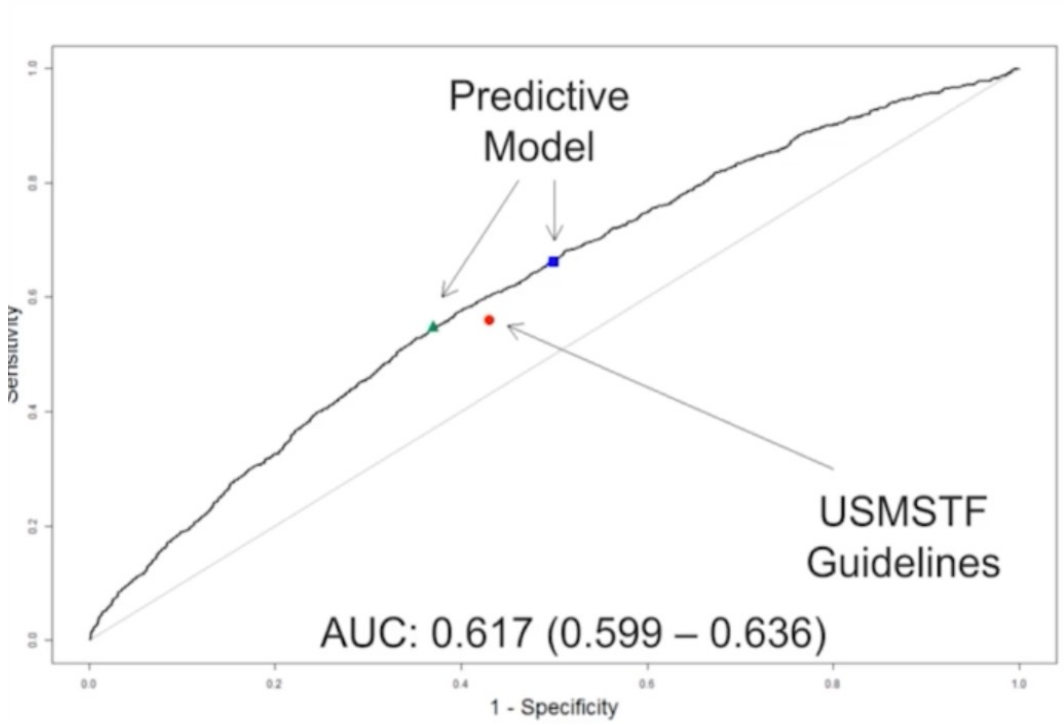
Study inclusion and exclusion flow



Diabetes, gender, ADR were associated with developing metachronous lesions

Association of Included Variables with MAN (Training Data)			
Predictor	**Multivariable OR**	**Predictor**	**Multivariable OR**
Age	1.02 (1.01, 1.03)*	**Sex**	
Diabetes	1.41 (1.27, 1.56)*	Male	1.99 (1.38, 2.88)*
Number of adenomas		Female	1.00
Zero (SSA/P only)	0.47 (0.19, 1.16)	**Adenoma size**	
One-Two	1.00	< 10 mm	1.00
Three-Four	1.22 (1.06, 1.39)*	≥ 10 mm	1.54 (1.38, 1.73)*
More than Four	1.61 (1.33, 1.95)*	Missing	0.84 (0.72, 0.97)*
Location, n (%)		**ADR quintile, n (%)**	
None	1.00	Q1 (<19.7%)	1.48 (1.20, 1.84)*
Proximal only	1.08 (0.91, 1.27)	Q2 (19.7-32.1%)	1.66 (1.42, 1.94)*
Rectal/distal only	1.05 (0.93, 1.19)	Q3 (32.2-39.2%)	1.49 (1.30, 1.72)*
Both	0.87 (0.76, 0.99)*	Q4 (39.3-46.9%)	1.00 (0.87, 1.15)
Tubulovillous/villous	1.31 (1.16, 1.49)*	Q5 (≥47.0%)	1.00
		Missing	1.11 (0.96, 1.28)

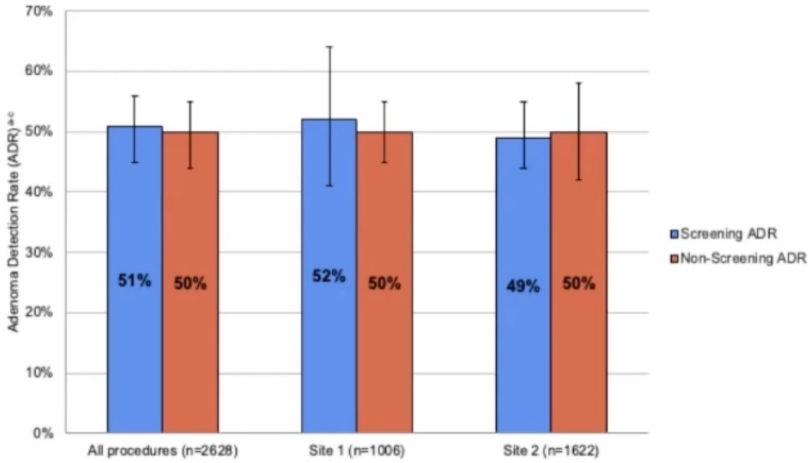
Novel model performed better across a range of cutoffs



Non-screening adenoma detection rate as a quality indicator

Adenoma Detection Rate (ADR) Irrespective of Indication Is Comparable to Screening ADR: Implications for Quality Monitoring

Tonya Kaltenbach,[*] Andrew Gawron,[‡] Craig S. Meyer,[*] Samir Gupta,[§] Amandeep Shergill,[*] Jason A. Dominitz,[‖] Roy M. Soetikno,[*] Tiffany Nguyen-Vu,[*] Mary Whooley,[*] and Charles Kahi[¶]

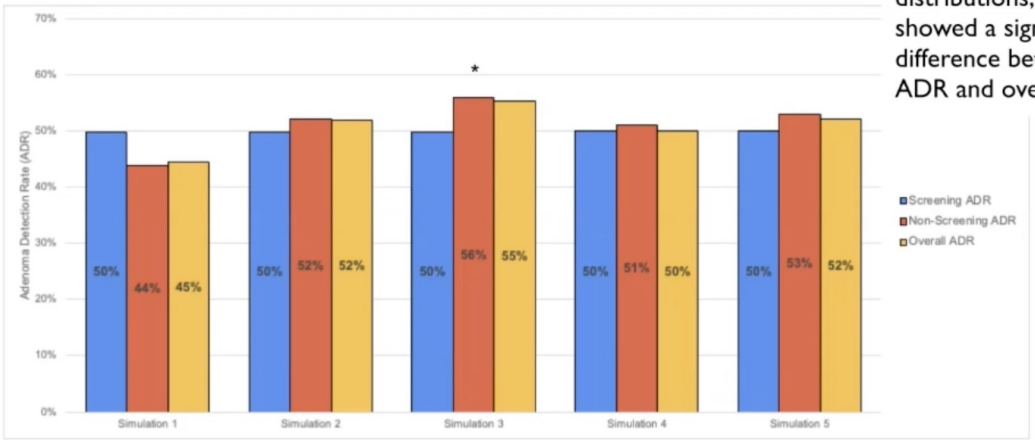


- Among 2628 colonoscopies and 21 endoscopists at 2 Veterans Affairs centers, we found no significant differences between screening ADR and non-screening ADR
- Simulation modeling with varying distributions of indication showed similar results for screening and overall ADR
- Overall ADR, irrespective of indication, is comparable to Screening ADR and should facilitate the broader implementation of quality measurement and reporting

[a]Adenoma detection rates adjusted for sex (male / female) and age (years), and standard errors clustered by endoscopist.
[b]Studies for positive fecal immunochemical test were classified as diagnostic exams.
[c]Indication distribution: Screening in 28.9%, Surveillance in 48.2%, Diagnostic in 22.9%

Non-screening adenoma detection rate as a quality indicator

Simulation Models



Out of 21 total simulations with varying indication distributions, only one model* showed a significant difference between screening ADR and overall ADR.

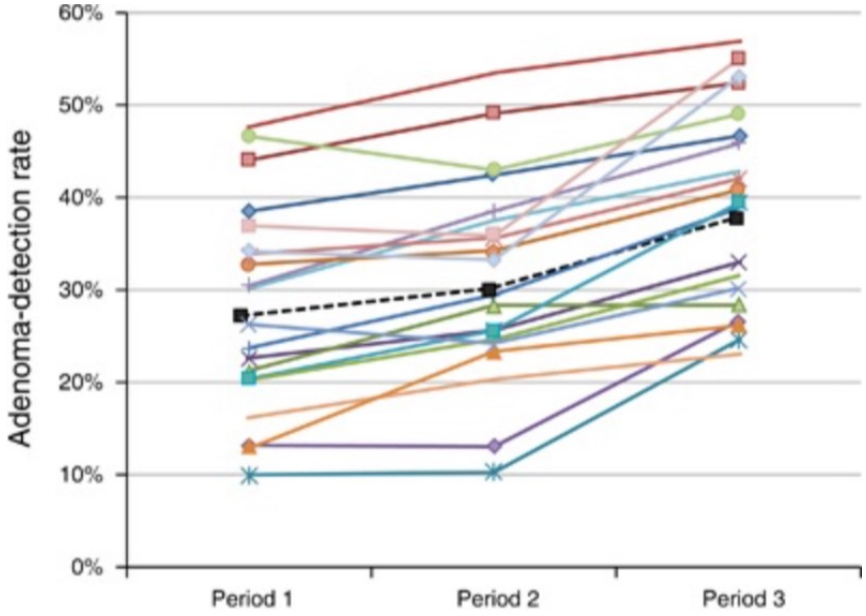
Simulation 1 (Screening 10%, Surveillance 10%, and Diagnostic 80%); Simulation 2 (Screening 10%, Surveillance 60%, and Diagnostic 30%); Simulation 3 (Screening 10%, Surveillance 70%, Diagnostic 10%, FIT+ 10%); Simulation 4 (Screening 30%; Surveillance 40% ; Diagnostic 30%); Simulation 5 (Screening 20%; Surveillance 60% ; Diagnostic 20%)

The endoscopist is the key variable in colonoscopy quality

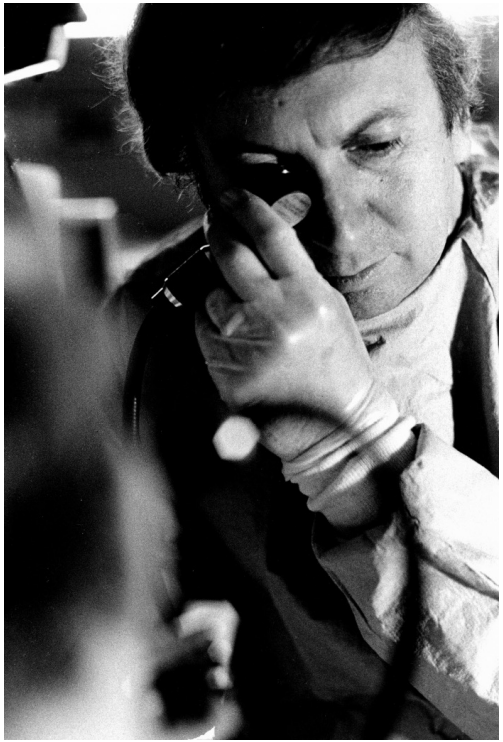
Inspection Tips for High Quality Colonoscopy

Mindset	1	Know the signature features of adenomas and serrated lesions
	2	Look for subtle lesions - think flat and depressed
Technique	3	Maintain a straight scope
	4	Clean the mucosa
	5	Look behind folds
	6	Expand & collapse the lumen
	7	Take adequate time - but be efficient with a plan
	8	Spend most time in the right colon - examine twice
Tools	9	Know when need adjustment- lighting, cap, chromoendoscopy
	10	Engage in quality assurance program

Audit & feedback improves colonoscopy quality



CRC screening & surveillance



"The best test is the one that gets done, and done well"

Sidney Winawer, MD
Memorial Sloan Kettering Cancer Center

Thank you!

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