



# 2021 SCSG GI SYMPOSIUM





# Colorectal Cancer Screening *(Part II)*

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# Disclosure Information

I have the following financial relationships to disclose:

**Consultant/Advisor for:**

California Health Benefits Review Program;  
Owl Peak Labs; Bayer Pharmaceuticals; Seed  
Global Health; Pythagoras/Saint Supply;  
Cottonelle/Kimberly-Clarke; BLKHLTH;  
Freenome; Takeda

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**Employee of:**

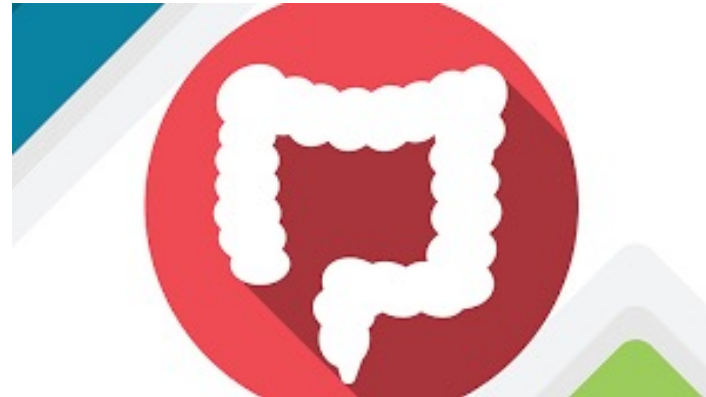
UCLA Health; Veterans Health Administration

I will not discuss off label use and/or investigational, device, product or medication  
use in my presentation.



# Outline

- Updated USPSTF CRC screening guidelines
- Advancing technologies in CRC screening







# 2021 SCSG GI SYMPOSIUM

## **2021 Update to the USPSTF Colorectal Cancer Screening Guidelines**





## 2021 Colorectal Cancer Screening Guidelines



**For adults aged 50 to 75 years:**

Screen all adults aged 50 to 75 years for colorectal cancer.



**For adults aged 45 to 49 years:**

Screen adults aged 45 to 49 years for colorectal cancer.



**For adults aged 76 to 85 years:**

Selectively screen adults aged 76 to 85 years for colorectal cancer, considering the patient's overall health, prior screening history, and patient's preferences.

# USPSTF Grading System

Grade	Definition	Suggestions for Practice
<b>A</b>	The USPSTF recommends the service. There is high certainty that the net benefit is substantial.	Offer or provide this service.
<b>B</b>	The USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.	Offer or provide this service.
<b>C</b>	The USPSTF recommends selectively offering or providing this service to individual patients based on professional judgment and patient preferences. There is at least moderate certainty that the net benefit is small.	Offer or provide this service for selected patients depending on individual circumstances.
<b>D</b>	The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.	Discourage the use of this service.
<b>I</b> Statement	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.	Read the clinical considerations section of USPSTF Recommendation Statement. If the service is offered, patients should understand the uncertainty about the balance of benefits and harms.

Population	Recommendation	Grade
Adults ages 50 to 75	USPSTF recommends screening for colorectal cancer in all adults ages 50 to 75 years.	<b>A</b>
Adults ages 45 to 49	USPSTF recommends screening for colorectal cancer in adults ages 45 to 49 years.	<b>B</b>
Adults ages 76 to 85	USPSTF recommends that clinicians selectively offer screening for colorectal cancer in adults ages 76 to 85. Evidence indicates that the net benefit of screening all persons in this age group is small. Patients and clinicians should consider the patient's overall health and prior screening history.	<b>C</b>





## 2021 Colorectal Cancer Screening Guidelines

Recommended screening strategies include:

- High-sensitivity guaiac fecal occult blood test (HSgFOBT) or fecal immunochemical test (FIT) every year
- Stool DNA-FIT every 1 to 3 years
- Computed tomography colonography every 5 years
- Flexible sigmoidoscopy every 5 years
- Flexible sigmoidoscopy every 10 years + annual FIT
- Colonoscopy screening every 10 years

# Emphasis on “Two-Step” Process



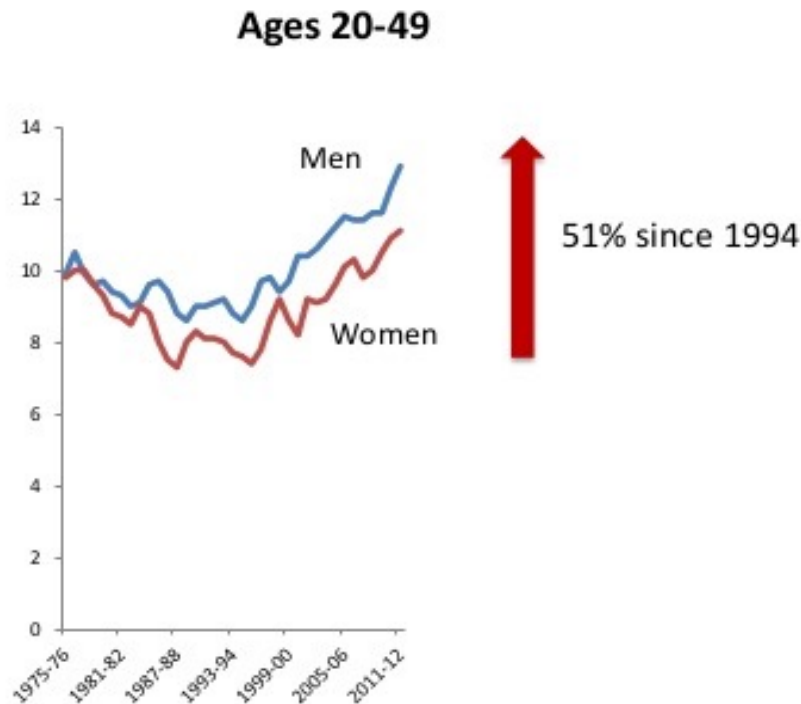
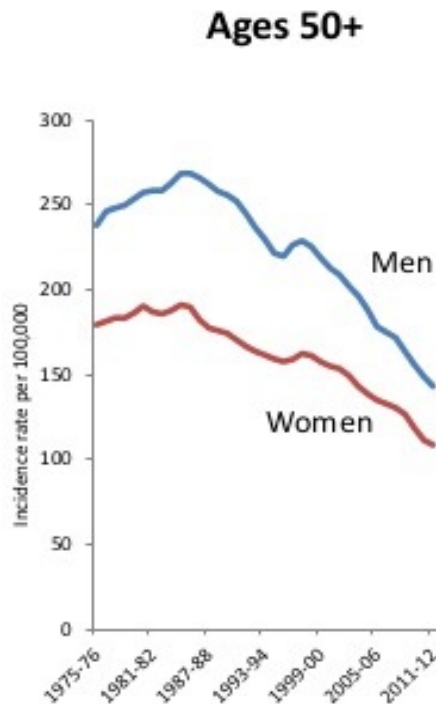
Abnormal (i.e. positive)  
non-colonoscopy screening test result



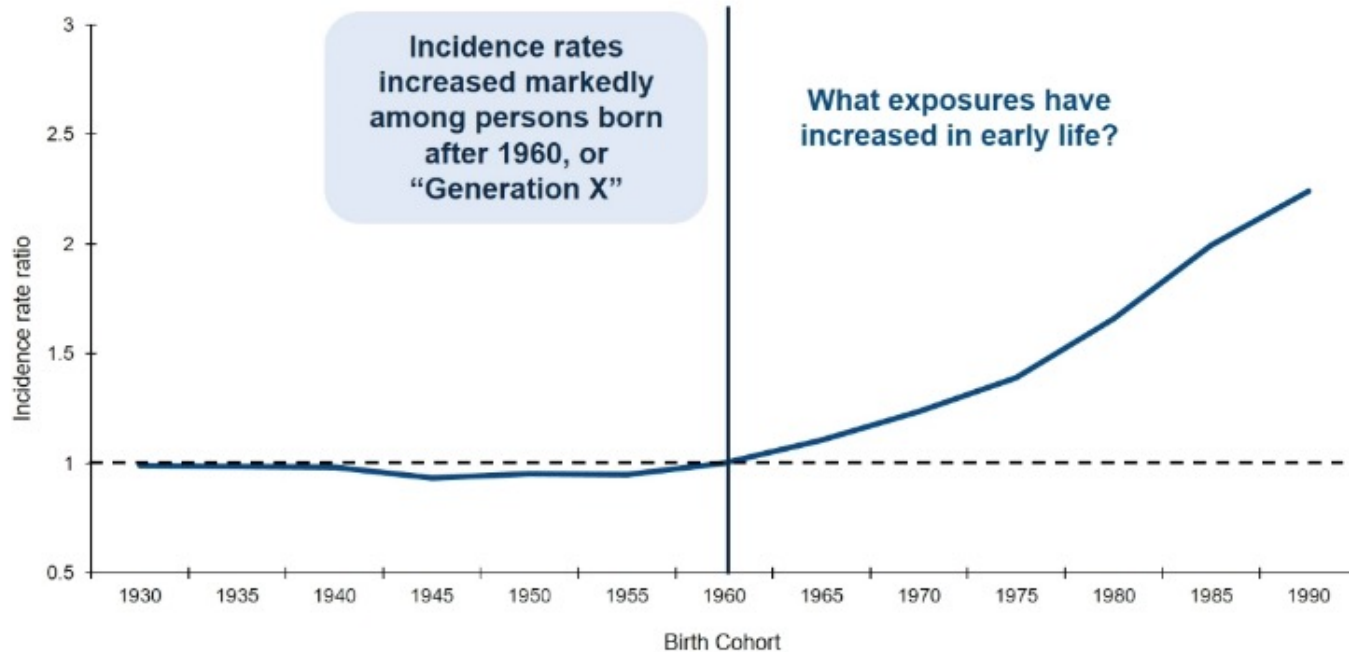
Follow-up colonoscopy  
to detect polyps and  
CRC



# Changing Epidemiology of Disease



# EOCRC Increases Successively Across Birth Cohorts





# American Cancer Society Recommendations (2018)



## 2018 American Cancer Society Colorectal Cancer Screening Guideline Overview

### Recommendations<sup>a</sup>

The ACS recommends that adults aged 45 y and older with an average risk<sup>b</sup> of CRC undergo regular screening with either a high-sensitivity stool-based test or a structural (visual) examination, depending on patient preference and test availability. As a part of the screening process, all positive results on noncolonoscopy screening tests should be followed up with timely colonoscopy.

The recommendation to begin screening at age 45 y is a *qualified recommendation*.

The recommendation for regular screening in adults aged 50 y and older is a *strong recommendation*.

The ACS recommends that average-risk adults in good health with a life expectancy of greater than 10 y continue CRC screening through the age of 75 y (*qualified recommendation*).

# Basis of USPSTF Recommendations

- Two commissioned reports:
  - 1) Systematic review to evaluate the benefits and harms of screening in adults 40 years or older.
    - a) Effectiveness of screening tests
    - b) Comparative effectiveness of screening tests
    - c) Accuracy of various screening tests to detect CRC and adenoma
    - d) Serious harms of different screening tests.
  - 2) Comparative modeling report from the CISNET Colorectal Cancer Working Group for life-years gained, CRC cases/deaths averted, colonoscopy burden, harms for different starting and stopping ages for various screening strategies.

# Systematic Review: Summary of Evidence

Key question		Total no. of Studies	Direct Visualization				Stool				Serum	Urine
			FS (+/- stool testing)	Colo	CTC	CE	gFOBT	HSgFOBT	FIT	sDNA	mSEPT9	Metab
1	Screening effectiveness	13	4*	2*	0	0	6*	0	1*	0	0	0
	Comparative effectiveness	21	11*	5*	3*	0	8	0	13*	0	0	0
2	Colonoscopy reference standard†	40	0	4	9	2*	NA	2*	26*	4*	1	1*
	Differential verification‡	19	0	0	0	0	NA	3	19*	0	0	0
3	Serious adverse events	110	19*	68* (S) 20* (F)	17*	1*	NA**	NA**	NA**	NA**	NA**	NA**
	Radiation	7	NA	NA	7	NA	NA	NA	NA	NA	NA	NA
	ECF	27	NA	NA	27*	NA	NA	NA	NA	NA	NA	NA

\* Includes new data since the 2016 USPSTF recommendation

† Differential verification consisted of direct visualization for those with an abnormal screening test and cancer registry followup for all participants.

\*\* No hypothesized harms for non-invasive screening tests beyond that of the followup testing.

‡ For colonoscopy and CTC studies, the reference standard could include colonoscopy plus CTC (segmental unblinding)



# Modeling Analysis: 2016 v. 2021

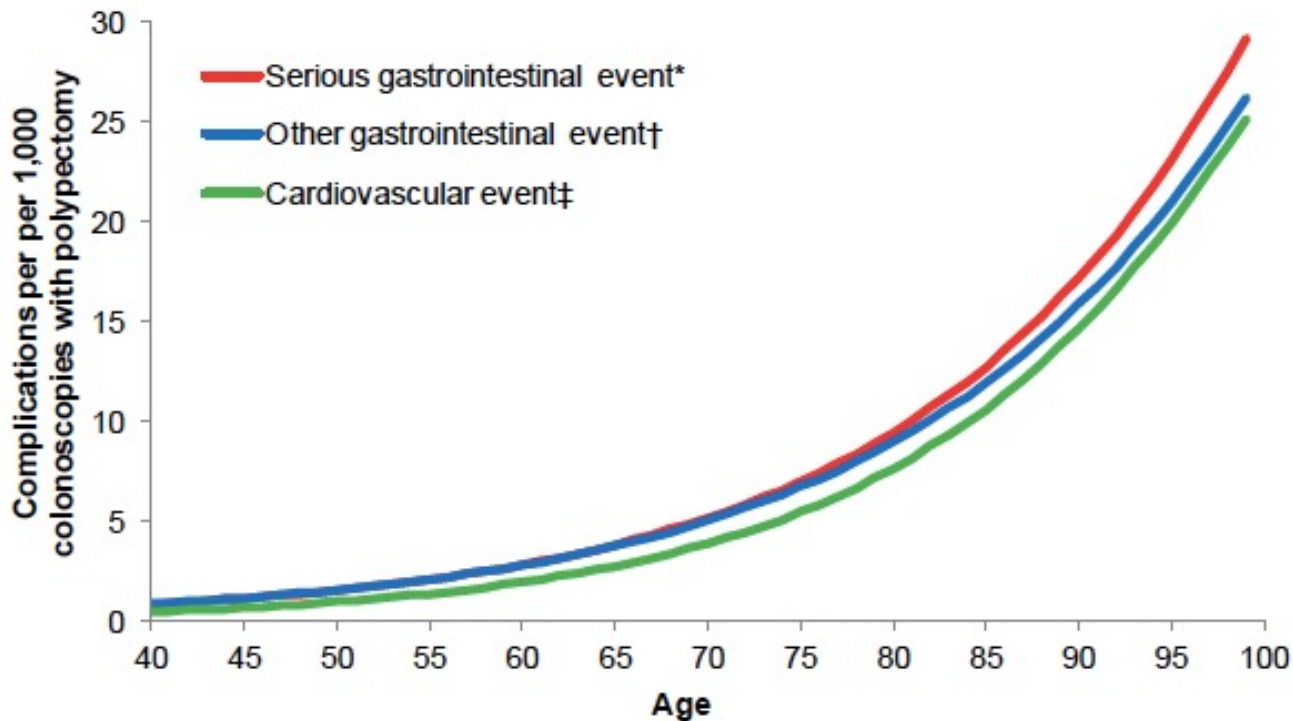
Characteristic	2021 analysis	2016 analysis
Simulation models	SimCRC, CRC-SPIN, MISCAN	SimCRC, CRC-SPIN, MISCAN
Cohort of interest	US average-risk 40-year-olds*	US average-risk 40-year-olds*
US life table (for other-cause mortality rates)	2017	2009
CRC incidence	Models calibrated to incidence rate ratio from SEER for 20- to 44-year-olds in 2012-2016 vs 1975-1979	Models calibrated to rates from 1975-1979 SEER data
CRC relative survival	SEER (1975-2003) <sup>†</sup>	SEER (1975-2003) <sup>†</sup>
Age to begin screening (y)	45, 50, 55	45, 50, 55
Age to end screening (y)	70, 75, 80, 85	75, 80, 85
Stool based screening modalities (intervals (y))	HSgFOBT (1, 2, 3) <sup>‡</sup>	HSgFOBT (1, 2, 3)
	FIT (1, 2, 3)	FIT (1, 2, 3)
	sDNA-FIT (1, 2, 3)	sDNA-FIT (1, 3, 5)
Other screening modalities (intervals (y))	COL (5, 10, 15)	COL (5, 10, 15)
	SIG (5, 10)	SIG (5, 10)
	SIG + FIT (10_1, 10_2)	SIG + FIT

# When to Stop Screening

- CRC risk
- History of prior screening
- Life expectancy/comorbidity
- Patient preferences

*Selective  
screening for  
age 76 to 85*

# Excess Risks of Colonoscopy Complications





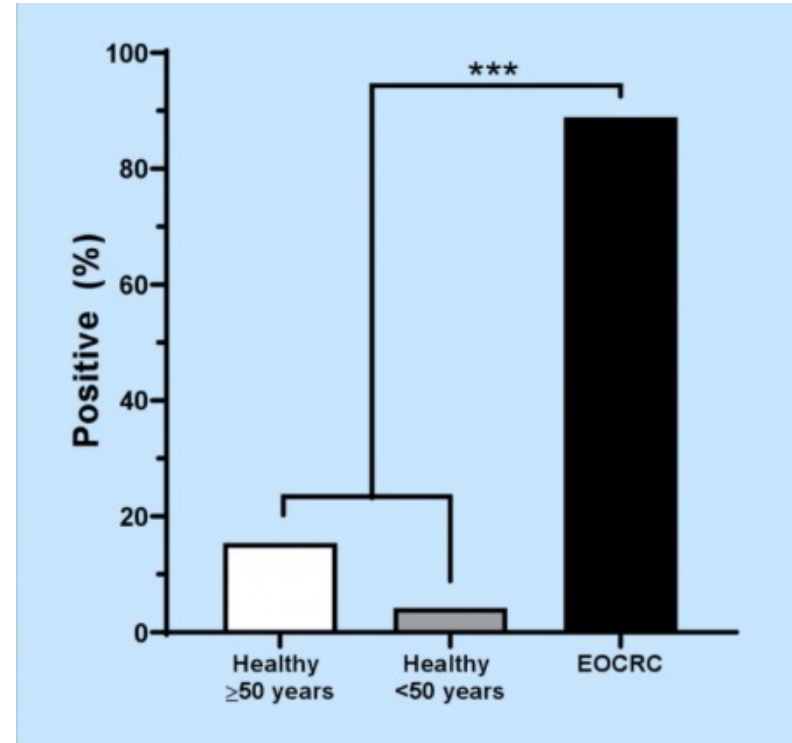
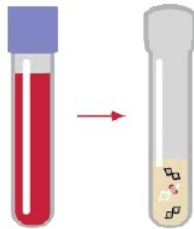


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GI SYMPOSIUM

# **Advancing Technologies in CRC Prevention and Control**

# Blood-based DNA Biomarkers for Colorectal Cancer Screening

- Methylated Septin9 (mSEPT9) is a sensitive and specific biomarker for the detection of EOCRC
- Detected in 89% EOCRC cases (compared to 15% controls)
  - Sensitivity: 91%
  - Specificity: 89%
  - PPV: 96%
  - NPV: 75%



# Focus on High-Quality Colonoscopy

ASGE/ACG Taskforce Quality Indicators	
Pre-procedure	
	Indication documented
	Informed consent obtained
	Surveillance interval
Intra-procedure	
	Bowel Preparation quality
	Cecal intubation rate
	Adenoma detection rate
	Withdrawal time
Post-procedure	
	Perforation incidence
	Post-polypectomy bleed incidence
	Post-polypectomy bleed requiring surgery
	Surveillance interval recommendation



ADR  
CRC Incidence  
CRC Mortality



# Technologies for Screening Colonoscopy

## Endoscopes that Increase Mucosal Visualization

Multiple lenses colonoscope systems

Retroview colonoscope systems

Wide angle views

Short turn radius



## Accessory Devices

Transparent caps

Endocuff

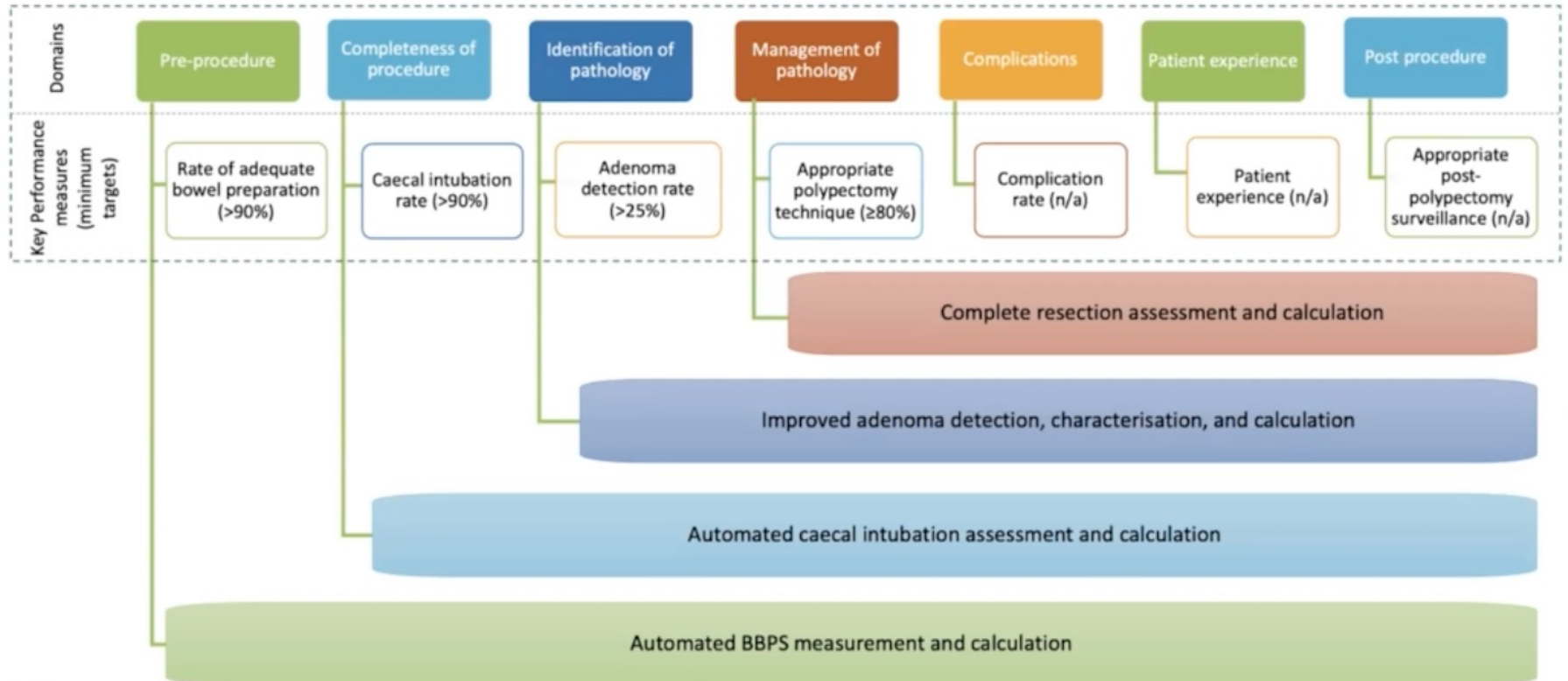
Endorings

G-Eye

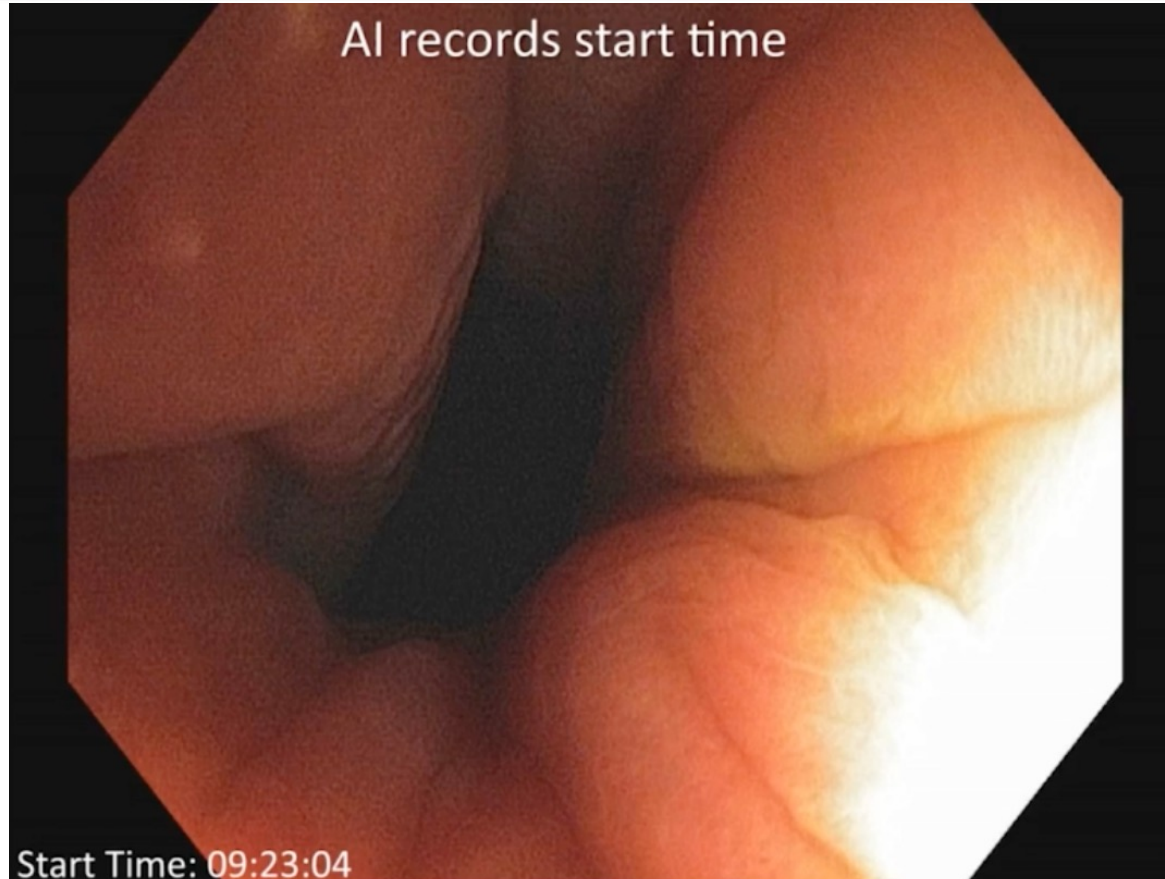
Third eye panoramic



# Artificial Intelligence in Colonoscopy



# AI Records Procedure Start Time





# AI Challenges to Improve Prep



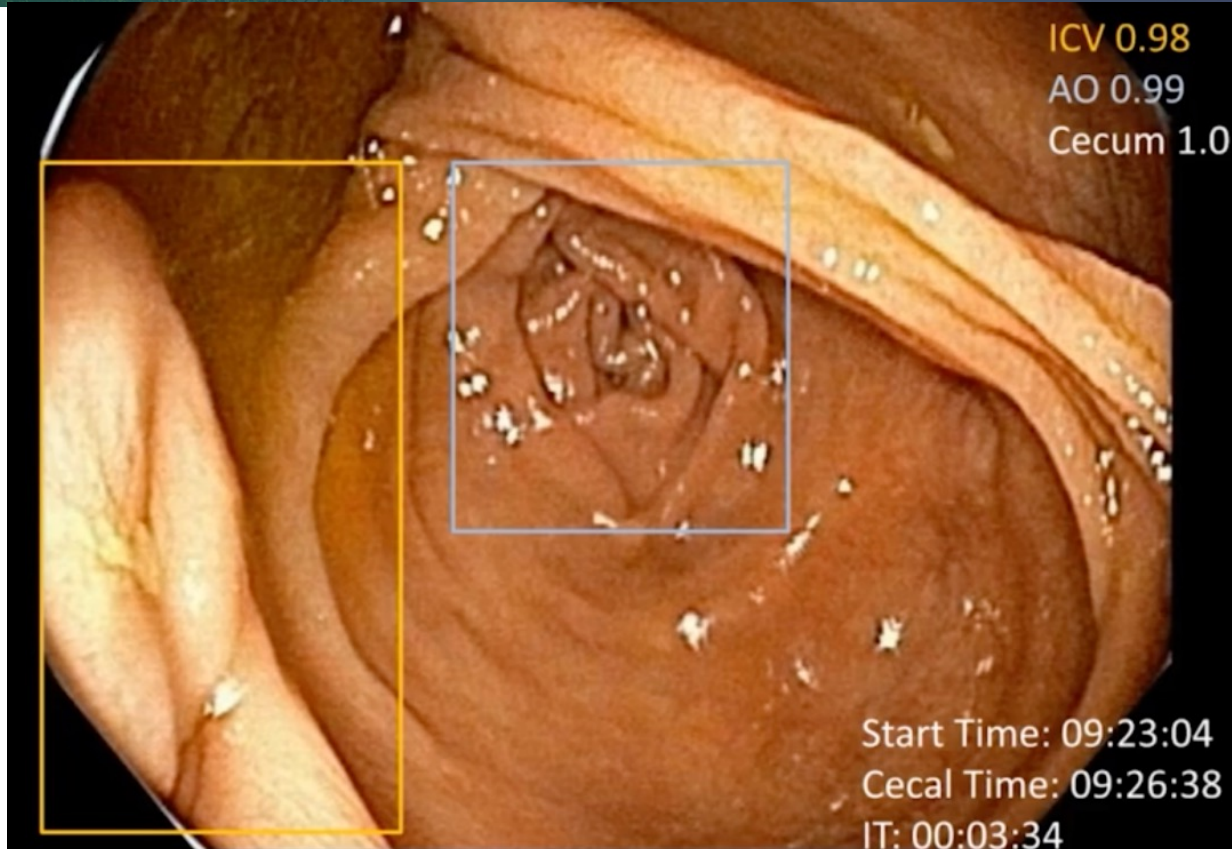
Start Time: 09:23:04



Start Time: 09:23:04

*Boston Bowel Preparation Scale (BBPS) or Ottawa Bowel Preparation Scale (OBPS) scores every 30 seconds and cumulatively*

# AI Identifies Landmarks and Marks Time



# Assessing Withdrawal Time

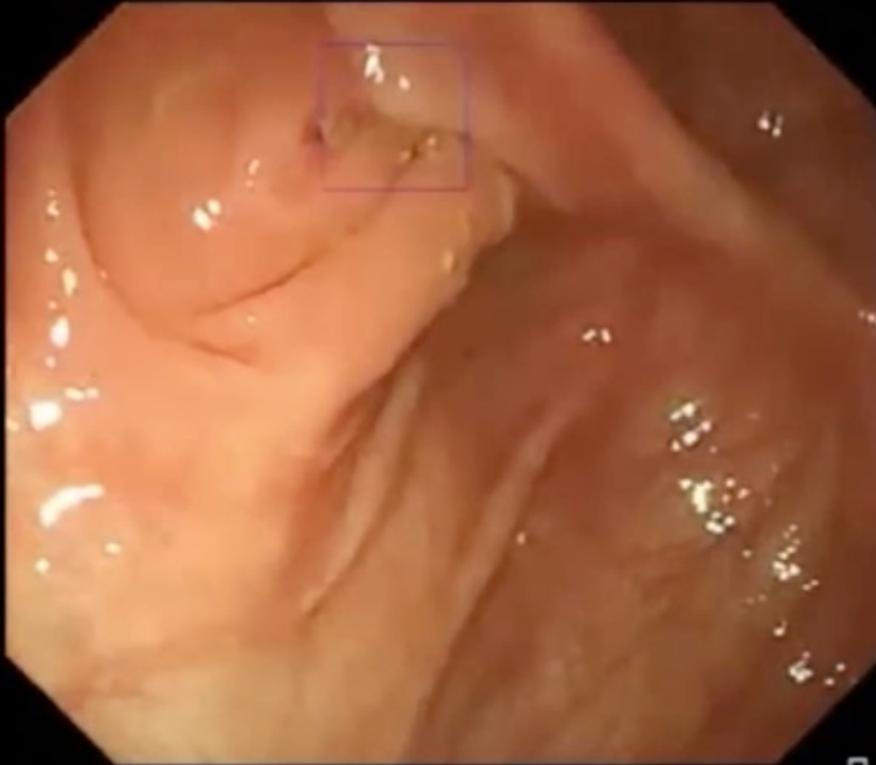
Insertion: 01:46

Withdrawal: 00:04

Loss of view: 0



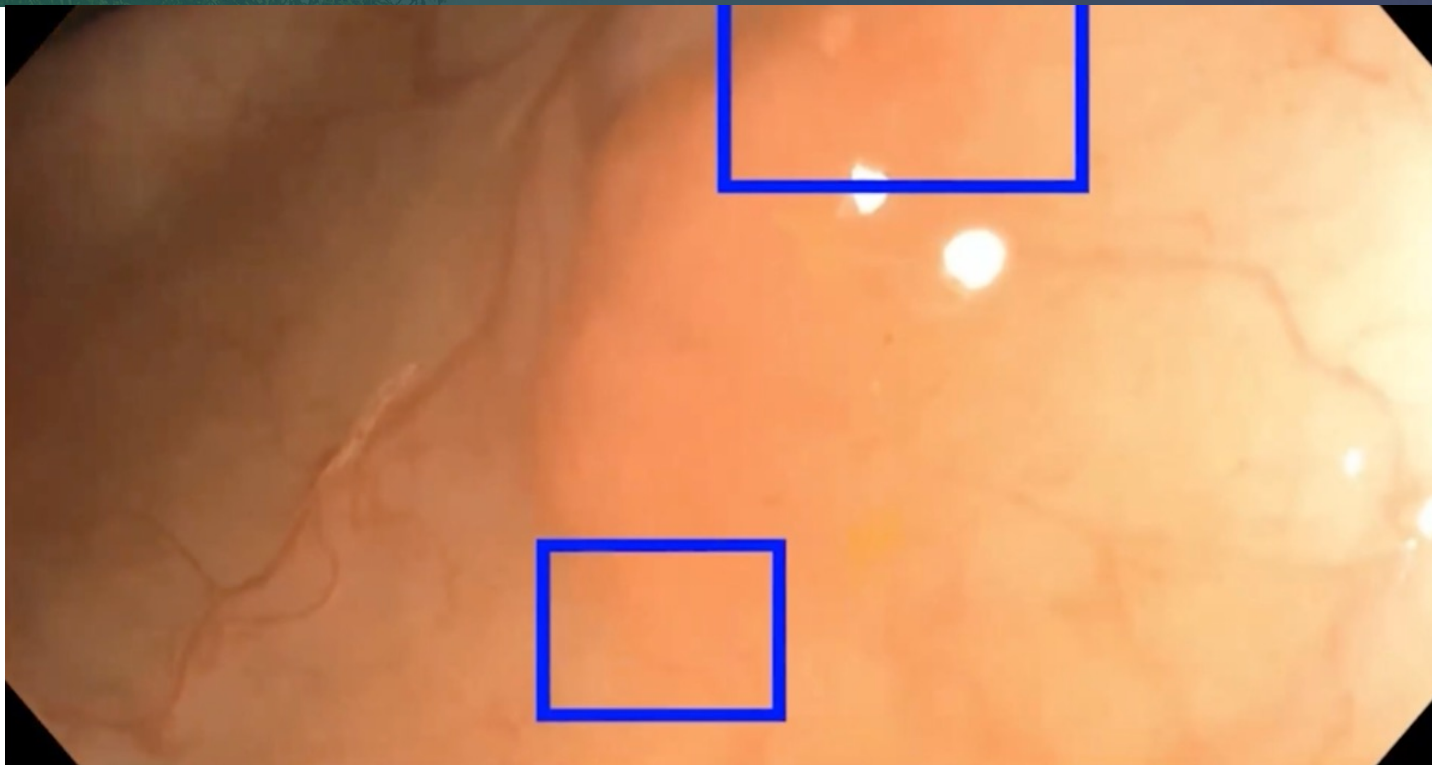
Appendix orifice reached,  
now we can withdraw  
appendix orifice



Sharma P. Digital  
Technologies and AI.  
DDW2021.

 drfolamay

# Polyp Detection During Colonoscopy



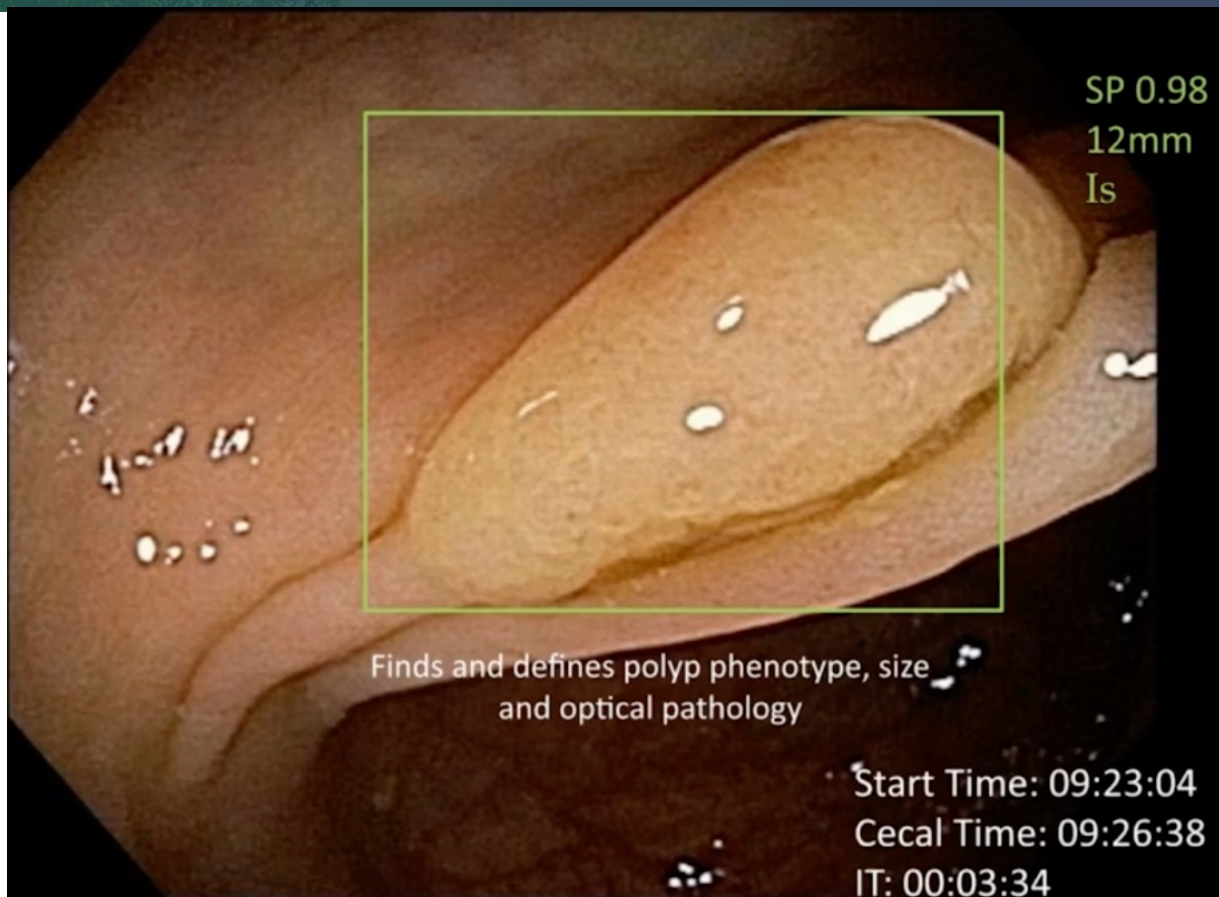


# AI for Polyp Detection: Systematic Review and Meta-Analysis

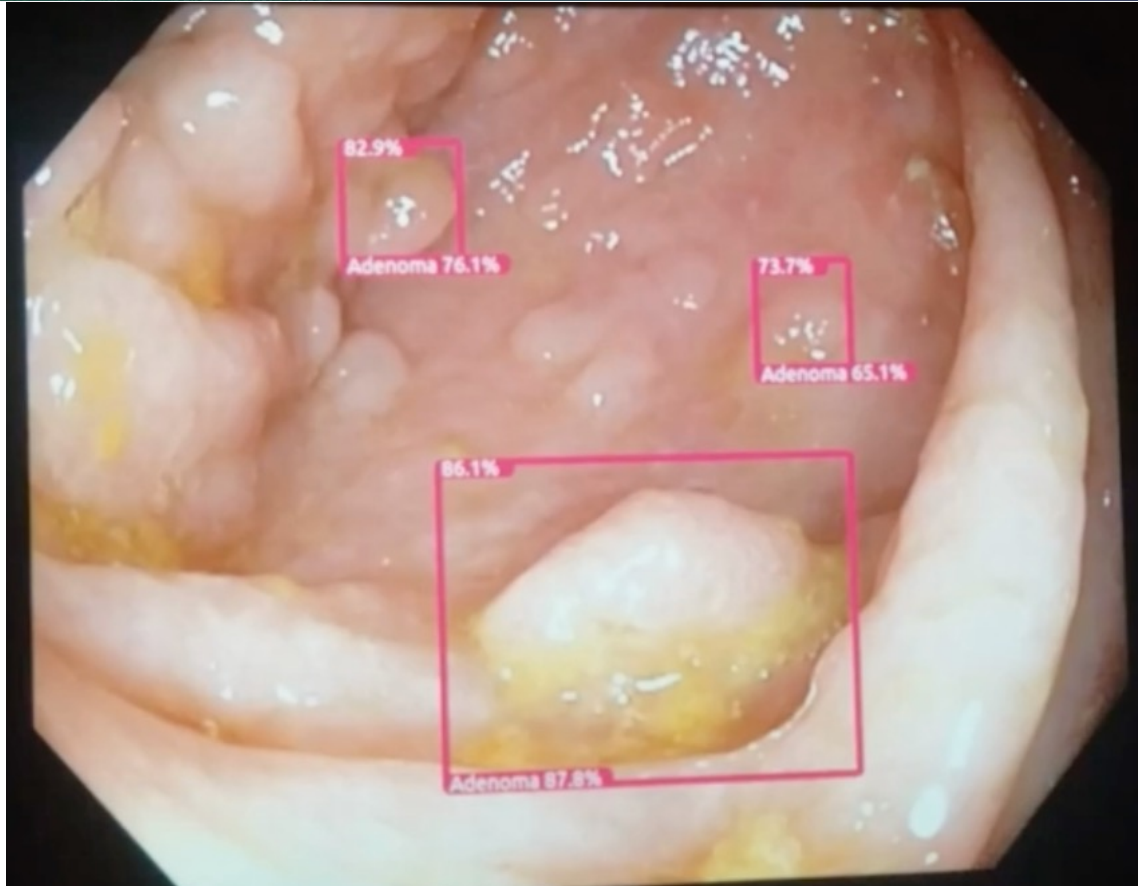
- 5 RCTs
- 4311 patients
- Published 2019-20
- Screening/surveillance or diagnostic colonoscopy

	With AI	Without AI	RR
ADR	30%	19%	1.52 (1.31-1.77)
PDR	45%	31%	1.48 (1.37-1.60)
Mean APC for small adenomas ( $\leq 5\text{mm}$ )		AI was better than No AI (mean diff 0.15 (0.12-0.18))	

# Characterization of Colorectal Polyps by AI



# Characterization of Colorectal Polyps by AI

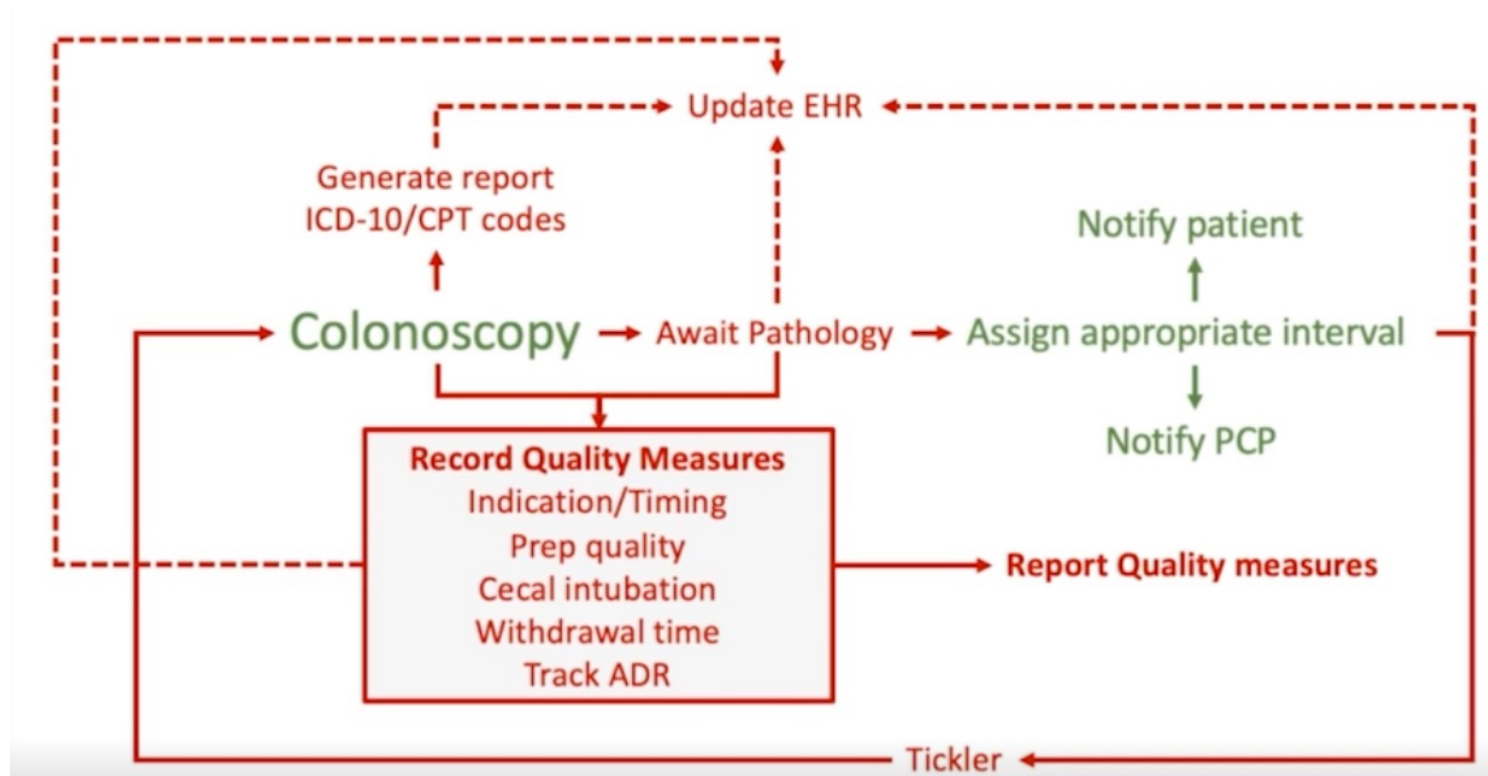


# AI Records Procedure End Time

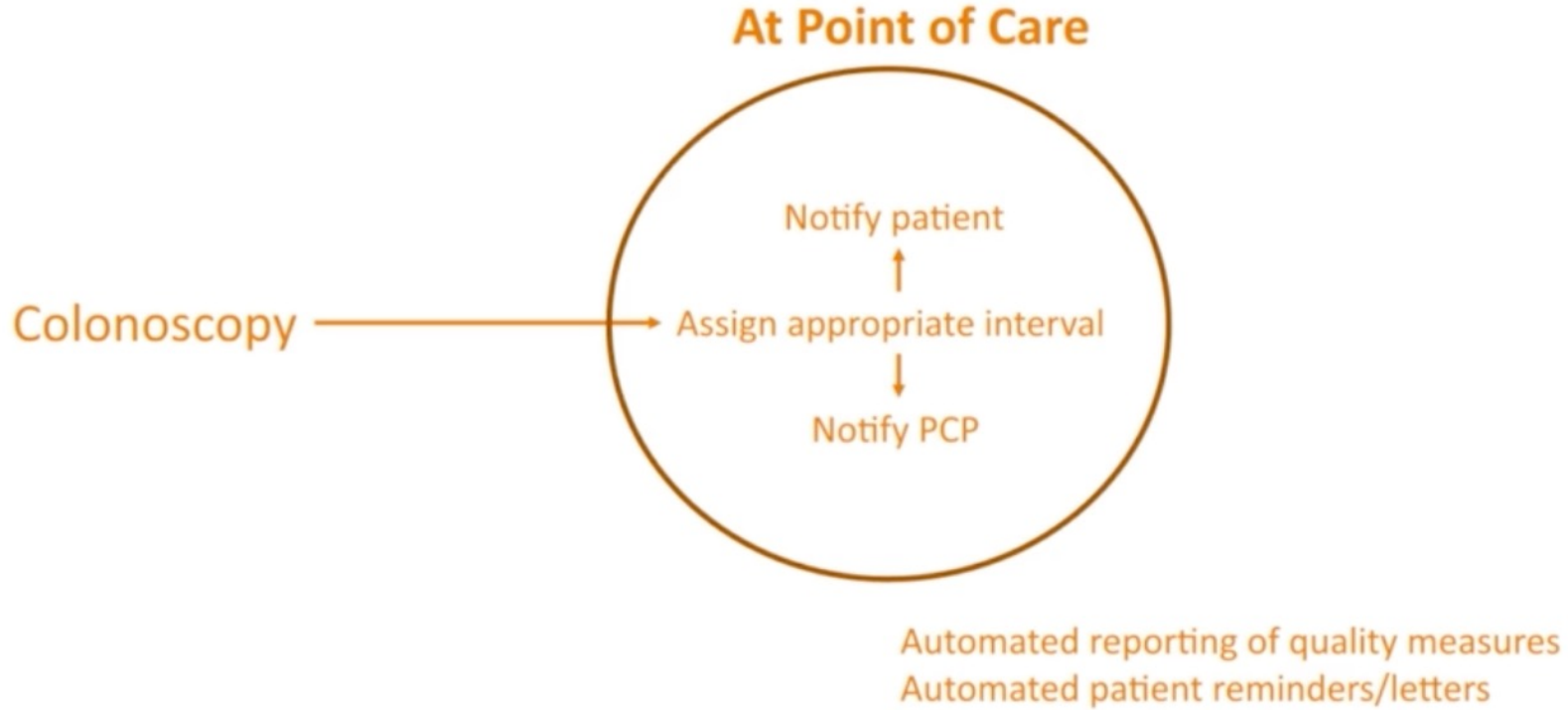




# Current Workflow for Screening Colonoscopy



# Future Workflow for Screening Colonoscopy



# Potential Downsides of AI

- False positive findings
- Missed lesions
- Biased algorithms
- Variable access to AI technologies
- Greater disparities by income and race/ethnicity
- Diminishing procedural skill

# Summary

- New USPSTF CRC screening guidelines (2021) recommend the initiation of screening at age 45 for average-risk Americans (grade B).
- The age to stop screening remains debated but selective screening is appropriate until age 85 after considering benefits and harms (grade C).
- High quality colonoscopy is essential to reduce interval cancers and reduce morbidity and mortality from CRC.
- Emerging technologies in CRC screening aim to improve the detection of early cancers and polyps and colonoscopy quality.



# Thank You!



**UCLA FIELDING**  
SCHOOL OF PUBLIC HEALTH



**Funding Sources:**  
NIH/NCI  
UCLA JCCC  
Broad Institute  
Ablon Scholars Program  
TRDRP



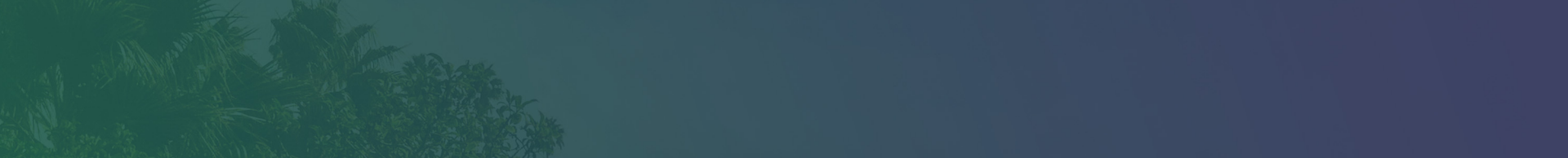
**<https://www.uclahealth.org/gastro/may-lab>**









- 
- AI and Mucosa exposed/seen
  - AI and Adequate retroflexion
  - Standardize titles



# Screening test options

## Stool-based strategies



gFOBT



Fecal Immunochemical Test (FIT)



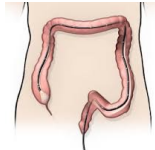
## Direct-visualization techniques



CT Colonography

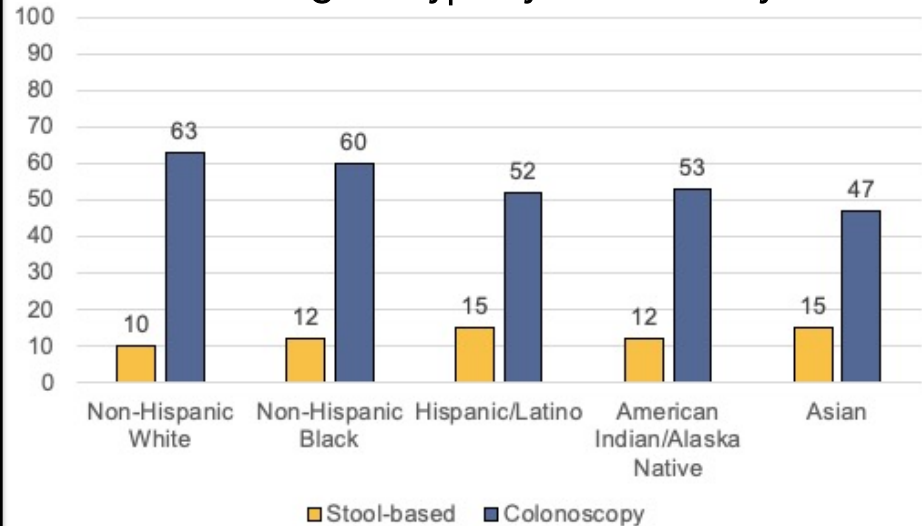


Flexible Sigmoidoscopy



Colonoscopy

Screening test type by race/ethnicity



## USPSTF 2021 Final Recommendation Statement

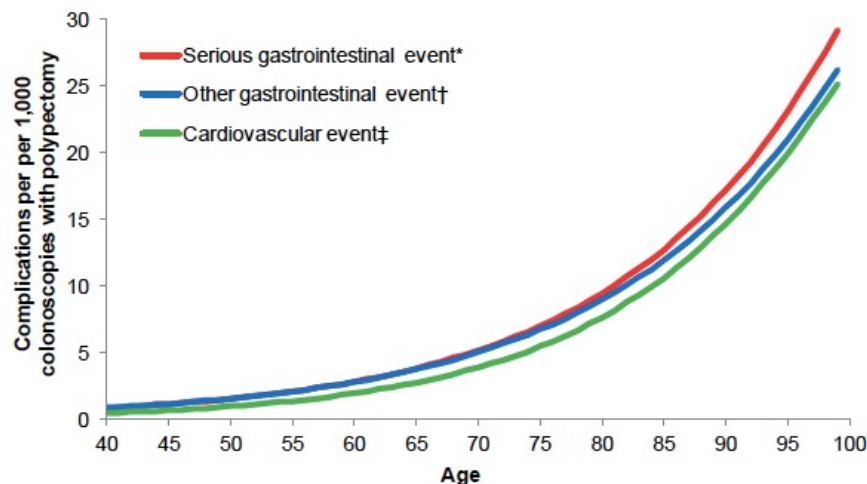
Recommended Screening Test(s)*	Screening Age	Recommended Screening Intervals	Addressing Disparities
<b>Stool-based tests</b> HSgFOBT, FIT, sDNA-FIT (Cologuard®)	<b>Screen adults 50 to 75 years</b> Grade A: High certainty that net benefit is substantial	<b>Stool-based tests</b> HSgFOBT, FIT: every 1 year sDNA-FIT (Cologuard®): every 1 to 3 years	Strongly encourages clinicians to ensure Black patients receive recommended colorectal cancer screening, follow-up, and treatment due to historically worse CRC health outcomes.
Positive results on stool-based screening tests require follow-up colonoscopy for the screening benefits to be achieved	<b>Screen adults 45 to 49 years</b> Grade B: Moderate certainty that net benefit is moderate	<b>Direct visualization</b> Colonoscopy: every 10 years CT colonography: every 5 years Flexible sigmoidoscopy: every 5 years (every 10 years + annual FIT)	Calls for more research on factors contributing to increased CRC incidence and mortality in Black adults.
<b>Direct visualization</b> Colonoscopy, CT Colonography, Flexible Sigmoidoscopy +/- FIT	<b>Screen adults 76 to 85 years</b> Grade C: Moderate certainty that net benefit is small		

*\*The USPSTF states: Because no direct evidence compares different screening tests, and because local resources or patient factors may influence feasibility of different screening strategies, the USPSTF is unable to determine which tests are unequivocally “better” or “worse.”*

Appendix Table 17.1. Summary of Differences Between Base-Case Analyses for the 2021 Decision Analysis for the USPSTF and for the 2018 Decision Analyses for the ACS<sup>27,28</sup>

Characteristics	2021 USPSTF analysis	2018 ACS analysis I <sup>22</sup>	2018 ACS analysis II <sup>23</sup>
Simulation models	MISCAN, SimCRC and CRC-SPIN	MISCAN	MISCAN and SimCRC
Cohort of interest	All 40-year-old adults at average risk of CRC	All 40-year-old adults at average risk of CRC	Race- and sex-specific 40-year-old adults at average risk of CRC
US life table (for other-cause mortality rates)	2017	2013	2013
CRC incidence	Models calibrated to incidence rate ratio from SEER for 20- to 44-year-olds in 2012-2016 vs 1975-1979 (IRR = 1.19)	Models calibrated to results from age-period-cohort modeling (IRR = 1.59)	1. Models calibrated to race- and sex-specific incidence in SEER 1975-1979 (SimCRC) and SEER 1990-1994 (MISCAN) 2. Race- and sex-specific results from age-period-cohort modeling
CRC localization	Models calibrated to localization in SEER 1975-1979	Models calibrated to localization in SEER 1975 birth cohort	1. Models calibrated to same sources as CRC risk 2. Models calibrated to localization in SEER 1975 birth cohort
Evaluated screening modalities	Single, hybrid and once-only test strategies	Single test strategies only	Single test strategies only
Age to begin screening (y)	45, 50, 55	40, 45, 50	45, 50, 55
Age to end screening (y)	70, 75, 80, 85	75, 80, 85	75, 80, 85
Selection of model-recommendable strategies (Yes/No)	No	Yes	Yes

Figure 9. Age-Specific Excess Risks of Complications From Colonoscopy With Polypectomy Relative to Colonoscopies Without Polypectomy as Estimated by Van Hees et al<sup>73</sup>



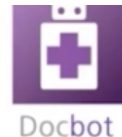
Note: Complications include serious gastrointestinal events, other gastrointestinal events, and cardiovascular events.

\* Perforations, gastrointestinal bleeding, or transfusions. Excess risk per colonoscopy with polypectomy =  $1/[\exp(9.27953 - 0.06105 \times \text{Age}) + 1] - 1/[\exp(10.78719 - 0.06105 \times \text{Age}) + 1]$ .

† Paralytic ileus, nausea and vomiting, dehydration, abdominal pain. Excess risk per colonoscopy with polypectomy =  $1/[\exp(8.81404 - 0.05903 \times \text{Age}) + 1] - 1/[\exp(9.61197 - 0.05903 \times \text{Age}) + 1]$ .

‡ Myocardial infarction or angina, arrhythmias, congestive heart failure, cardiac or respiratory arrest, syncope, hypotension, or shock. Excess risk per colonoscopy with polypectomy =  $1/[\exp(9.09053 - 0.07056 \times \text{Age}) + 1] - 1/[\exp(9.38297 - 0.07056 \times \text{Age}) + 1]$ .

# What your future could look like:



- **Colonoscopy is complete**
- **AI has recorded all quality metrics:** cecal intubation, withdrawal time, prep quality, ADR
- **AI completes colonoscopy report (for you to review/edit/sign)**
  - auto-labelled images, including cecum
  - accurate billing details
  - CADx replaces pathology in many cases (resect and discard = no need for path letter!)
  - autogenerates guideline recommendations
- **AI continuously learns and improves based on your input & edits**