Colon Cancer Screening update

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Disclosure

I have nothing to disclose

Learning objectives

1. Discuss endoscopic and non-endoscopic technologies for CRC screening
2. Review Post polypectomy surveillance guidelines

You are asked to provide CRC screening guidance for a 77-year old male. He has no personal or family history of colorectal cancer, denies gastrointestinal symptoms, and has never been screened.

Which approach is consistent with the USPSTF CRC screening recommendations?

a) Offer screening colonoscopy now; no further screening if normal

b) Offer no screening; patient exceeds eligible screening age

c) Offer FIT or FIT DNA (Cologuard) screening, followed by colonoscopy if abnormal

d) Discuss potential risks and benefits of screening and patient preferences

52 year old male with a negative colonoscopy at age of 40 and mother with colon cancer at age of 58. He does not want a colonoscopy?

How do you respond?

a) That is fine, we will order a Cologuard because it is over 90 % sensitive for picking up cancer

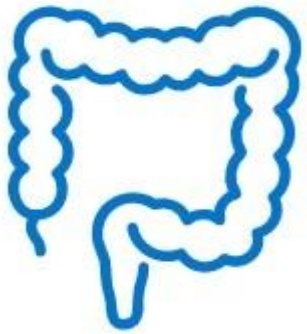
b) Let me introduce you to my dog who is trained to sniff out colon cancer

c) That will not work since only colonoscopy is appropriate for someone at high risk with a family history such as yours

d) That will work since your mother was genetically tested and was not found to have any high risk mutations

e) We can skip the colonoscopy and instead will do a blood test looking for cell free DNA

Common and Deadly but largely Preventable

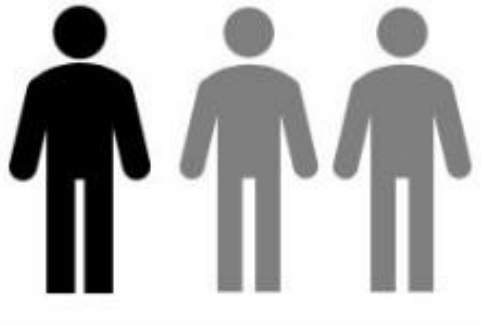


151,000 cases/ year (2022)

3rd most common cause of cancer for men and women in U.S.

52,000 deaths/ year

2nd most common cause of cancer-related deaths in U.S.

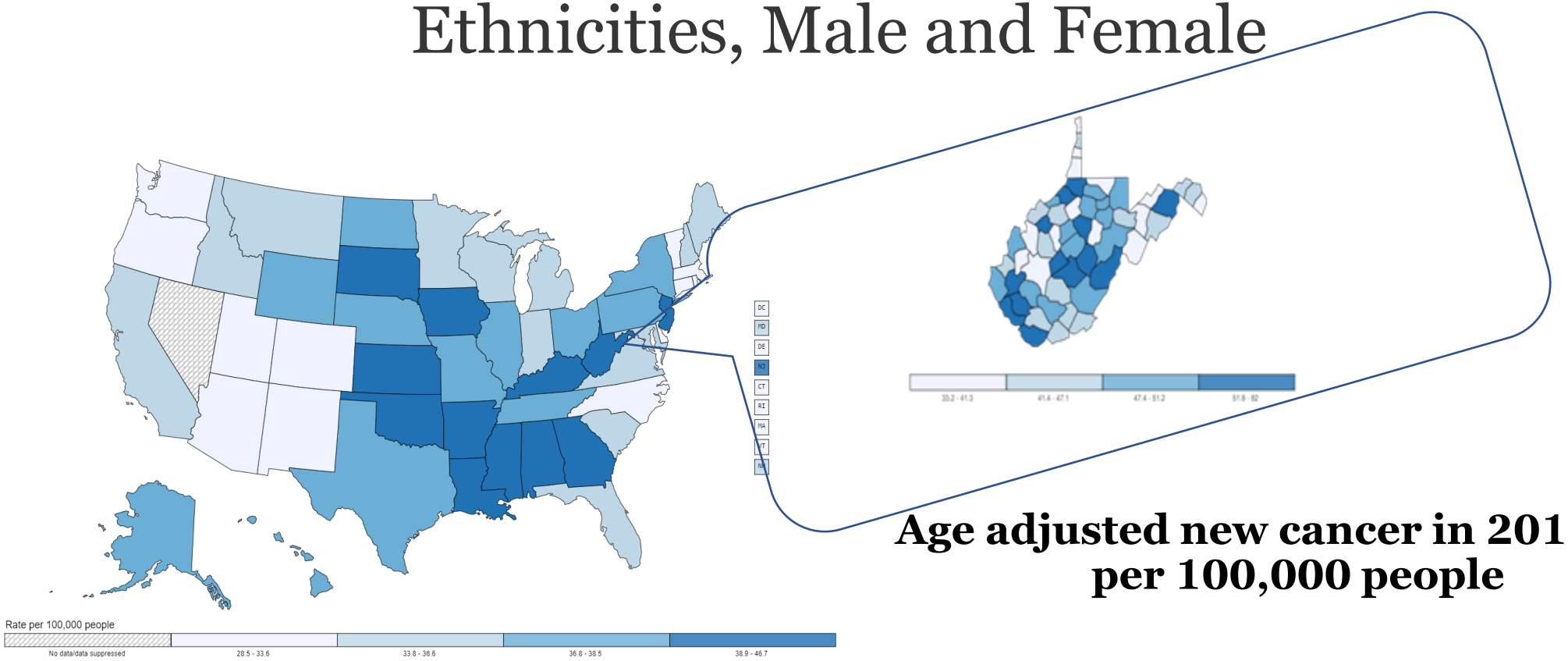


23 million unscreened

1 in 3 adults in U.S. not screened for CRC

CRC facts and figures 2022. American Cancer Society

Rate of New Cancers in the United States, 2019 Colon and Rectum, All Ages, All Races and Ethnicities, Male and Female

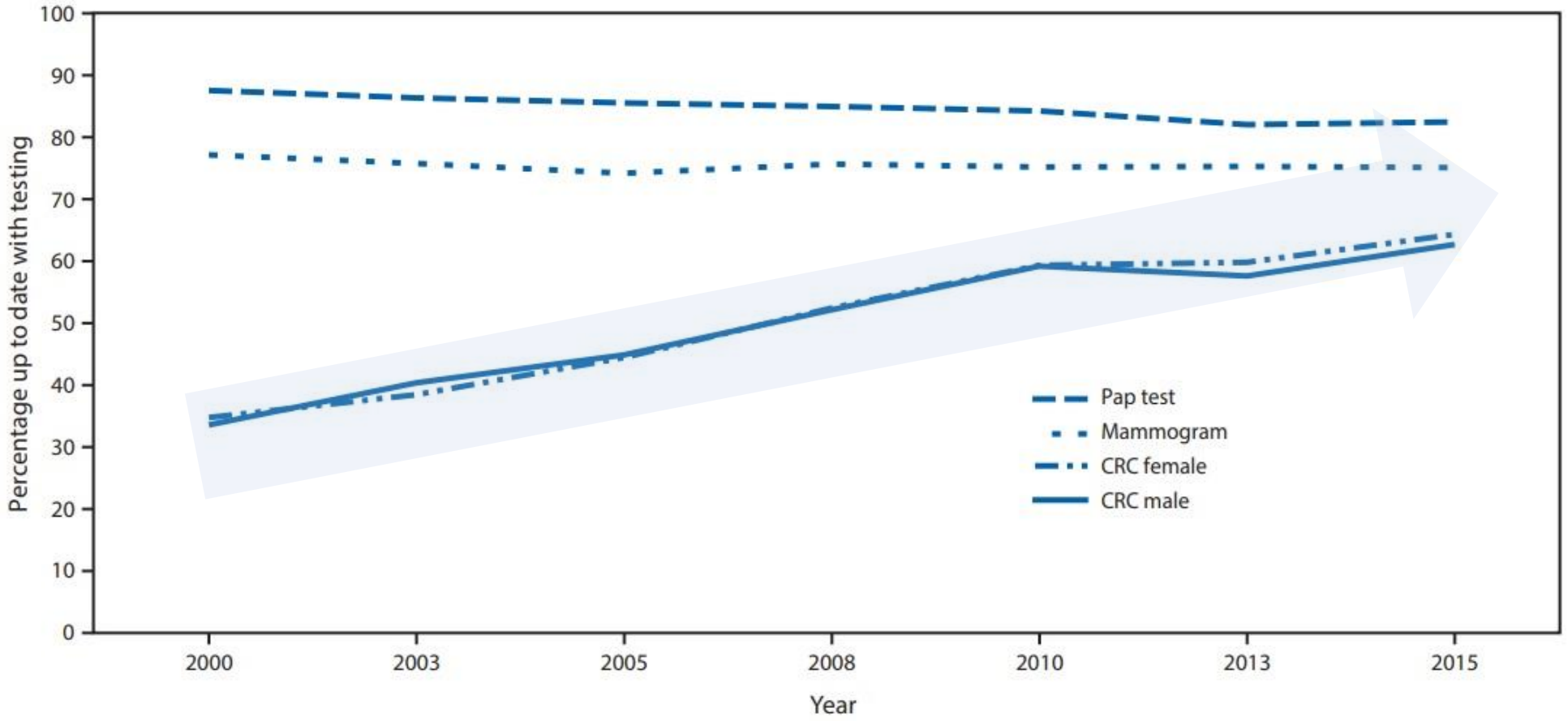


Age adjusted new cancer in 2019 43.2 per 100,000 people

Source - U.S. Cancer Statistics Working Group. U.S. Cancer Statistics Data Visualizations Tool, based on 2021 submission data (1999-2019): U.S. Department of Health and Human Services, Centers for Disease Control and Prevention and National Cancer Institute; https://www.cdc.gov/cancer/dataviz, released in June 2022.

USA Screening Rates for CRC

FIGURE. Percentage of adults who were up to date with screening for breast,* cervical,† and colorectal§ cancers, by test, sex, and year — United States, 2000–2015



Abbreviation: CRC = colorectal cancer.

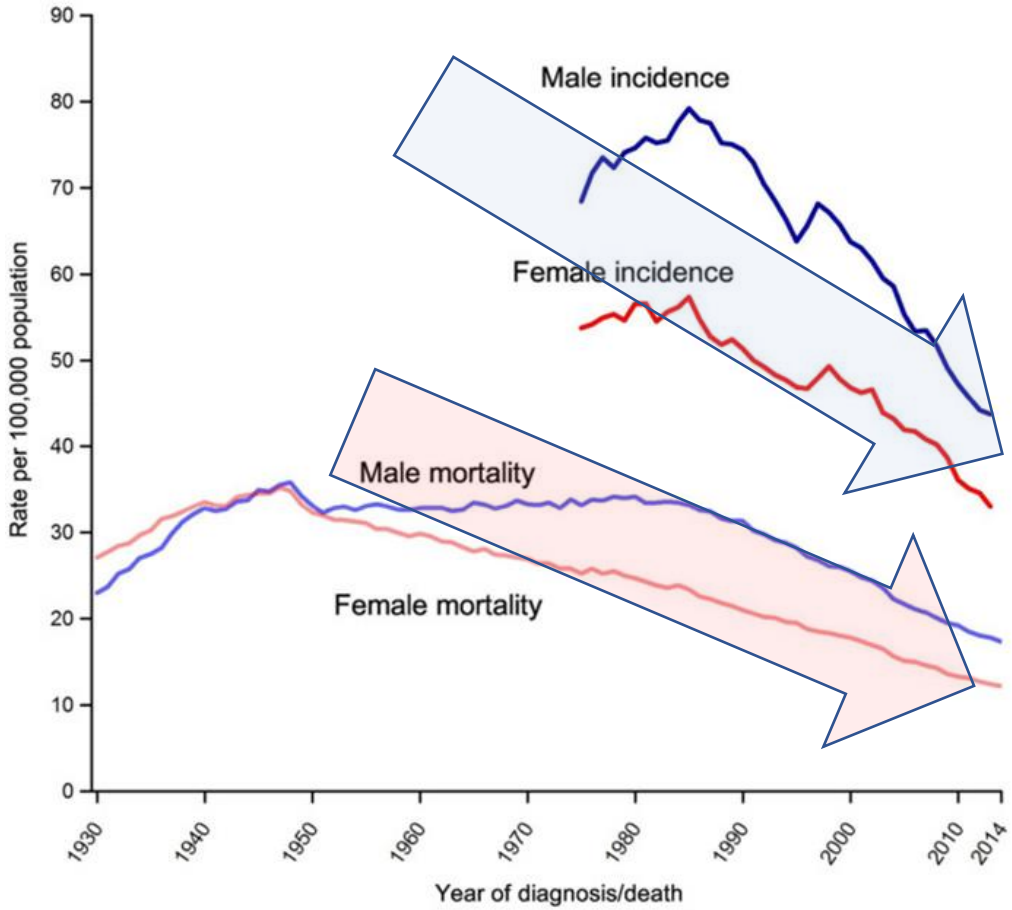
* The U.S. Preventive Services Task Force (USPSTF) recommends mammography within 2 years for women aged 50–74 years.

† USPSTF recommends Papanicolaou (Pap) test within 3 years for women aged 21–65 years without hysterectomy, or Pap test with human papillomavirus test within 5 years for women aged 30–65 years without hysterectomy. To account for changing screening recommendations over time for cervical cancer for women aged 21–65 years without hysterectomy, only trends for Pap test within 3 years for women aged 21–65 years without hysterectomy were assessed; Pap test data for 2003 are missing.

§ The USPSTF recommends three options for CRC screening: 1) fecal occult blood test within 1 year; 2) sigmoidoscopy within 5 years and fecal occult blood test within 3 years; or 3) colonoscopy within 10 years for respondents aged 50–75 years.

White A, Thompson TD, White MC, et al. Cancer Screening Test use – United States, 2015. MMWR morb Mortal Wkly Rep 2017;66:201-206

Decreasing CRC Incidence and Mortality USA



Sources: incidence: SEER Program, 2016.

Mortality: US mortality Volumes 1930 to 1959, US

Mortality Data: 1960-2014, NCHC, CDC, 2016.

Siegel et al. CA Cancer J Clin 2017;67:177-193

Colorectal cancer statistics, 2020

Increasing Incidence and Mortality for Young Adults and Middle-Aged Adults

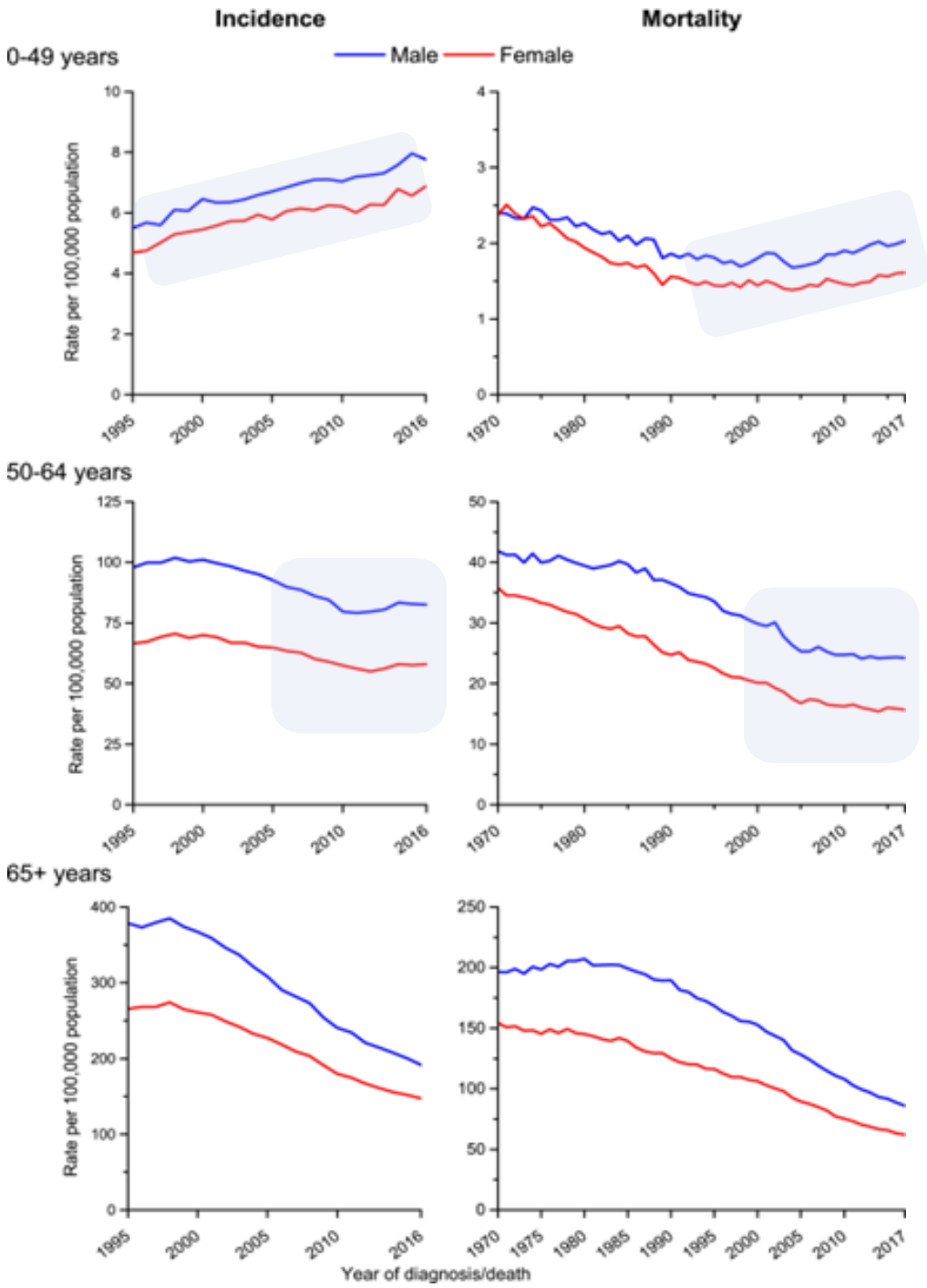
Siegel et al. CA Cancer J Clin 2020;70(3):145-164

Leveling off of CRC incidence and mortality for adults age 50-64

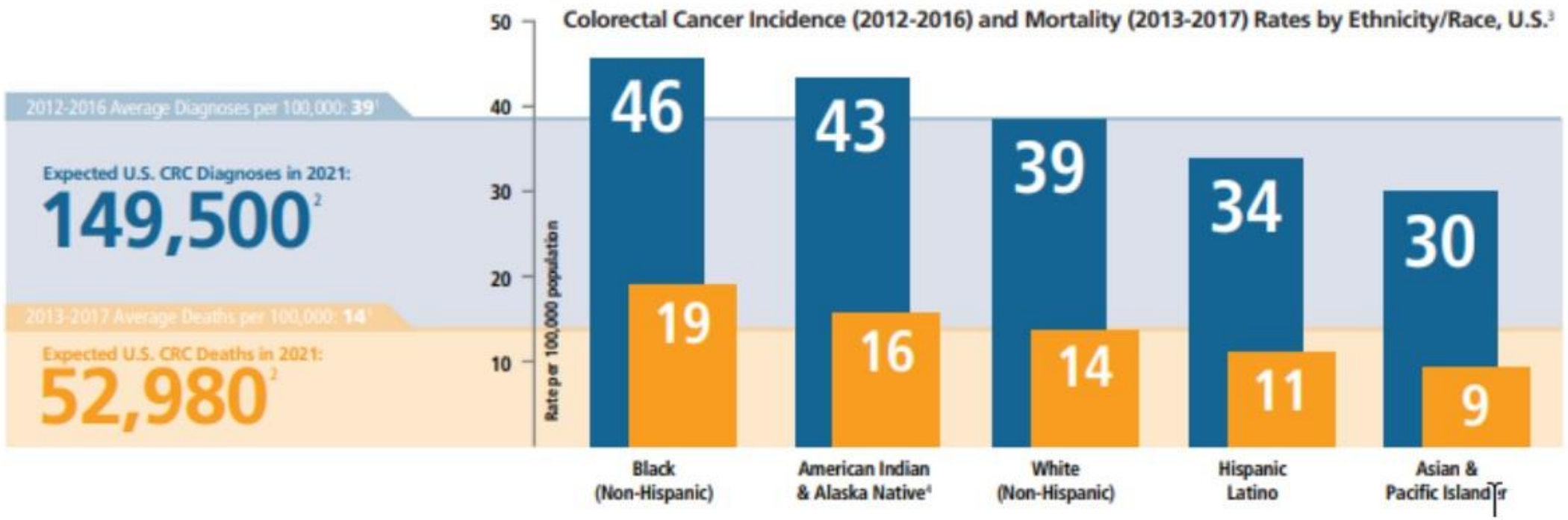
Increased incidence and mortality for ages 0-49

By 2030, colorectal cancer will be the leading cause of cancer related death in age 20-49

We Need to do Better!

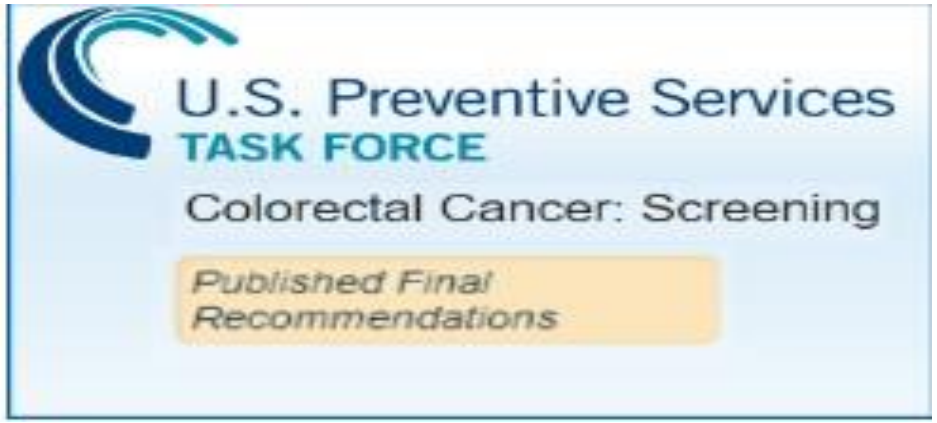


Disease Burden Varies by Race/Ethnicity



Compared to White individuals, **Black and American Indian/Alaska Native individuals have more cases and deaths from CRC.**

Gastroenterology Health Partners, 2021



Population	Recommendation	Grade
Adults aged 50 to 75 years	The USPSTF recommends screening for colorectal cancer in all adults aged 50 to 75 years. See the "Practice Considerations" section and Table 1 for details about screening strategies.	A
Adults aged 45 to 49 years	The USPSTF recommends screening for colorectal cancer in adults aged 45 to 49 years. See the "Practice Considerations" section and Table 1 for details about screening strategies.	B
Adults aged 76 to 85 years	The USPSTF recommends that clinicians selectively offer screening for colorectal cancer in adults aged 76 to 85 years. Evidence indicates that the net benefit of screening all persons in this age group is small. In determining whether this service is appropriate in individual cases, patients and clinicians should consider the patient's overall health, prior screening history, and preferences.	C

USPSTF Recommended Screening Modalities

Stool-based strategies

High Sensitivity FOBT
annually

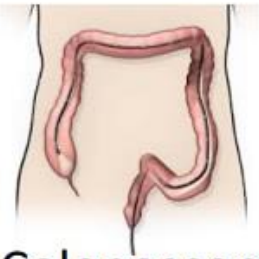
Fecal Immunochemical Test (FIT) *annually*

FIT-DNA (Cologuard)
Every 1-3 years

Direct-visualization techniques

Virtual (CT) Colonography
Every 5 years

Flexible Sigmoidoscopy with (Q10Y) or without FIT (Q5Y)



Colonoscopy
Every 10 years

Davidson K, et al. JAMA. 2021;325(19):1965-1977

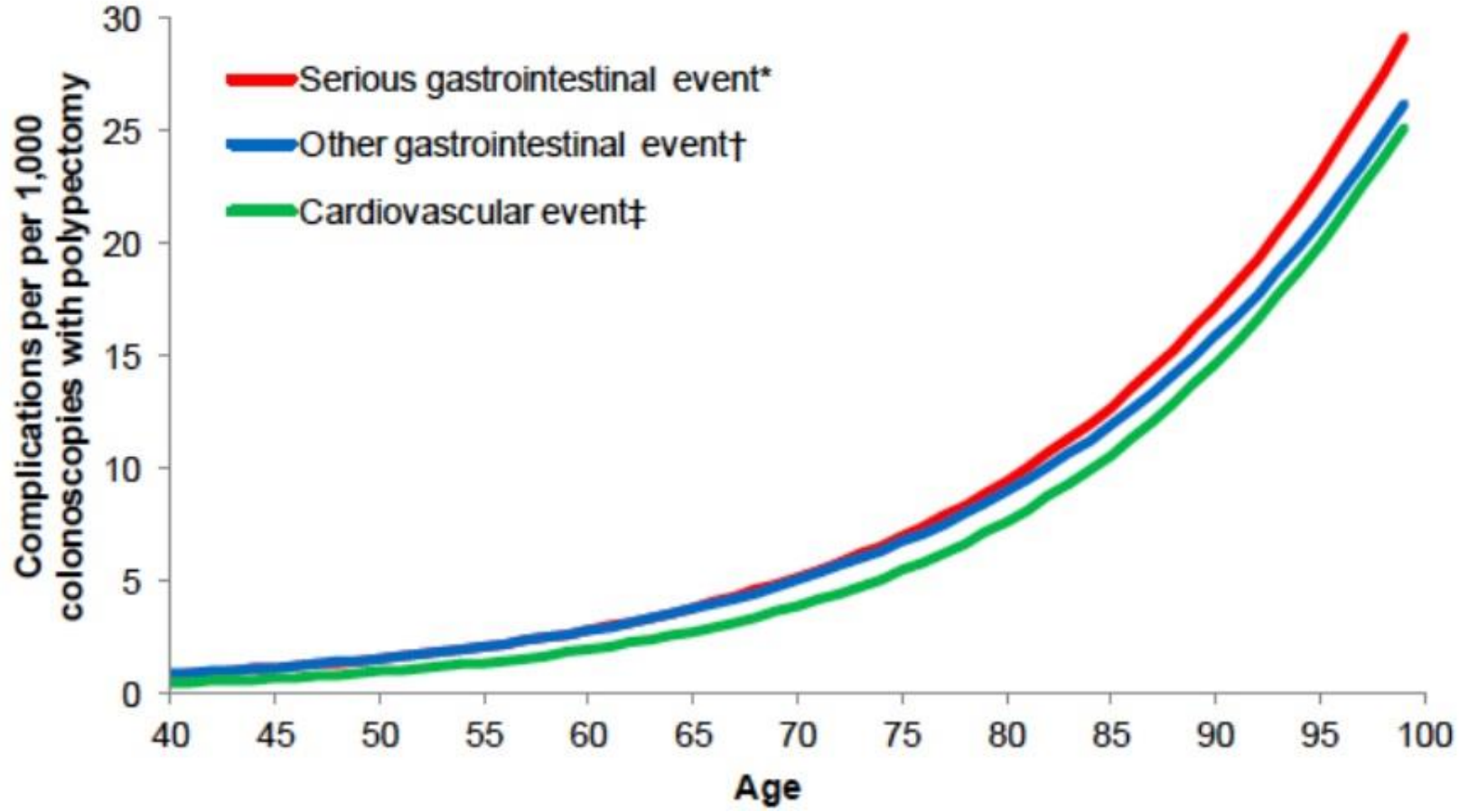
Age to stop screening

Individuals age 76-85

Selective offering of screening based on:

- Overall health (life expectancy, comorbidities)
- Prior screening history
- Patient preferences

Excess Risks of Colonoscopy Complications



ACA Preventive Services Coverage Clarification

Coverage of Colonoscopies Pursuant to USPSTF Recommendations

In 2016, the USPSTF recommended with an "A" rating screening for colorectal cancer starting at age 50 years and continuing until age 75 years. The Departments have issued several FAQs clarifying that if a colonoscopy is scheduled and performed as a screening procedure pursuant to the USPSTF recommendation, cost sharing may not be imposed for items and services that are an integral part of performing the colonoscopy.[23] These items and services include:

- Required specialist consultation prior to the screening procedure;[24]
- Bowel preparation medications prescribed for the screening procedure;[25]
- Anesthesia services performed in connection with a preventive colonoscopy;[26]
- Polyp removal performed during the screening procedure;[27] and
- Any pathology exam on a polyp biopsy performed as part of the screening procedure.[28]

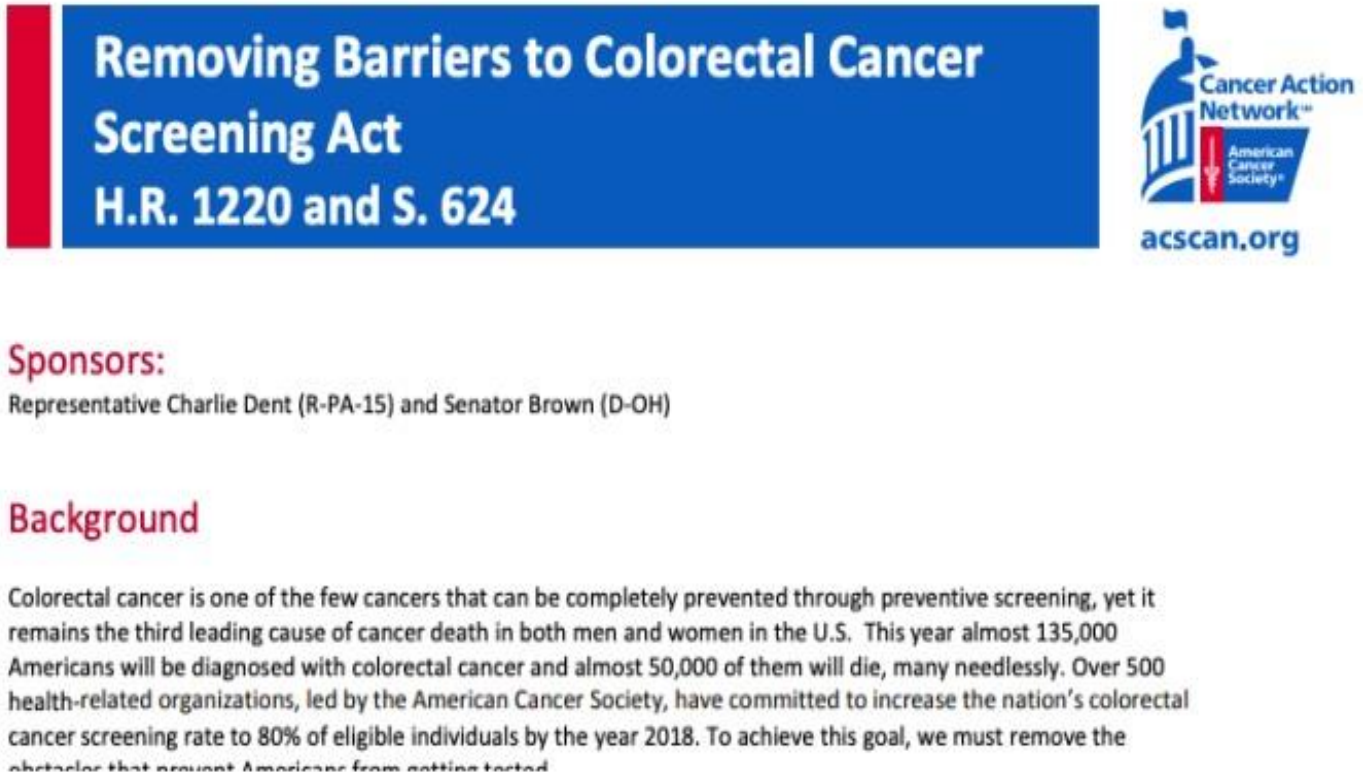
On May 18, 2021, the USPSTF updated its recommendation for colorectal cancer screening. The USPSTF continues to recommend with an "A" rating screening for colorectal cancer in all adults aged 50 to 75 years and extended its recommendation with a "B" rating to adults aged 45 to 49 years. In its "Practice Considerations" section detailing screening strategies, the Final Recommendation Statement provides: "When stool-based tests reveal abnormal results, follow-up with colonoscopy is needed for further evaluation.... Positive results on stool-based screening tests require follow-up with colonoscopy for the screening benefits to be achieved."[29] Additionally, the Final Recommendation Statement provides with respect to direct visualization

January 2022

Surprise bills for a colonoscopy done after a positive result from a stool-based screening test will be prevented under new federal rules. (Private insurers)

Departments of Labor, Health and Human Services (HHS), and the Treasury. January 10, 2022

Removing Barriers to Colorectal Cancer Screening Act



Removing Barriers to Colorectal Cancer Screening Act
H.R. 1220 and S. 624

Cancer Action Network
American Cancer Society
acscan.org

Sponsors:

Representative Charlie Dent (R-PA-15) and Senator Brown (D-OH)

Background

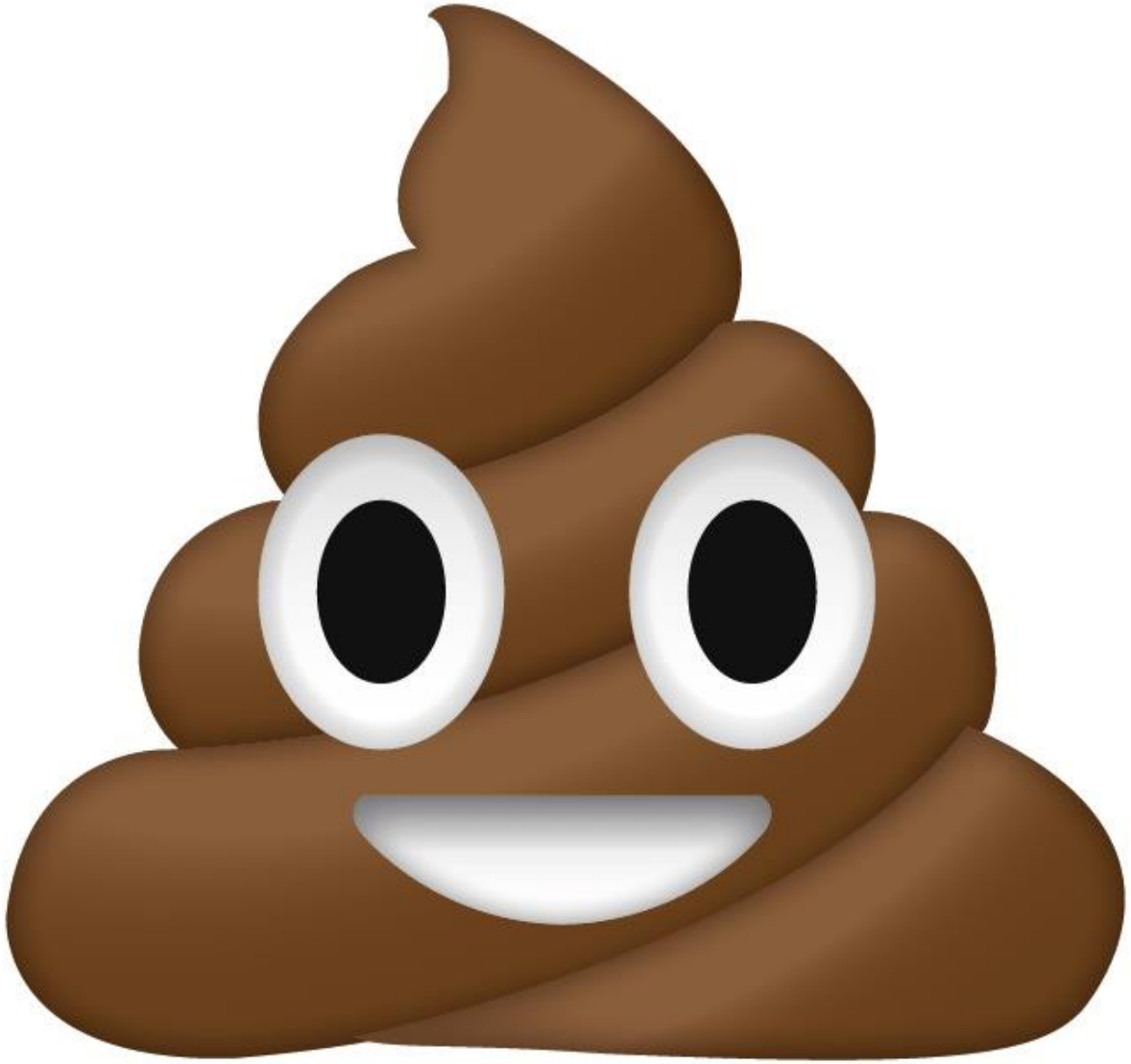
Colorectal cancer is one of the few cancers that can be completely prevented through preventive screening, yet it remains the third leading cause of cancer death in both men and women in the U.S. This year almost 135,000 Americans will be diagnosed with colorectal cancer and almost 50,000 of them will die, many needlessly. Over 500 health-related organizations, led by the American Cancer Society, have committed to increase the nation's colorectal cancer screening rate to 80% of eligible individuals by the year 2018. To achieve this goal, we must remove the obstacles that prevent Americans from getting tested

December 2020

Waives coinsurance requirements with respect to CRC screening tests, regardless of the code billed for a resulting diagnosis or procedure. The bill phases in implementation over an eight-year period.

U.S. Congress Bill: H.R. 1570/S.668

Stool based tests



1990s: Early FOBT Studies show ↓ Mortality

- 4 large randomized FOBT trials:
  - 15 %- 33 % reduction in CRC mortality
  - No change in all-cause mortality

- Minnesota Colon Cancer Control Study:

30-year follow up

  - 32 % reduction in CRC mortality
  - No change in all-cause mortality

Ransohoff DF, Lang CA. Ann intern Med 1997; 126:811-822.
Shaukat A, Mongin S, Geisser M. N Engl J Med 2013; 369:1106-1114.

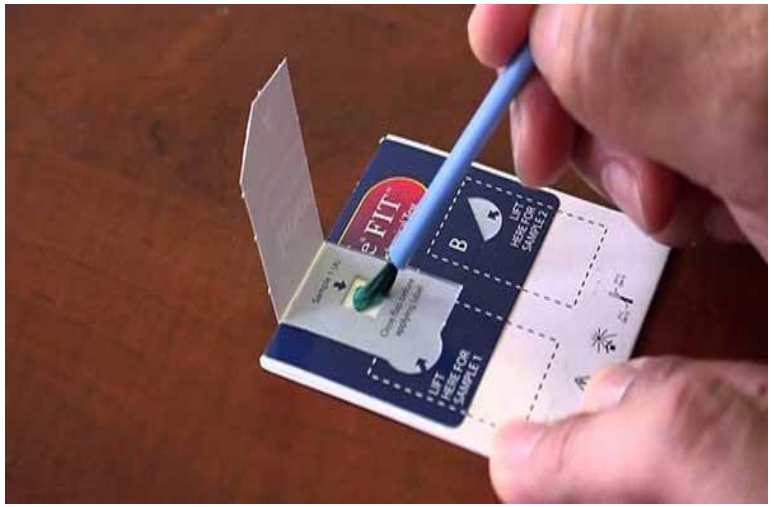
FOBT After Digital Rectal Exam

- 24 %-64 % of primary care providers use only digital FOBT as their primary screening test
- VA study of 3,121 asymptomatic patients, age 5-75
- Sensitivity for detection of advanced neoplasia (284 pts)
  - Six-sample at-home FOBT 23.9%
  - Digital FOBT 4.9%
- Conclusion: Single-sample digital FOBT is a poor screening method and is not recommended

Collins J, Liberman D, Durbin T, et al. Accuracy of screening for fecal occult blood on a single stool sample obtained by digital rectal examination: a comparison with recommended sampling practice. *Ann Intern Med* 2005; 142(2):81-85

FIT: Fecal Immunochemical Test

- Detects globin protein of hemoglobin molecule
- Does not require dietary modification
- Must be done yearly (Europe q 2 years)
- Can be quantitated
- If positive – MUST be followed with a timely colonoscopy
- " 2-step" Screening



Accuray of FIT Meta Analysis

Lee JK et al. Ann Intern Med 2014;160:171-181

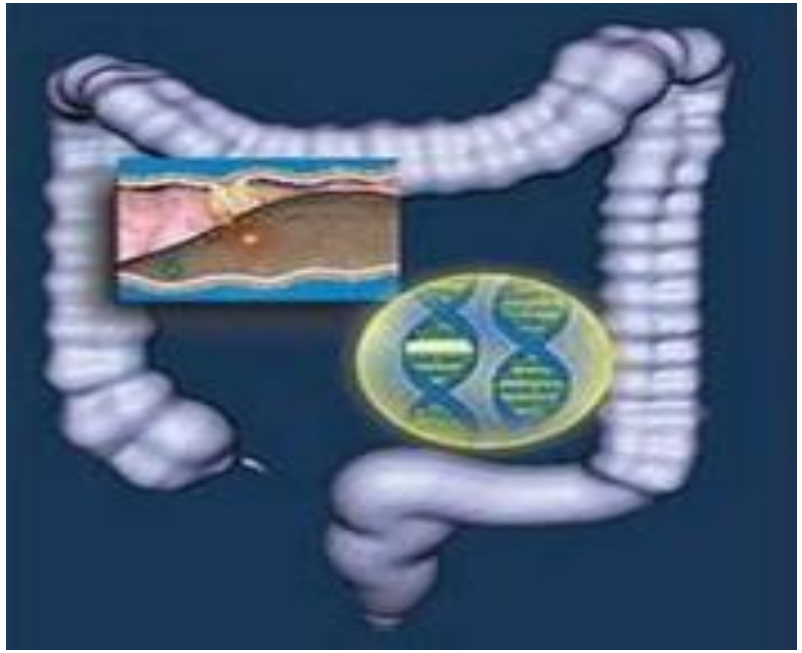
Pooled Sensitivity:	•70 % (69 %- 86%)
Pooled Specificity:	•94 % (92%-95%)

First Stool DNA testing: 2003

- Multi-target assay panel
- 21 point mutations in KRAS, APC, and P53 genes
- Microsatellite instability (MSI) marker (BAT-26)
- DNA Integrity Assay (DIA)

Stool DNA Testing: Early Result 2004

- Sensitivity 52 %
- Specificity 93 %- 97 %
- Not covered by insurance
- Expensive



Imperiale et al, NEJM 351:2704-14, 2004

Multi-targeted Test: FIT + DNA

Multi-Target DNA/FIT DeeP-C Results

Three Components

1. Two gene Methylation markers (NDRG4 and BMP3)
2. 7 KRAS Mutation markers
3. Fecal Hb (FIT)

Cancer Sensitivity: **92%** for CRC (**73.8 %** FIT alone)

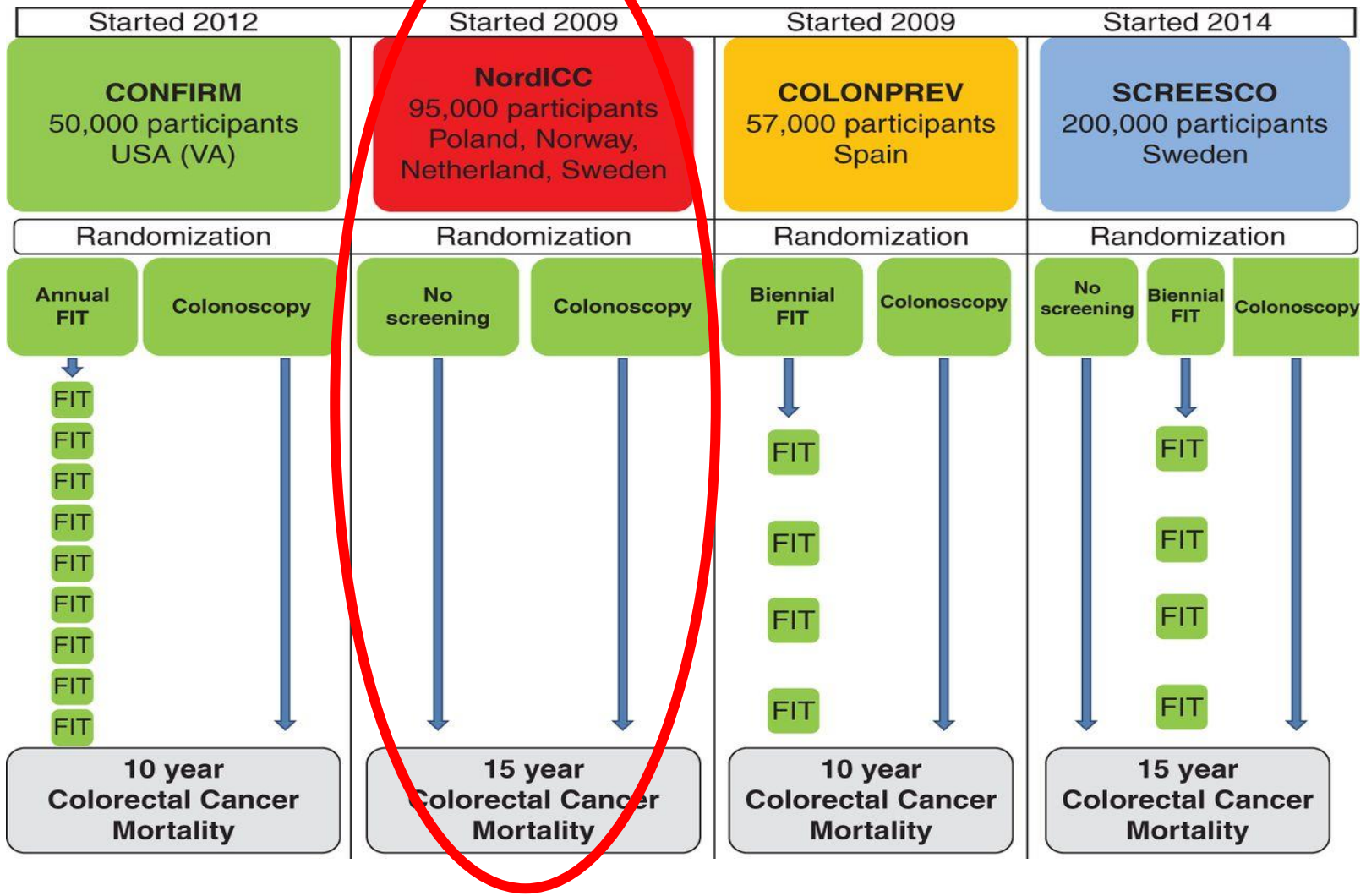
Polyp Sensitivity: **42%** polyps > 1 cm (**23.8 %** FIT alone)

Sessile Serrated: **42%** (**5.1 %** FIT alone)

Specificity: **87%** (**95%** FIT alone)

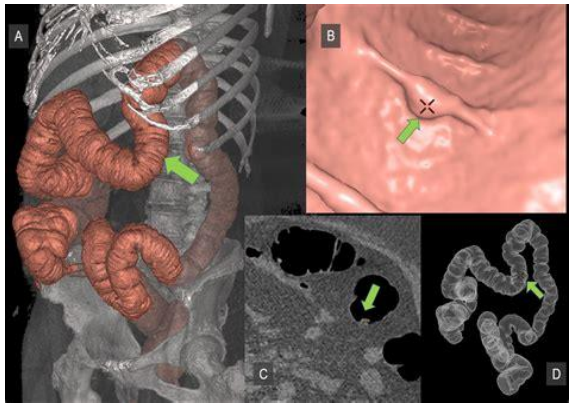
Imperiale et al. N Engl J Med. 2014;370(14):1287-1297

Ongoing Randomized Trials of CRC screening



Robertson et al. Gut 2015;64:982-990

CT Colonography:
ACRIN Data



Polyp size (MM)	≥ 5	≥ 6	≥ 7	≥ 8	≥ 9
Sensitivity	65 %	78 %	84 %	87 %	90 %

- Colonoscopy referral for all lesions ≥ 5 mm: 17%
- Extracolonic findings: 66%
- Extracolonic findings requiring evaluation: 16%

Johnson et al. N Engl J Med. 2008;359(12): 1207-1217 (ACRIN)

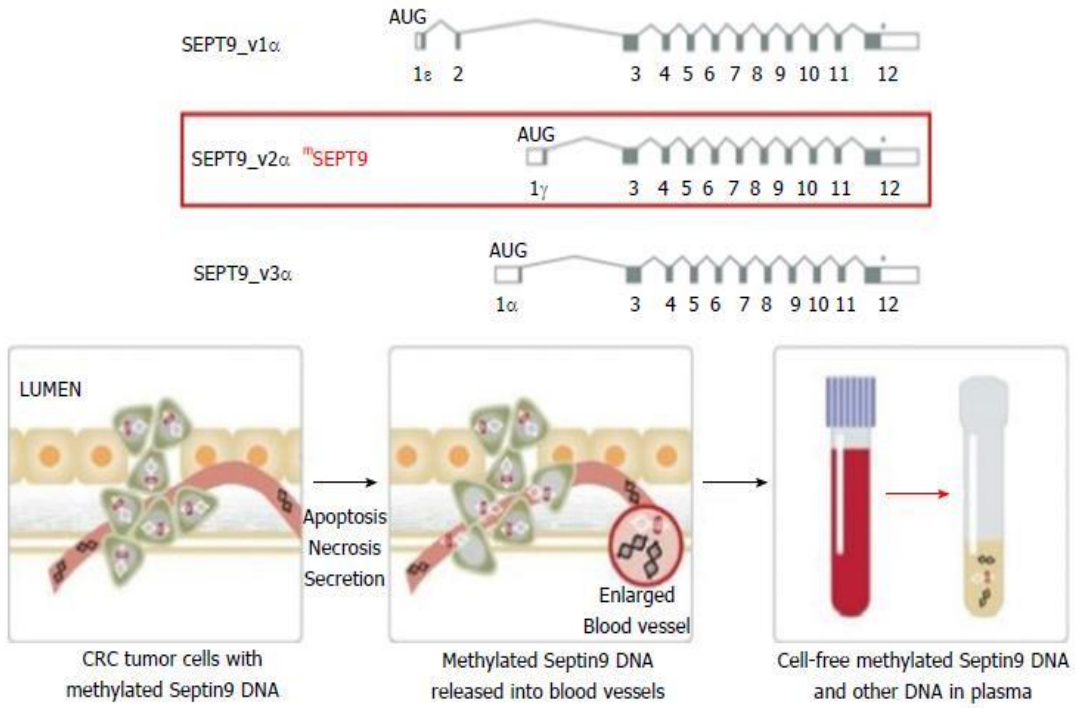
Colon Capsule Endoscopy (CCE)

- 8 studies used CCE as a filter test after a positive FIT result
- 5 studies used CCE for primary screening
- Polyp detection: **24 % - 74 %**
- Polyps > 6 m, sensitivity = **79 % - 96 %**
- Polyps >10 mm, sensitivity = **84 % - 97 %**
- CCE failed to evaluate the entire colon in approximately one-third of participants due either to inadequate bowel preparation or to incomplete examination

Vuik FER, Nieuwenburg SAV, Moen S, Spada C, Senore C, Hassan C, Pennazio M, et al.: Colon capsule endoscopy in colorectal cancer screening: a systemic review. Endoscopy. 2021 August;53(8):815-824

Septin 9: Not Recommended

- 25 studies were included for analysis
- Cell cycle related protein (cytokinesis)
- The pooled Data:
  - Sensitivity = 71 %
  - Specificity = 92 %
  - Positive ratio of mSEPT9 was higher in advanced CRC stage:
    - 45 % in I
    - 70 % in II
    - 76 % in III
    - 79 % in IV



Nian J, Sun X, Ming S, et al. Diagnostic Accuracy of Methylated SEPT 9 for blood-based Colorectal cancer Detection: A systematic Review and Meta-analysis. Clin Transl Gastroenterol. 2017;8(1):e216.

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Cancer - Blood-Based Biomarker Tests

National Coverage Analysis (NCA) Proposed Decision Memo

Screening for Colorectal Cancer - Blood-Based Biomarker Tests

CAG-00454N

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Decision Summary

The Centers for Medicare & Medicaid Services (CMS) proposes that the evidence is sufficient to cover a blood-based biomarker test as an appropriate colorectal cancer screening test once every 3 years, or at the interval designated in the Food and Drug Administration (FDA) label if the FDA indicates a specific test interval, for Medicare beneficiaries when performed in a Clinical Laboratory Improvement Act (CLIA)-certified laboratory, when ordered by a treating physician and when all of the following requirements are met:

The patient is:

- age 50-85 years, and,
- asymptomatic (no signs or symptoms of colorectal disease including but not limited to lower gastrointestinal pain, blood in stool, positive guaiac fecal occult blood test or fecal immunochemical test), and,
- at average risk of developing colorectal cancer (no personal history of adenomatous polyps, colorectal cancer, or inflammatory bowel disease, including Crohn's Disease and ulcerative colitis; no family history of colorectal cancers or adenomatous polyps, familial adenomatous polyposis, or hereditary nonpolyposis colorectal cancer).

Sensitivity for CRC	74 %
Specificity for CRC	90 %
FDA approval	Yes
Guideline endorsed	Yes

Test Characteristics of Screening Tests

Test	Sensitivity for CRC	Sensitivity for Adv adenoma	Specificity for CRC	Evidence	Risk	Deaths averted per 1000 screened
High sensitivity guaiac FOBT	62-79%	7%	87%-96%	Strong	Low	26
FIT	76-95%	27%-47%	89%-96%	Weak	Low	26
FIT-DNA (Cologuard)	93 %	43%	85%	Early	Low	28 (yearly) 25 (Q 3 years)
CT Colonography	96 %	67%-94% (>10mm) 73%-98% (6mm)	86%-98% (>10mm) 80%-93% (>6mm)	Weak	Low	26
Flexible Sigmoidoscopy	58 – 76 %	72%-86%	92%	Strong	Intermediate	24 (28 with FIT)
Colonoscopy	95 %	89%-98% (>10mm) 75%-93% (>6mm)	90%	Intermediate	High	28

Davidson K, et al. JAMA. 2021;325(19):1965-1977.
Knudsen et al. JAMA. 2021; 325(19): :1998-2011.

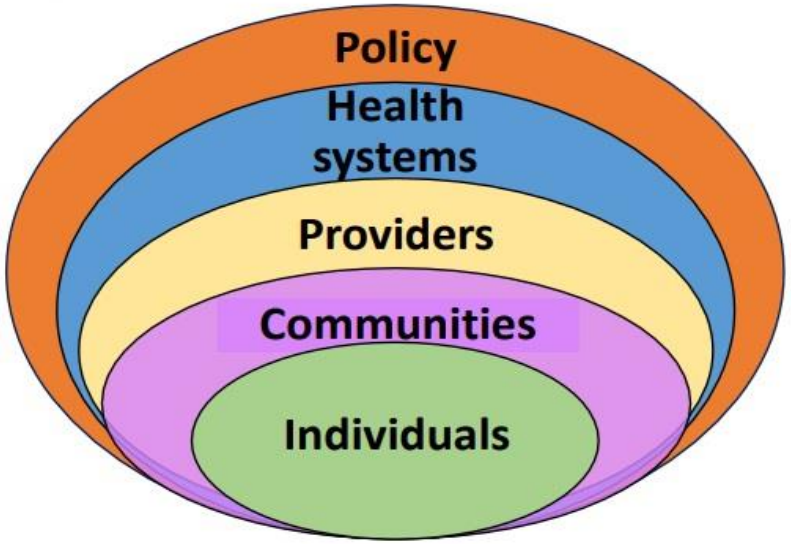
Patient Considerations for Screening Options

	HSgFOBT	FIT	FIT-DNA	CT Colonography	FS (+ FIT)	Colonoscopy
Invasiveness	+	+	+	++	++	+++
Home test	Yes	Yes	Yes	No	No	No
Dietary restrictions	Yes	No	No	Yes	Yes	Yes
Interval	1 year	1 year	1-3 years	5 years	5 (10 years)	10 years (if normal)
Complications	Negligible	Negligible	Negligible	Few	Few	Most (0.1%)
Patient Participation	Moderate	Moderate	Moderate	Moderate	Moderate	Lowest
Cost	$	$	$$	$$	$	$$

Robertson et al. AJG; 2017: 112; 37-53
Inadomi. NEJM; 2017; 376:1598-1600

Goal: 80% in Every Community

Various evidence based patient, provider, heath system, and policy level interventions

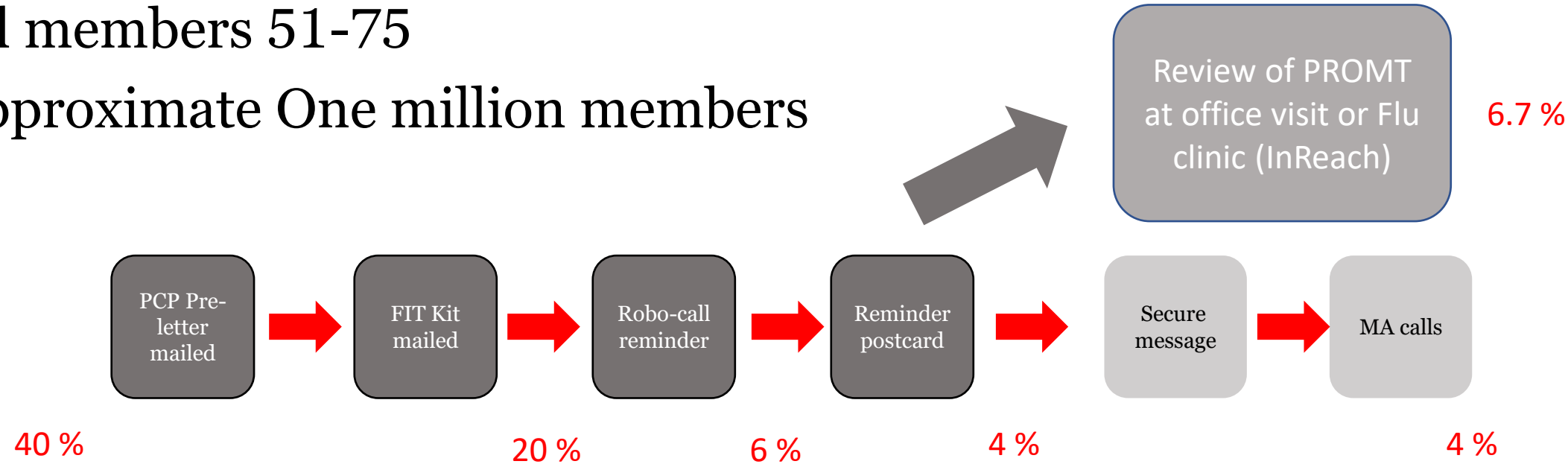


The best evidence-based interventions:

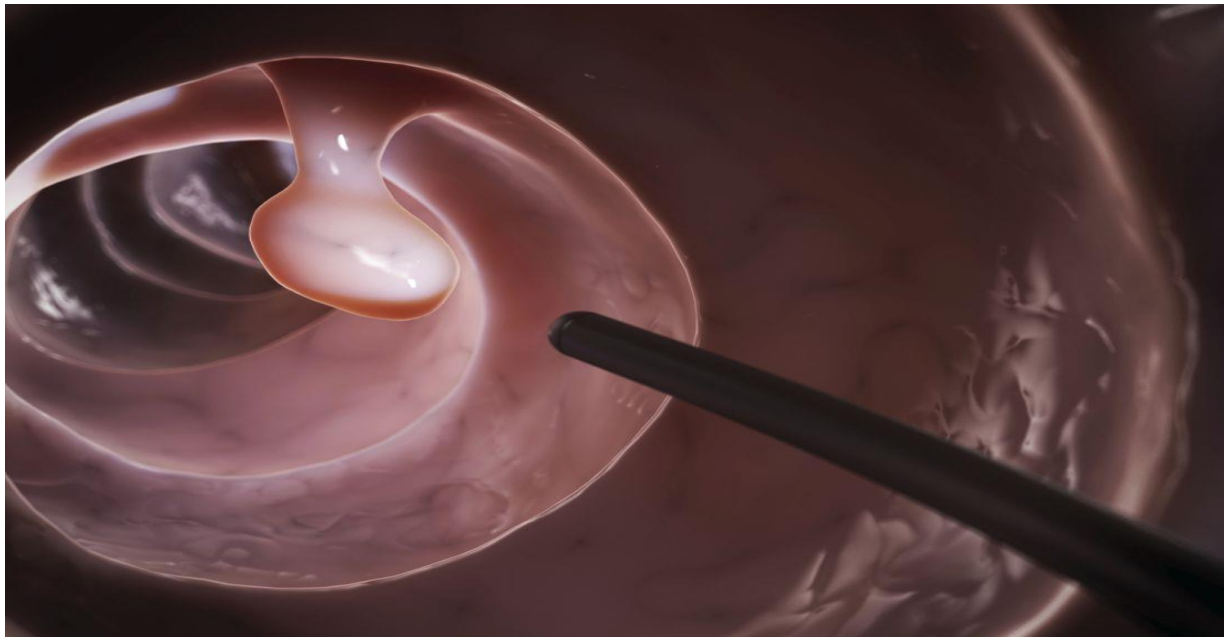
- Involve community stakeholders and members
- Have multiple components
- Address multi-level barriers to screening
- Are culturally tailored to the population
- Are sustainable over time
- Are disseminatable to other settings

Kaiser Permanente N. California CRC screening Program

- All members 51-75
- Approximate One million members

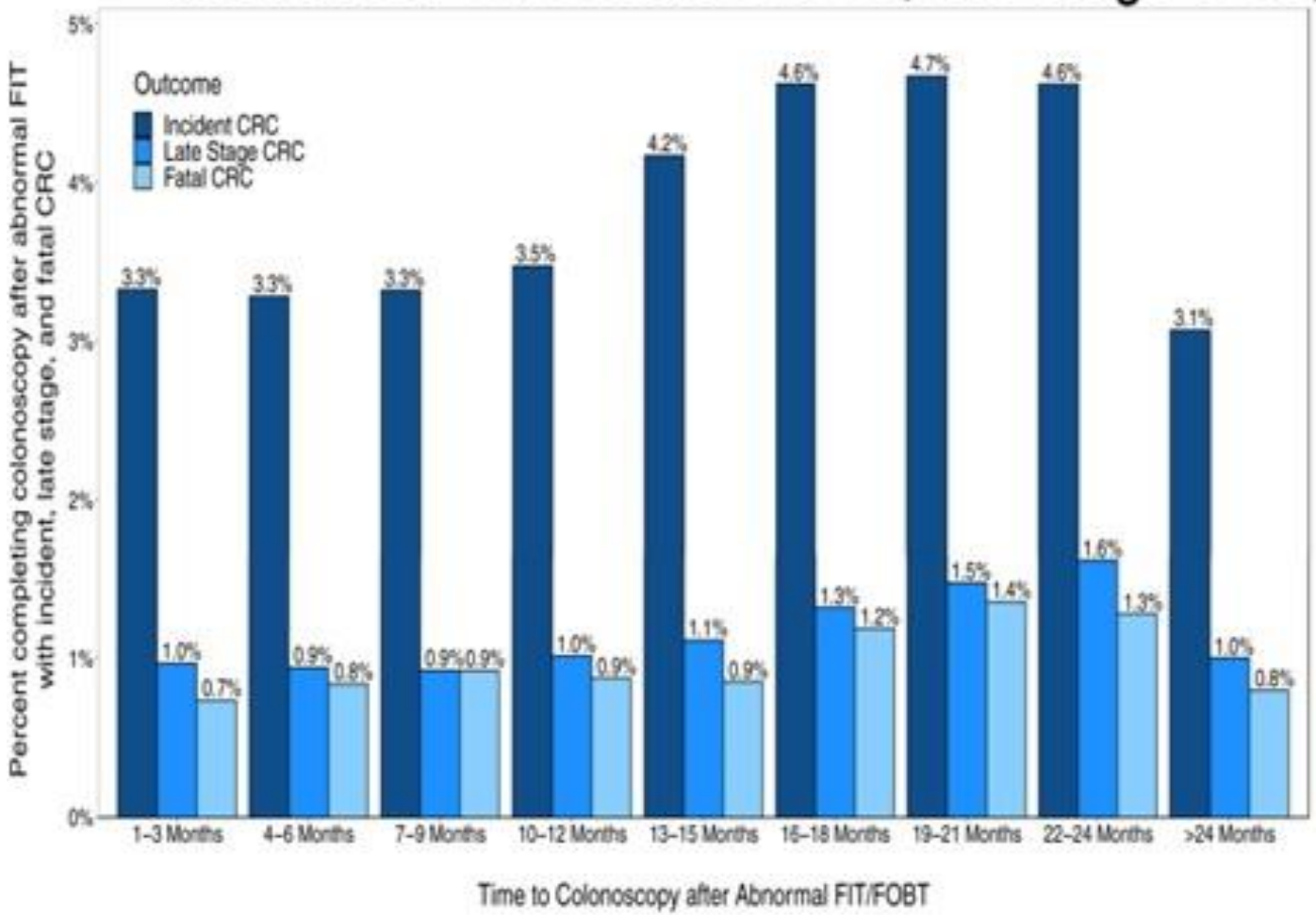


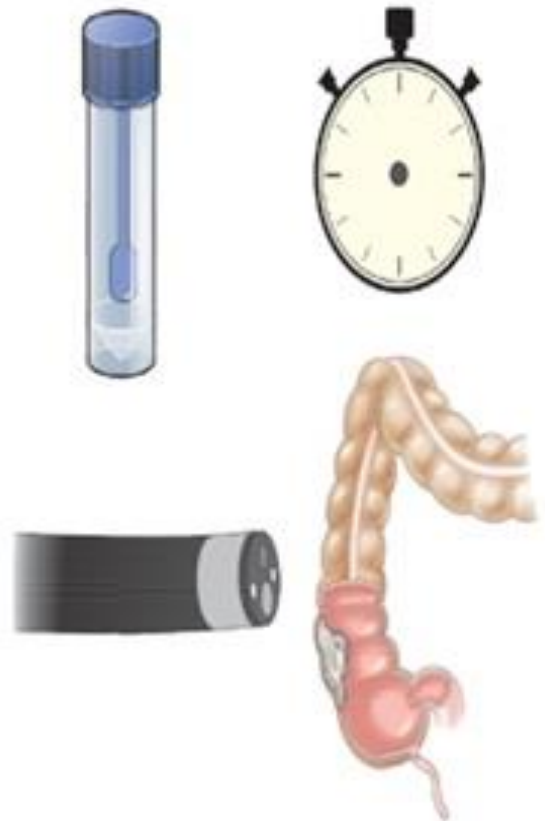
Other than a colonoscopy, all other screening tests are a "2-step" process



All positive screening tests require a colonoscopy

Increasing time to colonoscopy after abnormal stool-based testing is associated with incident CRC, late stage CRC, and fatal CRC





Gastroenterology

San Miguel et al. Gastro 2021

Colonoscopy

Quality Quality Quality

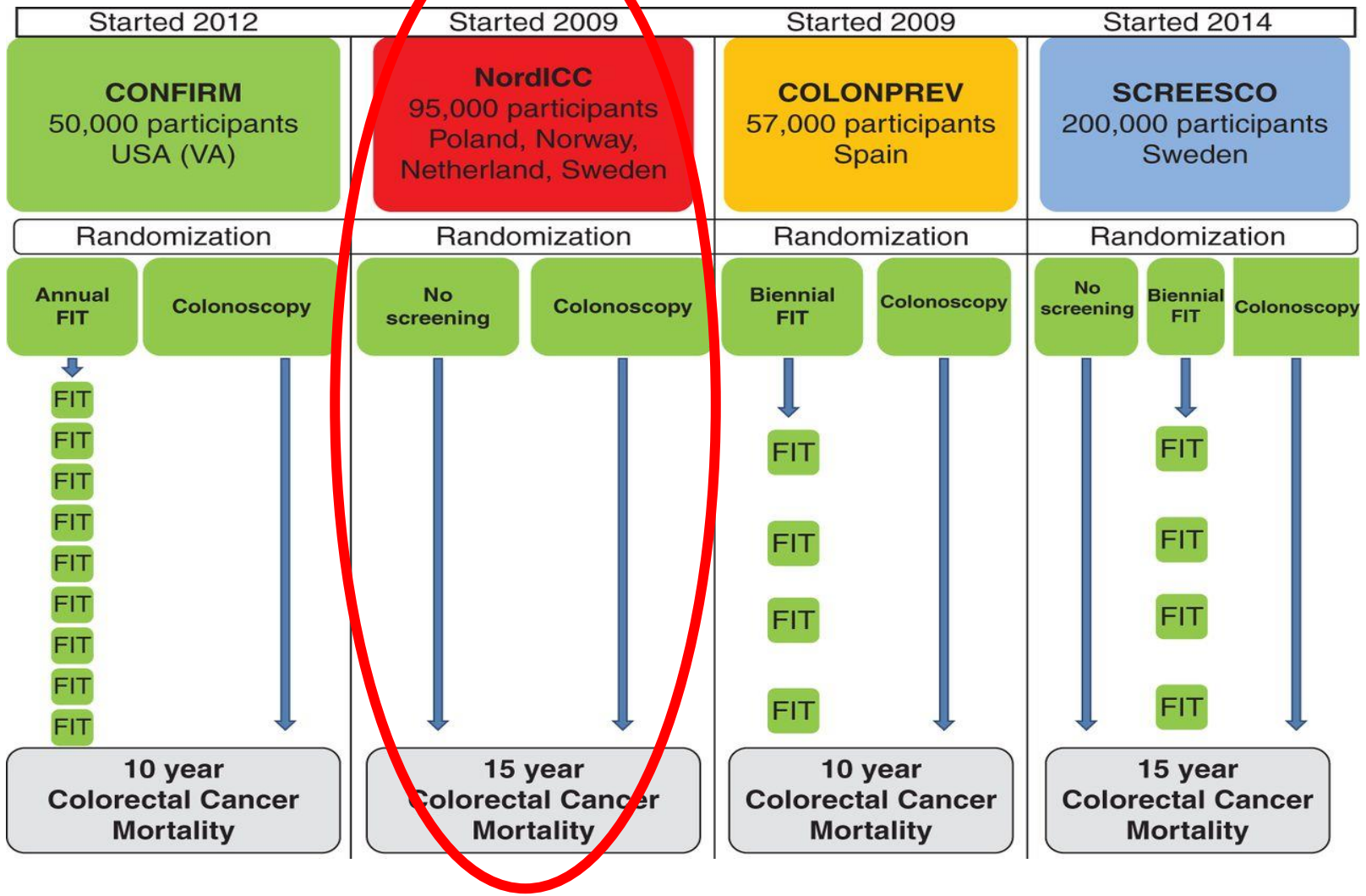
- ADR
- Withdrawal Time
- Technique
- Report Card
- Split Prep

Screening Colonoscopy Studies

	US 2009	Canada 2005	Germany 2014	Switzerland 2012	US (NHS) 2013	US 2013[b]	US (VHA) 2018	US (Kaiser Permanente) 2018
Design	Cohort	Case control	Case control	Cohort	Cohort	Case control	Case control	Case Control
N[a]	715	2,915[a]	6,332[a]	22,686	88,902[a]	980	24,820[a]	5,207
CRC incidence	0.52 (0.22–0.82)	0.69 (0.44–1.07)	0.09 (0.07–0.13)	0.31 (0.16–0.59)	NR	0.29 (0.15–0.58)	NR	NR
Relative risk reduction in CRC incidence	48%	31%	91%	69%	NR	71%	NR	NR
Proximal CRC incidence	NR	1.02 (0.72–1.45)	0.22 (0.14–0.33)	NR	NR	0.36 (0.16–0.80)	NR	NR
Relative risk reduction in proximal CRC incidence	NR	2% increase	78%	NR	NR	64%	NR	NR
CRC mortality	0.35 (0.0–1.06)	NR	NR	0.12 (0.01–0.93)	0.32 (0.24–0.45)	NR	0.30 (0.24–0.38)	0.33 (0.21–0.52)
Relative risk reduction in CRC mortality	65%	NR	NR	88%	68%	NR	70%	67%
Proximal CRC mortality	NR	NR	NR	NR	0.47 (0.29– 0.76)	NR	0.48 (0.35–0.66)	0.35 (0.18–0.65)
Relative risk reduction in proximal CRC mortality	NR	NR	NR	NR	53%	NR	52%	65%

CRC, colorectal cancer; NHS, Nurses Health study; NR, not reported; VHA, Veterans Health Administration.
[a]N is total for study and the screening colonoscopy cohort was a subgroup.
[b]Included late stage cancers (stage IIB and higher only).

Ongoing Randomized Trials of CRC screening



Robertson et al. Gut 2015;64:982-990

RESEARCH SUMMARY

Effect of Colonoscopy Screening on Risks of Colorectal Cancer and Related Death

Bretthauer M et al. DOI: 10.1056/NEJMoa2208375

CLINICAL PROBLEM

Although colonoscopy is widely used as a screening test to detect colorectal cancer, it is more invasive and requires more resources than fecal occult blood tests and sigmoidoscopy. To determine whether its benefits outweigh these costs, additional high-quality data are needed from randomized trials.

CLINICAL TRIAL

Design: A multinational, pragmatic, randomized trial assessed the 10-year effects of population-based colonoscopy screening on the risks of colorectal cancer and related death.

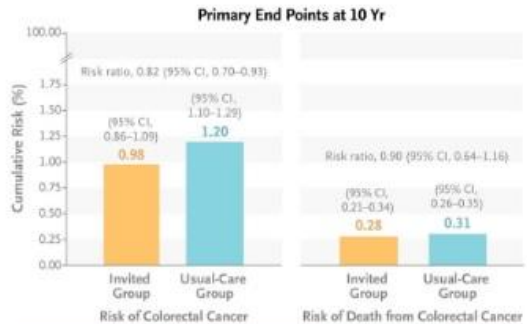
Intervention: 84,585 men and women 55 to 64 years of age who lived in Poland, Norway, and Sweden and who had not previously undergone screening were randomly assigned either to receive an invitation to undergo one-time colonoscopy screening (invited group) or to receive no invitation or screening (usual-care group). The primary end points were the risks of colorectal cancer and related death after median follow-ups of 10 years and 15 years.

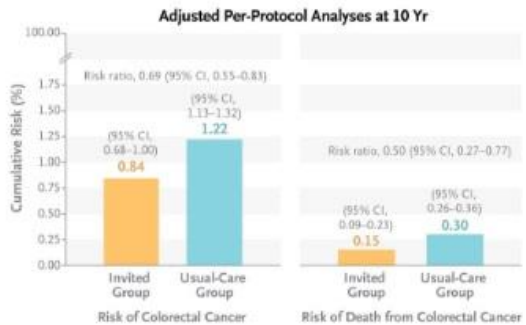
RESULTS

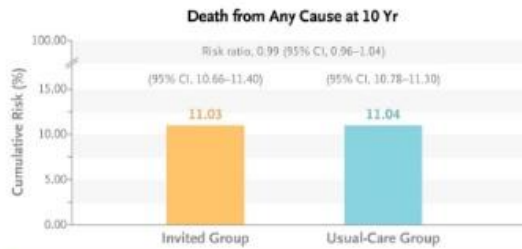
As compared with usual care, invitation to one-time screening colonoscopy reduced the risk of colorectal cancer over 10 years; 455 persons needed to be invited to undergo screening to prevent one case of colorectal cancer. Between-group differences in the risk of death from colorectal cancer were not significant.

LIMITATIONS

- Participation in screening was lower than expected in some countries (range, 33.0% to 60.7%).
- Information on adherence to recommendations regarding surveillance for polyps was lacking.
- Event rates were too low to assess variability according to quality indicators among endoscopists.
- Benefits with respect to the risk of colorectal cancer are expected to be apparent earlier than those with respect to the risk of death related to this disease; planned analyses after a median of 15 years of follow-up may be more informative in assessing the risk of death.







CONCLUSIONS

In participants 55 to 64 years of age who had not previously undergone screening, invitation to one-time screening with colonoscopy reduced the risk of colorectal cancer over a 10-year period.

Colorectal Cancer Incidence
Adjusted per-protocol analyses

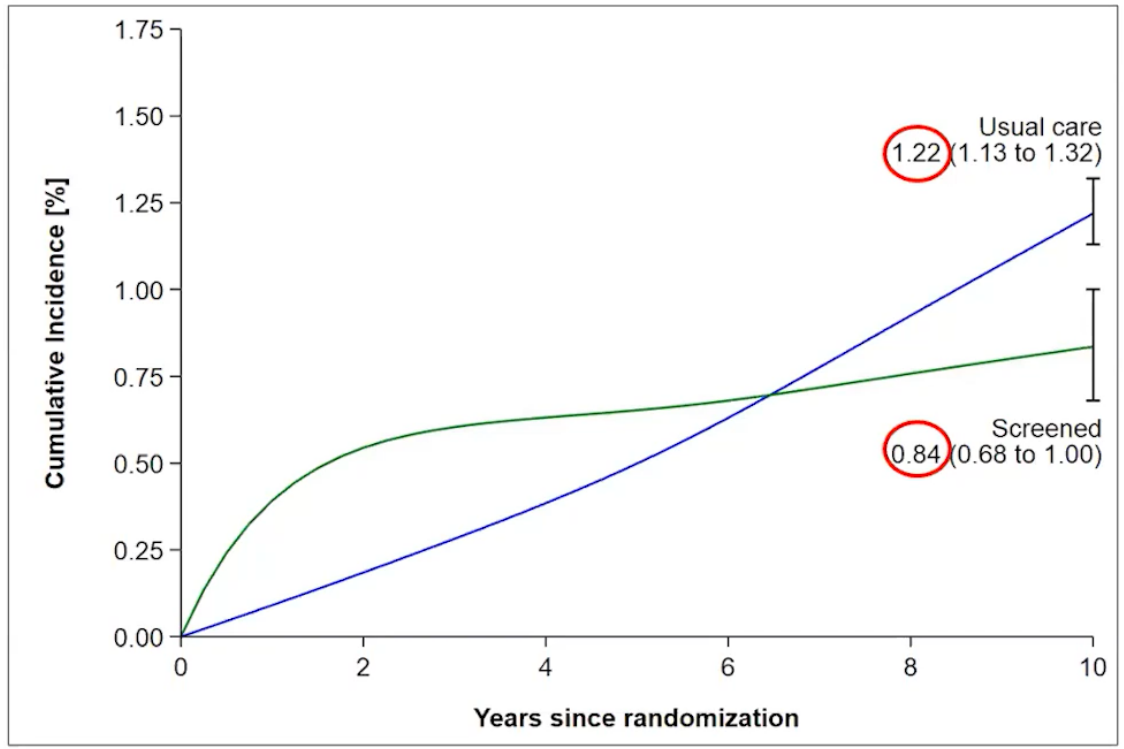
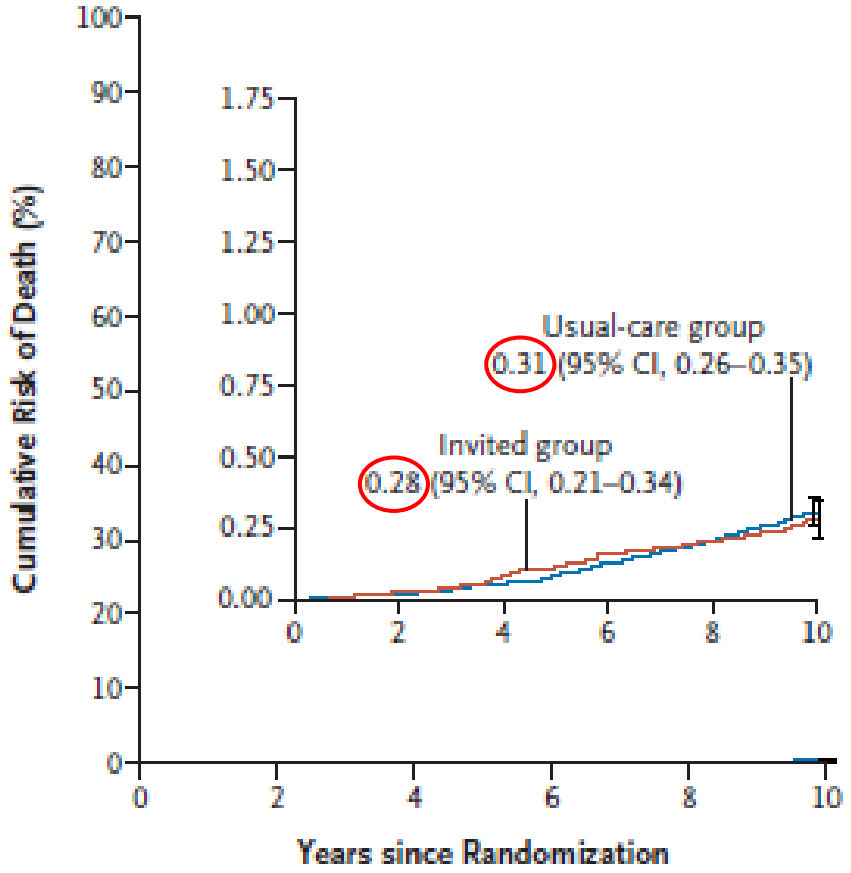


Table 2. Primary and Secondary End Points.

End Point	Invited Group		Usual-Care Group		Risk Difference (95% CI)	Risk Ratio (95% CI)
	Participants	10-Yr Risk (95% CI)	Participants	10-Yr Risk (95% CI)		
	number	*percent*	*number*	*percent*	*percentage points*	
Colorectal cancer	259	0.98 (0.86 to 1.09)	622	1.20 (1.10 to 1.29)	−0.22 (−0.37 to −0.07)	0.82 (0.70 to 0.93)
Death						
From colorectal cancer	72	0.28 (0.21 to 0.34)	157	0.31 (0.26 to 0.35)	−0.03 (−0.11 to 0.05)	0.90 (0.64 to 1.16)
From any cause	3036	11.03 (10.66 to 11.40)	6079	11.04 (10.78 to 11.30)	−0.01 (−0.47 to 0.44)	0.99 (0.96 to 1.04)

Table S7: Colorectal cancer stages in screening and no-screening groups based on Dukes[4].

	Screening, Number (%)	**No-screening, Number (%)**
Stage A	39 (0.14%)	78 (0.14%)
Stage B	69 (0.24%)	169 (0.30%)
Stage C	66 (0.23%)	174 (0.31%)
Stage D	47 (0.17%)	107 (0.19%)
Unknown stage	38 (0.13%)	94 (0.17%)



No. at Risk						
Invited group	28,220	27,768	27,224	26,591	25,273	18,856
Usual-care group	56,365	55,469	54,362	53,086	50,356	37,604

Figure 3. Cumulative Risk of Death from Colorectal Cancer at 10 Years in Intention-to-Screen Analyses.

The inset shows the same data on an enlarged y axis. I bars indicate 95% confidence intervals.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Effect of ~~Colonoscopy Screening~~ Mailing Letters to People on Risks of Colorectal Cancer and Related Death

M. Bretthauer, M. Løberg, P. Wieszczy, M. Kalager, L. Emilsson, K. Garborg, M. Rupinski, E. Dekker, M. Spaander, M. Bugajski, Ø. Holme, A.G. Zauber, N.D. Pilonis, A. Mroz, E.J. Kuipers, J. Shi, M.A. Hernán, H.-O. Adami, J. Regula, G. Hoff, and M.F. Kaminski, for the NordICC Study Group*

Colonoscopy is Operator dependent

1997: Study with Tandem Colonoscopies

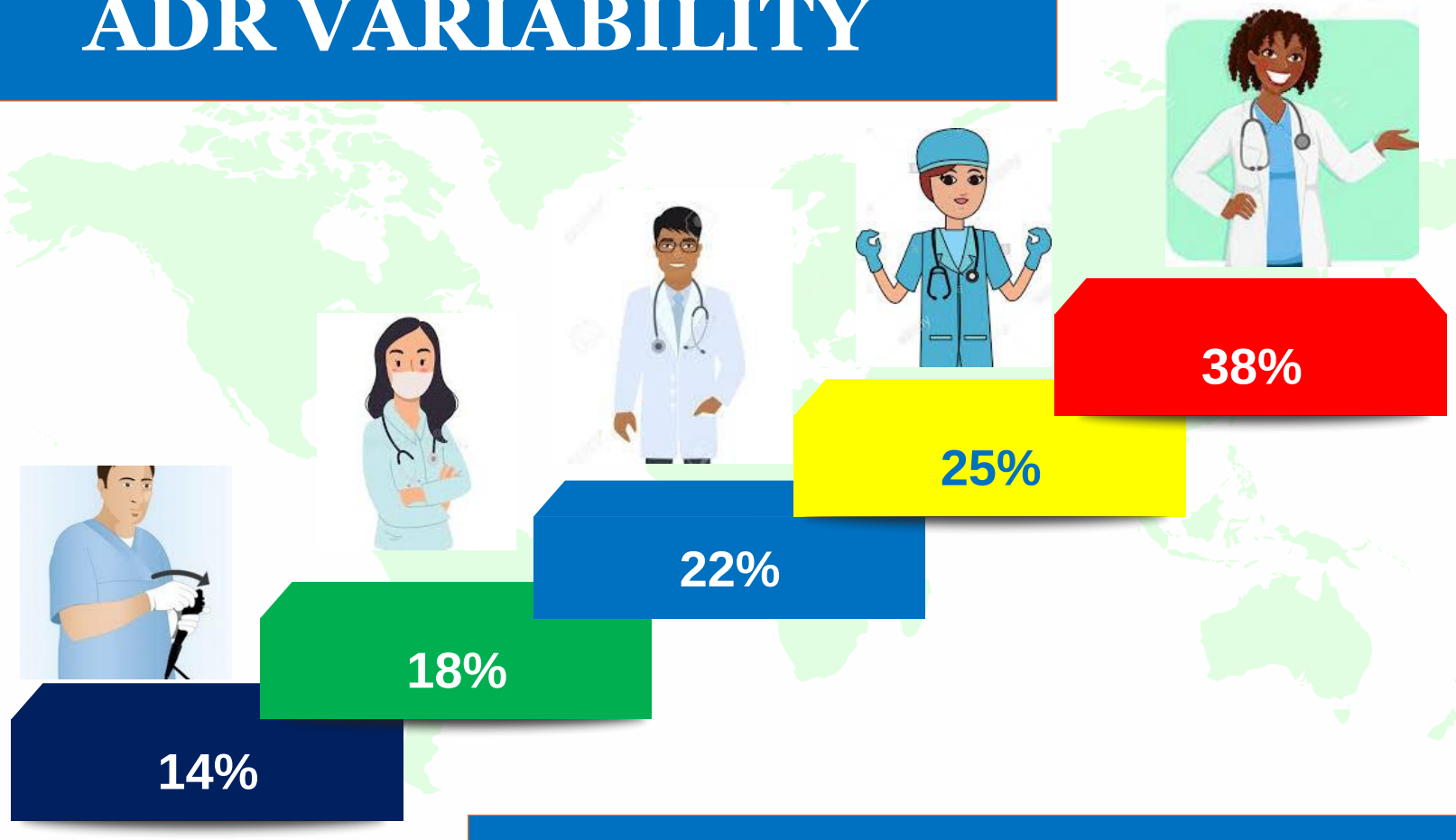
Overall adenoma miss rate = 24 %

Miss rates by endoscopist: 17-48 %

Size	Adenoma Miss rate
Less than or = 5 mm	27 %
6-9 mm	13 %
Greater than or = 1 cm	6 %

Rex DK et al. Colonoscopic miss rates of adenoma determined by back to back colonoscopies. Gastroenterology 1997;112:24-28

ADR VARIABILITY



Adenoma Miss Rate

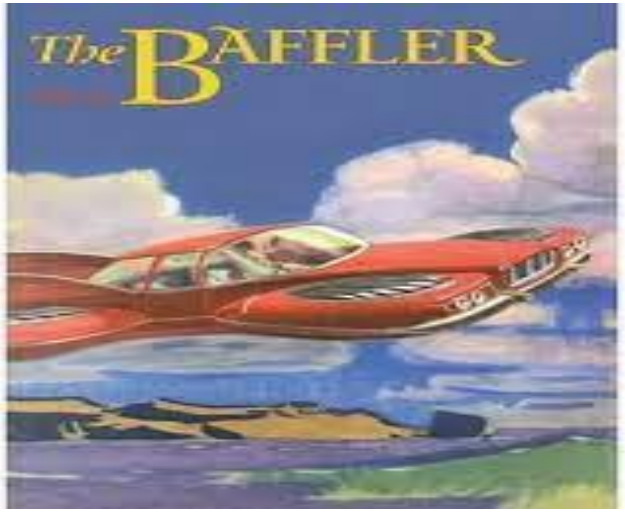
ADR Targets: Primary screening and + FIT

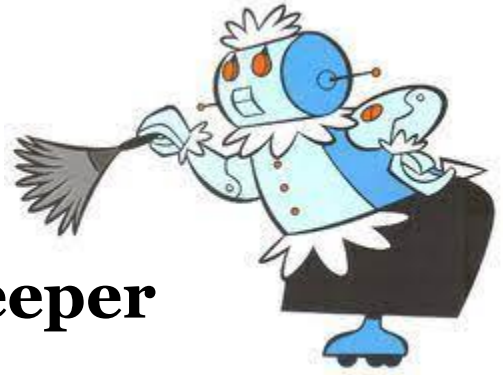
Primary screening	**FIT +**
Minimum acceptable	Minimum acceptable
25 %	40 %
Optional or aspirational	Optional or aspirational
50 %	70 %

- ✓ 9 mins withdrawal time
- ✓ Combined mechanical enhancement and AI
- ✓ Institutional target for SSA 7-8 %


BETTER
GOOD

Flying cars





Robot housekeeper

What About Colonoscopy Technology?

- Seeing better
- Identifying polyps better

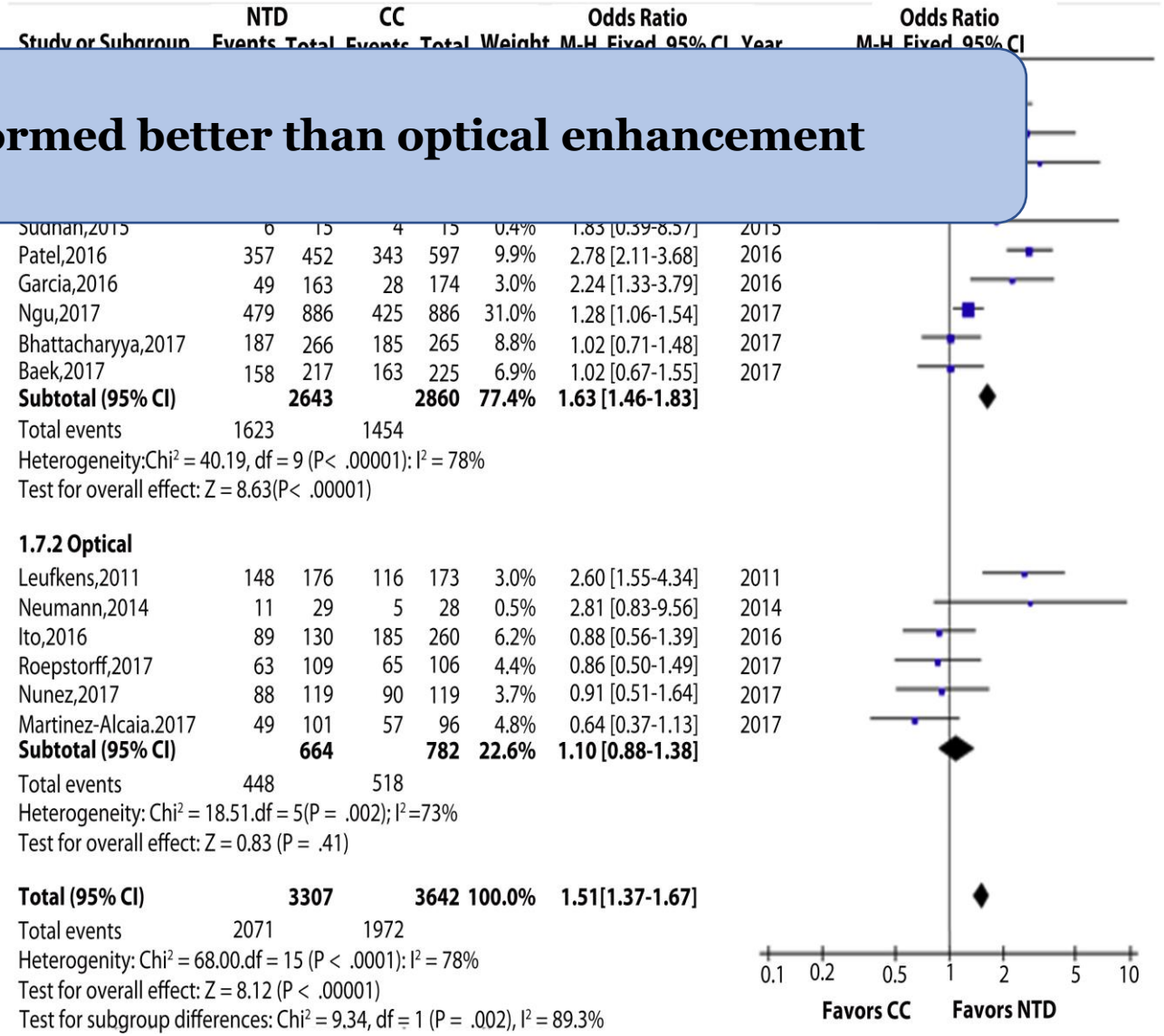
Innovations in Colonoscopy

Attachments

Scope Design

Mechanical Enhancement performed better than optical enhancement

Mechanical
Vs.
Optical Enhancement



Castaneda D, Popov VB, Verheyen E. et al. New technologies improve adenoma detection rate, adenoma miss rate, and polyp detection rate: a systematic review and meta-analysis. Gastroentist Endosc. 2018 Aug;88(2):209-222

Artificial Intelligence and polyp detection: meta-analysis

- 44 % relative increase in ADR
- 70 % relative increase in adenoma per colonoscopy (APC)
- No effect on the efficiency of colonoscopy
- Similar withdrawal time between the 2 arms

Hassan C, et al. Performance of artificial intelligence in colonoscopy for adenoma and polyp detection: a systematic review and meta-analysis, Gastrointestinal Endoscopy 2021;93:77-85

RCTs AI for detection

Author	Country	Year	Number of patients	ADR without AI	ADR with AI	P-value
Wang	China	2019	1058	20.3	29.1	<0.001
Su	China	2020	659	16.5	28.9	<0.001
Repici	Italy-U.S.	2020	685	40.4	54.8	< 0.001
Wang	China	2020	1046	28	34	0.03
Liu	China	2020	1026	23.8	39.1	<0.001

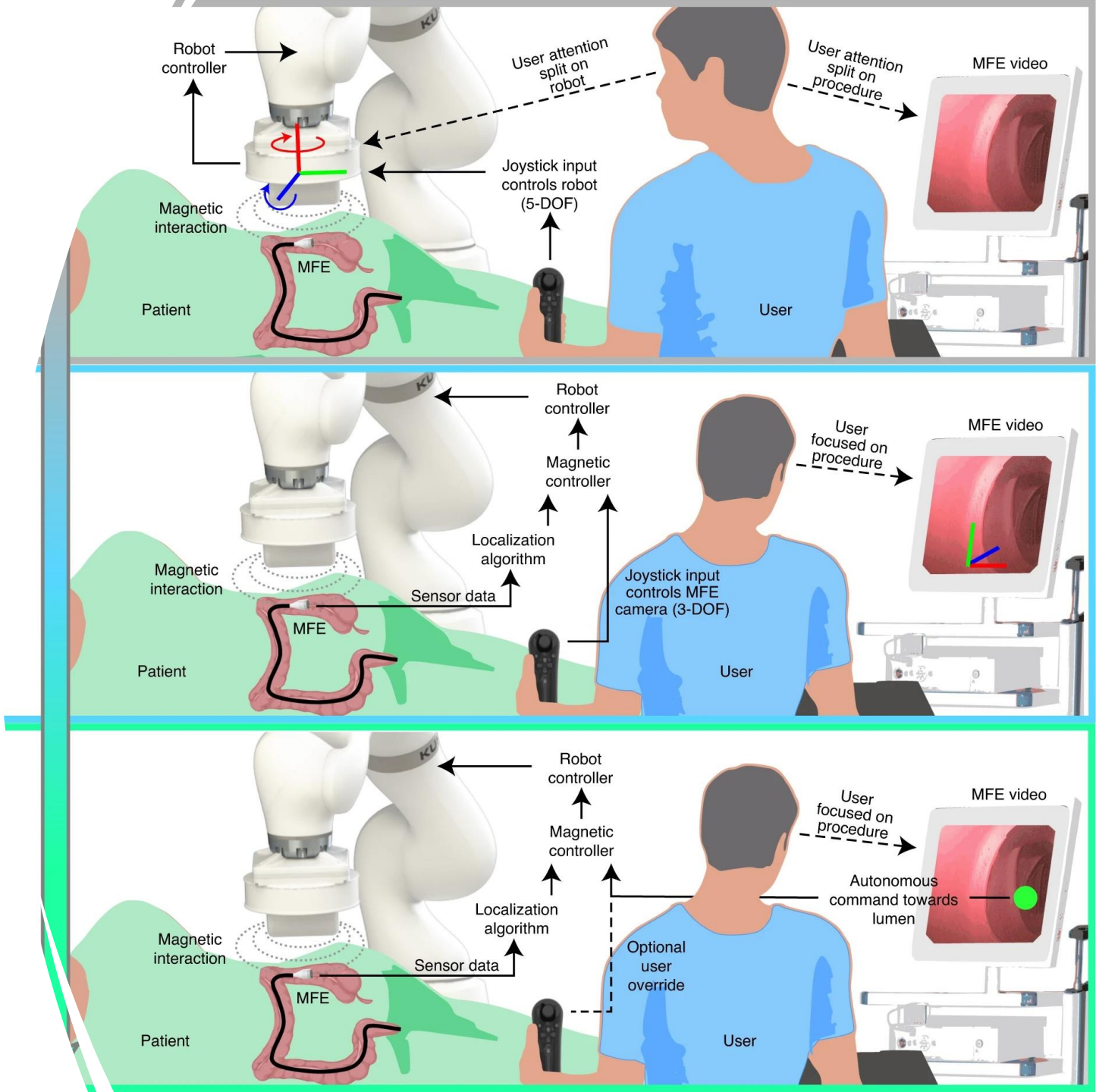
Where are the:

Self-propelled scopes?

Auto pilot scopes?

Joystick controlled scopes?

3D scopes?



What About other non-colonoscopy Non-Invasive Tests?

New Non-Invasive CRC Tests

1. Molecular Markers
2. DNA
   - mutations
   - methylation markers
3. RNA
   - microRNAs
4. Gut microbiome composition
5. Volatile organic Compounds (VOC)

VOC Dog Scan

- Volatile organic compounds (VOCs)
- Breath/ Stool evaluated by a trained Labrador Retriever
- Healthy controls vs. Patients with colorectal cancer

	Breath (N=33)	Stool (N=37)
Sensitivity	91 %	97 %
Specificity	99 %	99 %

Sonoda H, Kohnoe S, Yamazato T, et al. Colorectal cancer screening with odor material by canine scent detection. Gut 2011;60(6) 814-819

Electronic nose

Colorectal cancer and Advanced Adenomas versus Controls

Analysis[a]	Cases	Controls	AUC	Sens (%)	Spec (%)	PPV (%)	NPV (%)
CRC vs. controls							
Training model	42	68	0.76	83	60	56	85
Blind predictions (validation)	20	36	0.74	80	64	41	85
Final model with all data	62	104	0.84	95	64	61	96
AA vs. controls							
Training model	74	68	0.71	82	59	69	75
Blind predictions (validation)	38	36	0.61	67	45	69	59
Final model with all data	112	104	0.73	79	59	67	73

Abbreviations: AA, Advanced adenomas; AUC, area under the curve; CRC, colorectal cancer; NPV, negative predictive value; PPV, positive predictive value; Sens, sensitivity; Spec, specificity; vs, versus.

[a]These analysis only included breath tests performed before the bowel preparation.

CRC Sensitivity: 80- 95 %

CRC Specificity: 60- 64 %

Van Keulen, et al. Volatile organic compounds in breath can serve as a non-invasive diagnostic biomarker for the detection of advanced adenomas and colorectal cancer. Aliment Pharmacol Ther. 2020. Feb;51(3):334-346

Post endoscopy surveillance

Predictor/endpoint	Definition
Low-risk adenoma/non-advanced adenoma	1-2 tubular adenomas, <10 mm in size
Advanced adenoma	Adenoma >10 mm, villous features, and/or high grade dysplasia
Advanced neoplasia	Advanced adenoma or colorectal cancer (CRC)
High-risk adenoma	Advanced neoplasia or 3 or more adenomas any size
Sessile serrated adenoma/polyp/lesion (SSA/P)	Histologically confirmed lesion
Serrated polyp	SSA/P/L or hyperplastic polyp

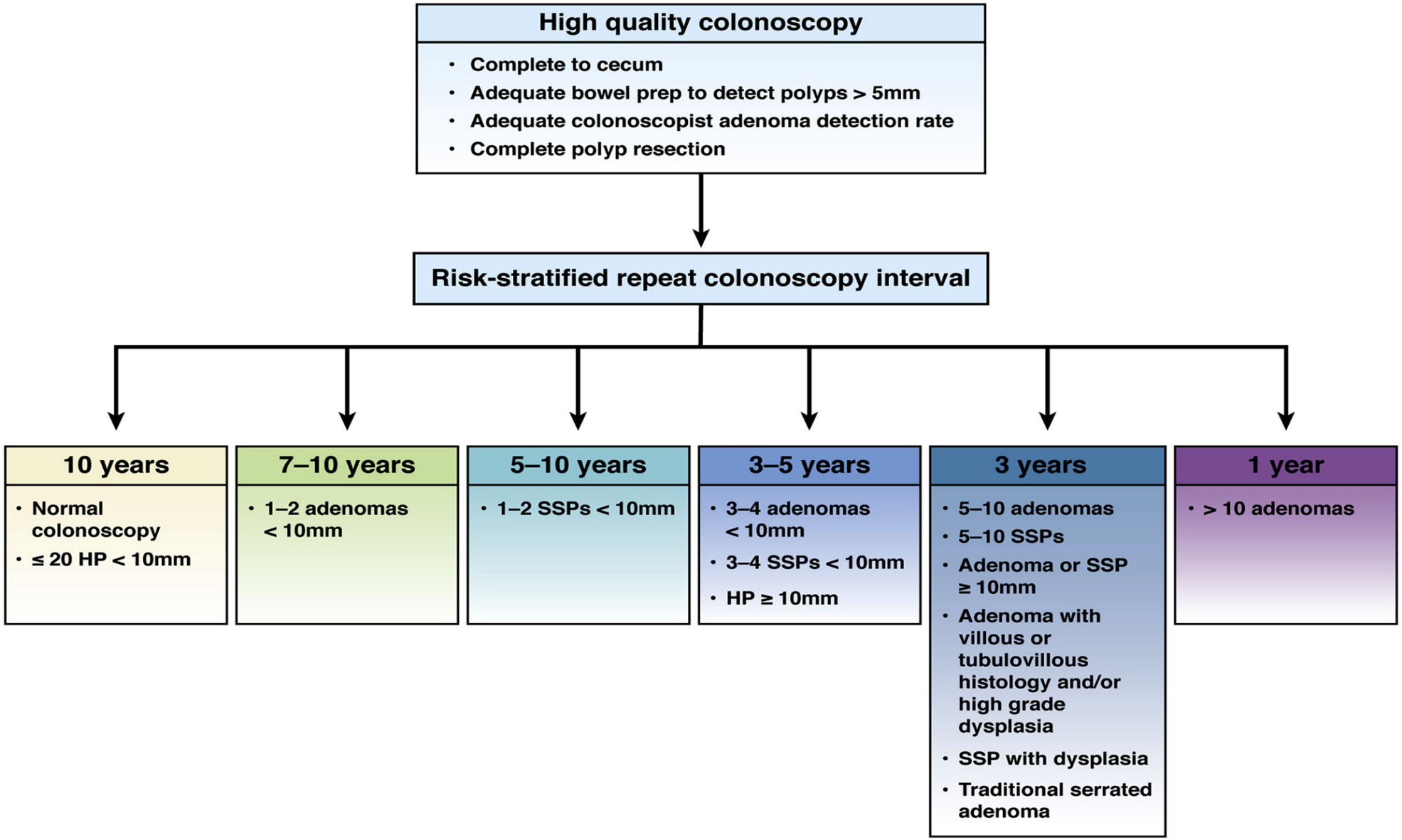


Figure 1. Recommendations for follow-up after colonoscopy and polypectomy. Recommendations for post-colonoscopy follow-up in average risk adults are depicted. After high-quality colonoscopy defined by examination complete to cecum adequate to detect polyps >5 mm, performed by a colonoscopist with adequate ADR with complete polyp resection, risk-stratified repeat colonoscopy intervals are provided. SSP, sessile serrated polyp/sessile serrated adenoma/sessile serrated lesion.

Diagnostic and therapeutic strategy

Screening colonoscopy

Some ↓ suspicious lesions

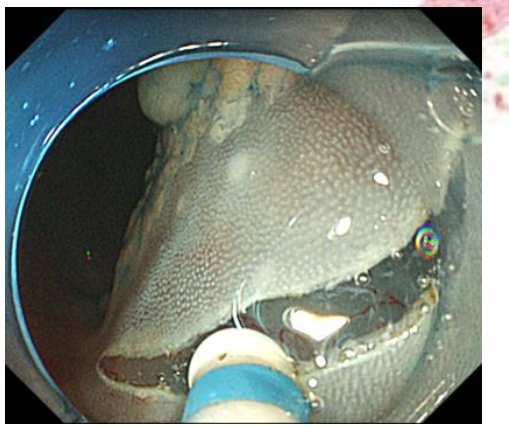
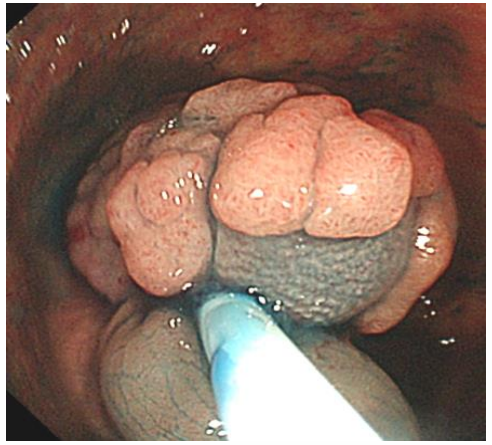


Image Enhanced Endoscopy (NBI, Indigocarmin)



Small adenoma
Small mucosal ca.

Large lesion or sm suspected

Magnification (crystal violet)

Large adenoma
Large mucosal ca.

Deep sm suspected

EUS

Slightly invasive
sm ca.

sm massive

Polypectomy, EMR

EPMR

ESD

Surgery

Approach to Colon Cancer screening

1 Step tests

2 Step tests

Colonoscopy

Stool based
Imaging based
*Blood based

You are asked to provide CRC screening guidance for a 77-year old male. He has no personal or family history of colorectal cancer, denies gastrointestinal symptoms, and has never been screened.

Which approach is consistent with the USPSTF CRC screening recommendations?

a) Offer screening colonoscopy now; no further screening if normal

b) Offer no screening; patient exceeds eligible screening age

c) Offer FIT or FIT DNA (Cologuard) screening, followed by colonoscopy if abnormal

d) Discuss potential risks and benefits of screening and patient preferences

52 year old male with a negative colonoscopy at age of 40 and mother with colon cancer at age of 58. He does not want a colonoscopy?

How do you respond?

a) That is fine, we will order a Cologuard because it is over 90 % sensitive for picking up cancer

b) Let me introduce you to my dog who is trained to sniff out colon cancer

c) That will not work since only colonoscopy is appropriate for someone at high risk with a family history such as yours

d) That will work since your mother was genetically tested and was not found to have any high0risk mutations

e) We can skip the colonoscopy and instead will do a blood test looking for cell free DNA

Take-home Points

- ✓Screening for CRC is evidence-based and recommended for all adults but underutilized.
- ✓Screening should begin at age of 45 for average risk individuals and earlier in high risk group
- ✓Refer patients for abnormal stool based test within 1 year, ideally before 9 months.
- ✓Endoscopic options are available for early colon cancer treatment