



Annual

**Advances and Innovations in Endoscopic Oncology
and Multidisciplinary Gastrointestinal Cancer Care**

Opportunities for Precision Interception of Early Onset Colorectal Cancer

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Disclosures

- This is a Non-CME Accredited session.

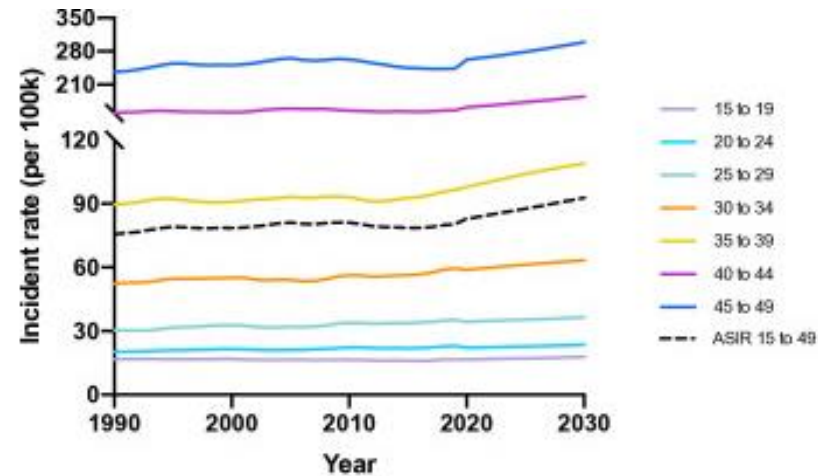
Overview

- Epidemiology of early-onset colorectal cancer
- Strategies for interception
 - Improve screening uptake in adults aged 45-49
 - Develop risk stratification and precision interception approaches in adults aged 18-44

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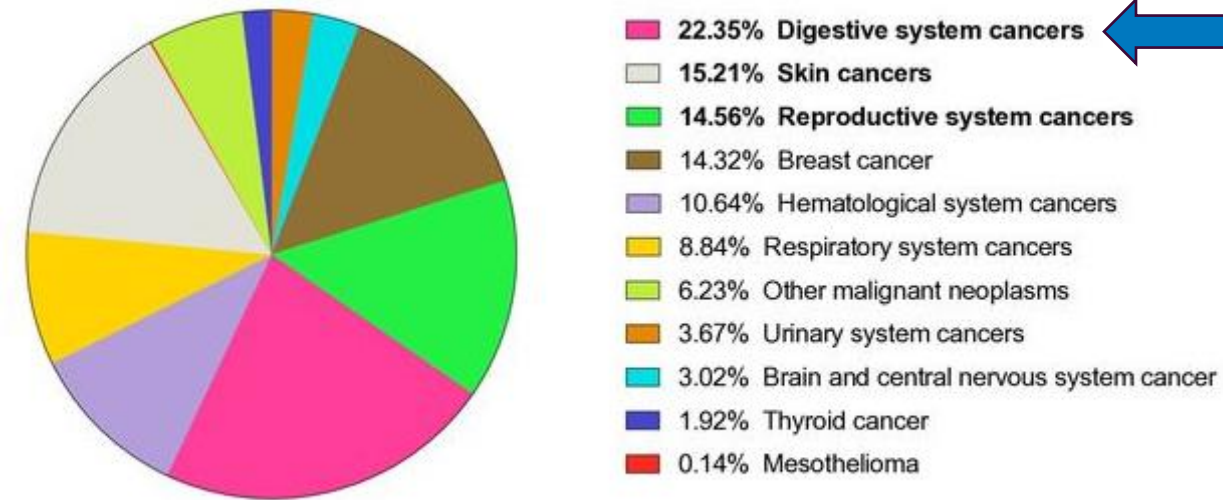
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The Global Rise in Early-Onset Cancer

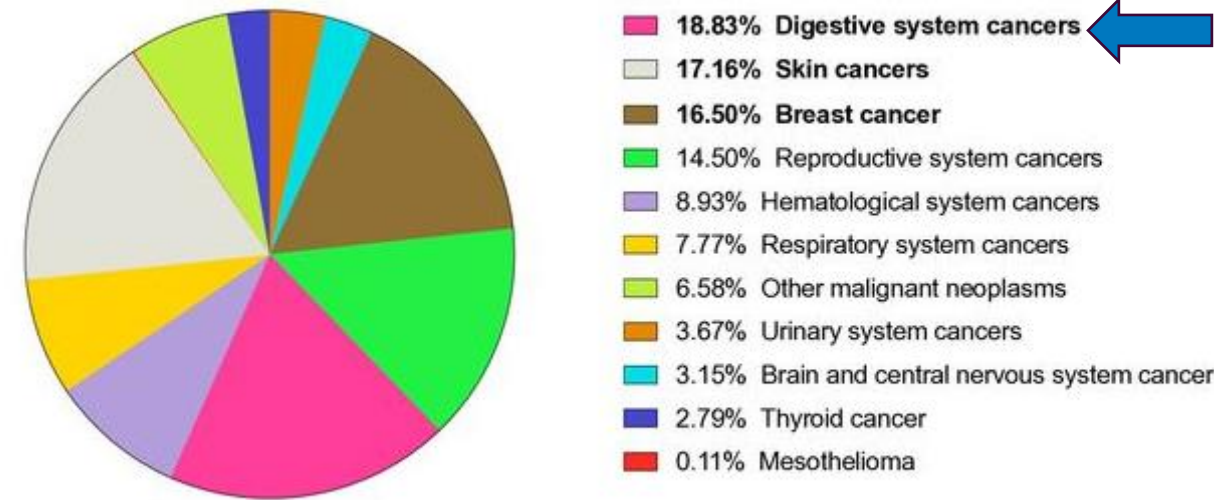


1990 Incidence

2019 Incidence



Total = 1.82 million



Total = 3.26 million

Early-Onset Cancer in the U.S. (2010–2019)

B By age group

Age, y

0-29 (n = 101 528)

30-39 (n = 136 479)

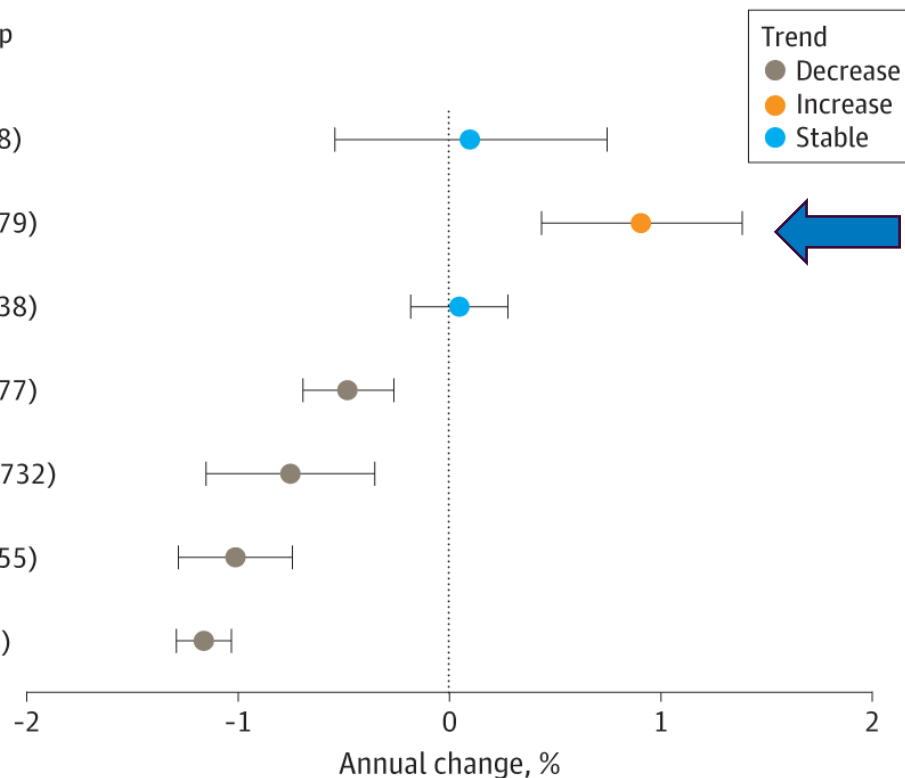
40-49 (n = 324 138)

50-59 (n = 772 177)

60-69 (n = 1 182 732)

70-79 (n = 988 155)

≥80 (n = 668 711)



C By organ system

System

Urinary system

Skin

Respiratory system

Other

Male reproductive system

Head and neck

Hematological malignant neoplasm

GI system

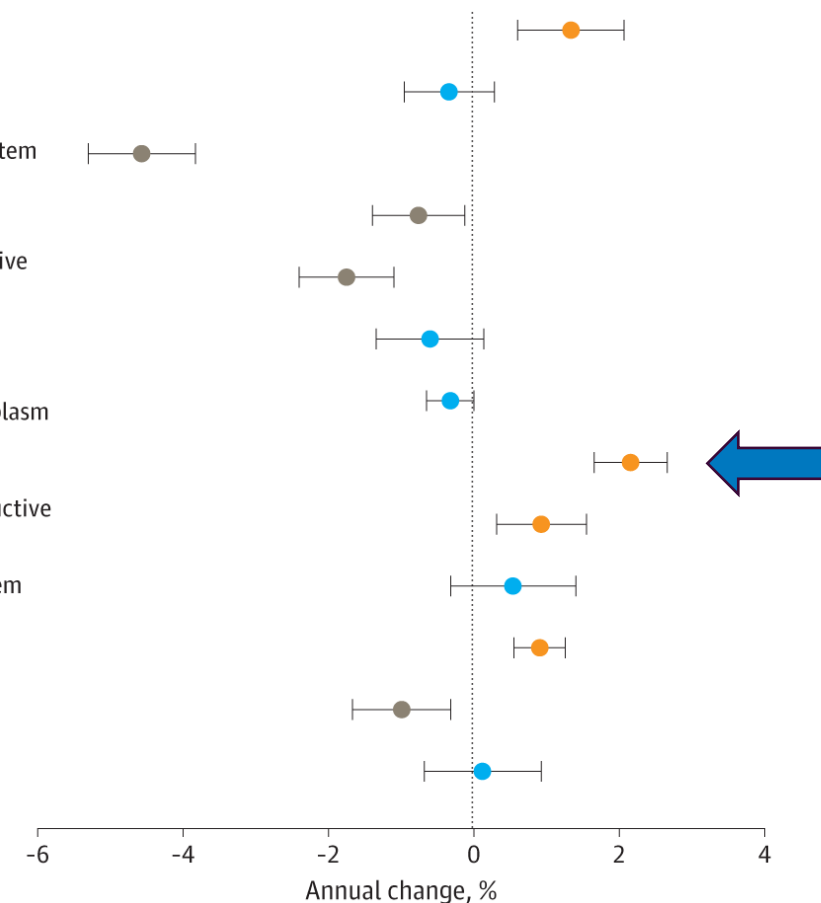
Female reproductive system

Endocrine system

Breast

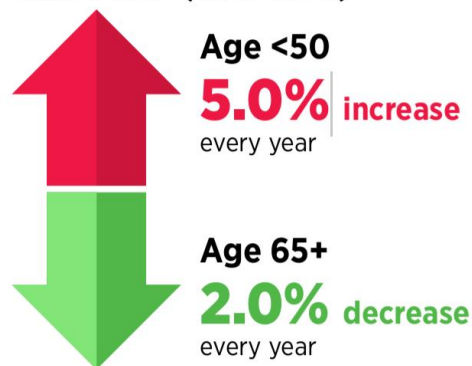
Brain and other nervous system

Bones, joints, and soft tissues

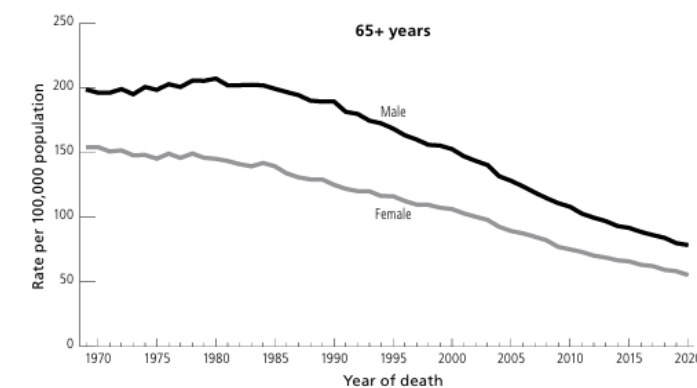
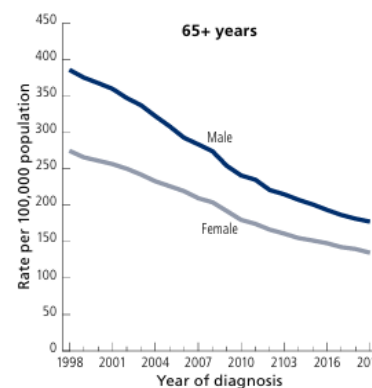
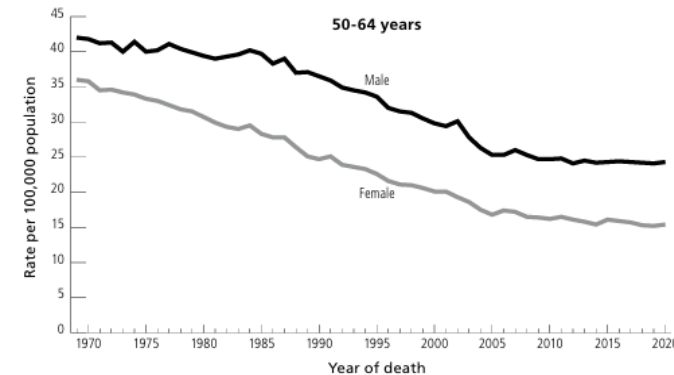
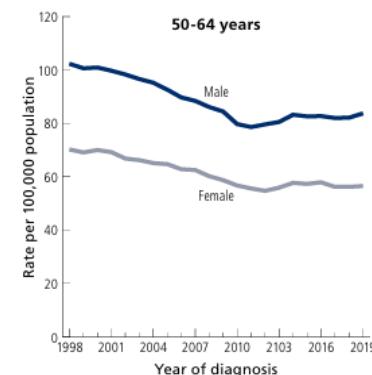
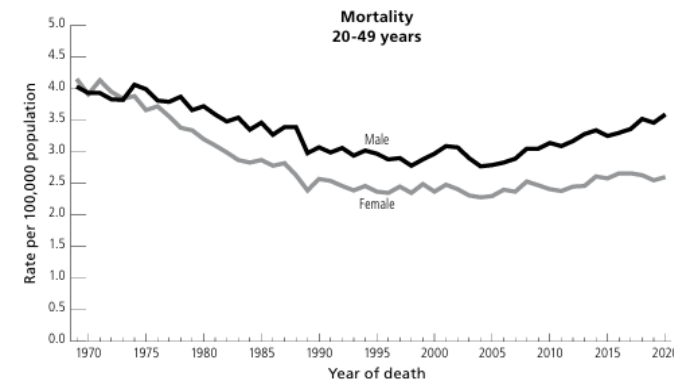
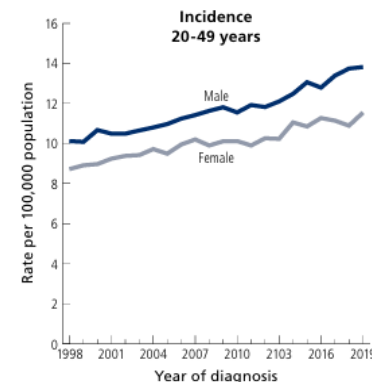
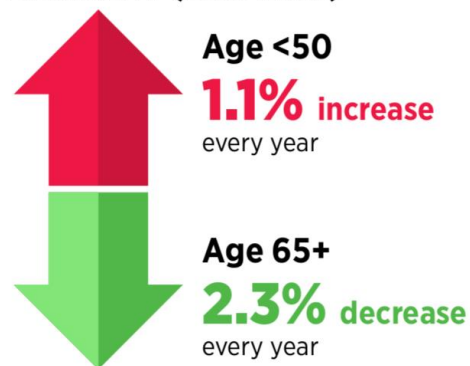


Trends in Colorectal Cancer (CRC)

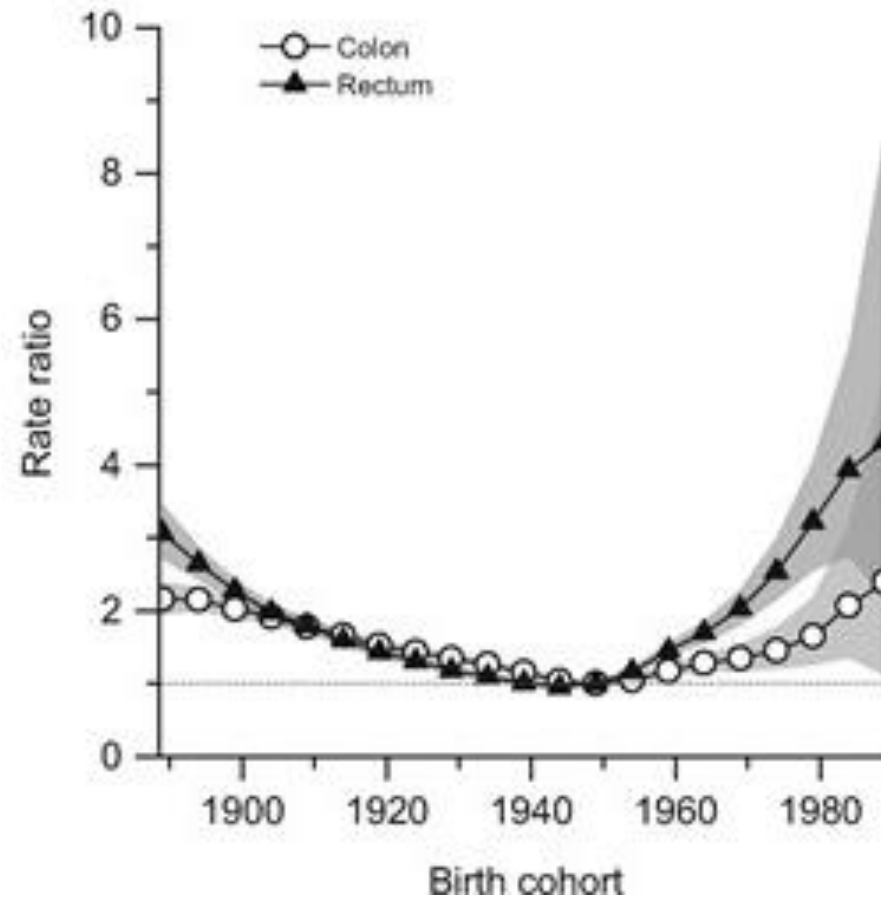
INCIDENCE (2018–2022)



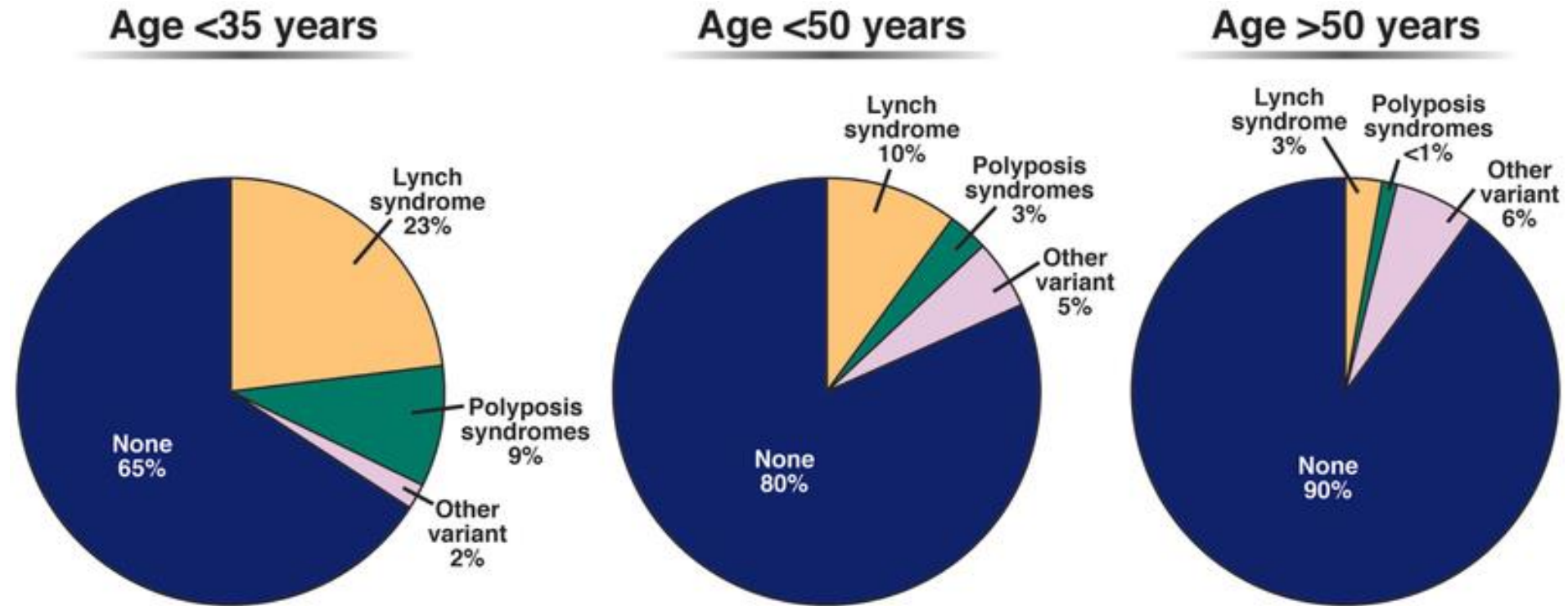
MORTALITY (2019–2023)



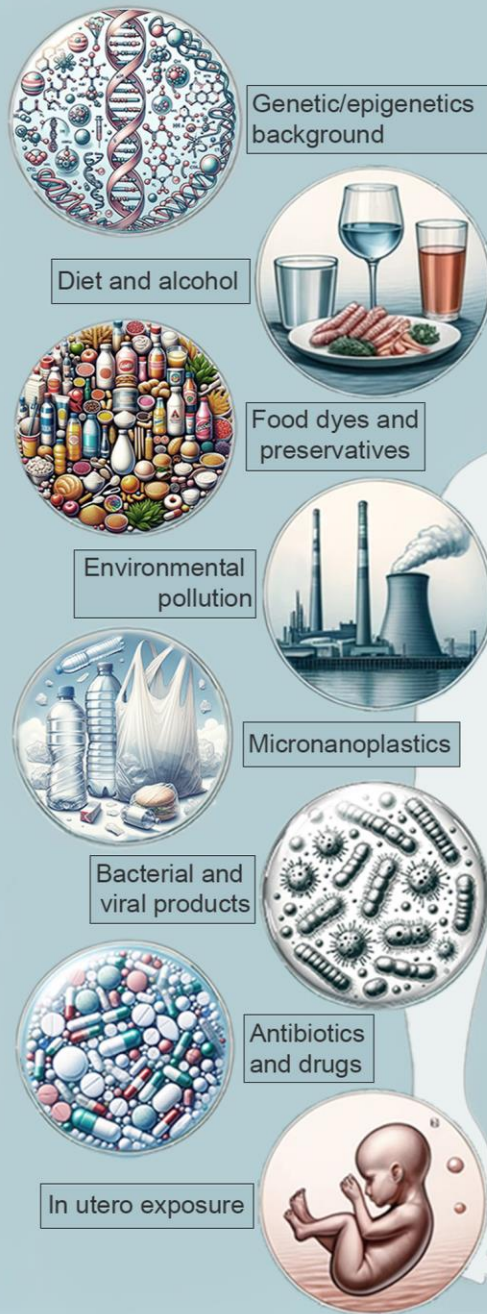
Birth Cohort Effect



Most Early-Onset CRC (EOCRC) is Sporadic



Potential drivers



Translational platforms (EO-cancer integrome)

Annual percentage change

Oropharynx +5.04%

Breast +0.91%

Stomach +1.59%

Pancreas +2.53%

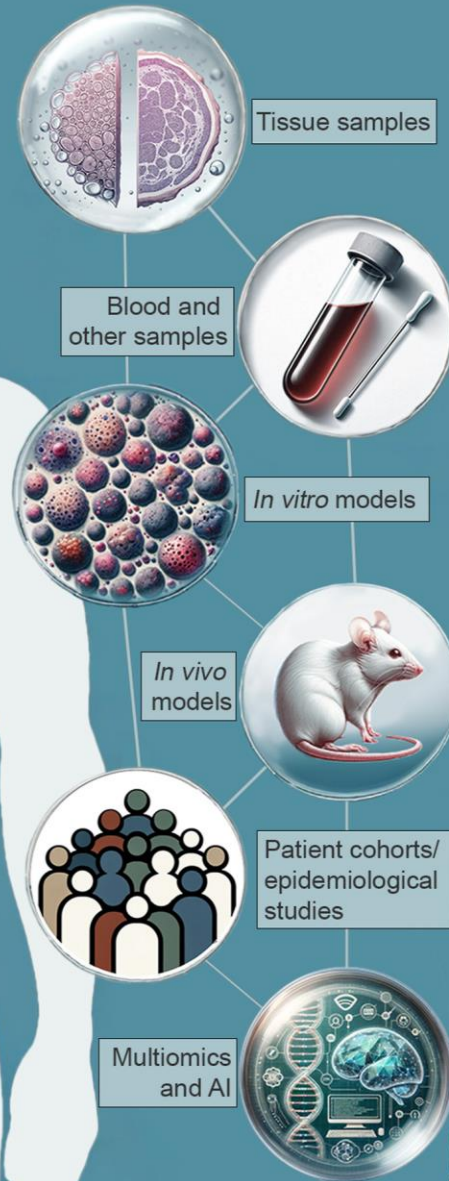
Biliary tract +8.21%

Small intestine +2.11%

Kidney +2.16%

Corpus uteri +2.22%

Colon and rectum +1.72%



2030s

2020s

2010s

2000s

1990s

1980s

EO-cancer incidence

SIDEBAR 4

What Is Causing the Rise in Early-onset Cancers?

From 2011 to 2019, in the United States, 2,020,829 new cancer cases were diagnosed among individuals ages 15 to 49 years. Although researchers are not sure of the exact reasons why these cancers are rising, several possible causes are under investigation:



Unhealthy diet and the microbiome



Obesity



Chemicals in the environment



Repeated and long-term use of antibiotics



Alcohol consumption



Sedentary behaviors

Understanding how these risk factors lead to early-onset cancers will help to inform approaches for screening, prevention, and treatment.

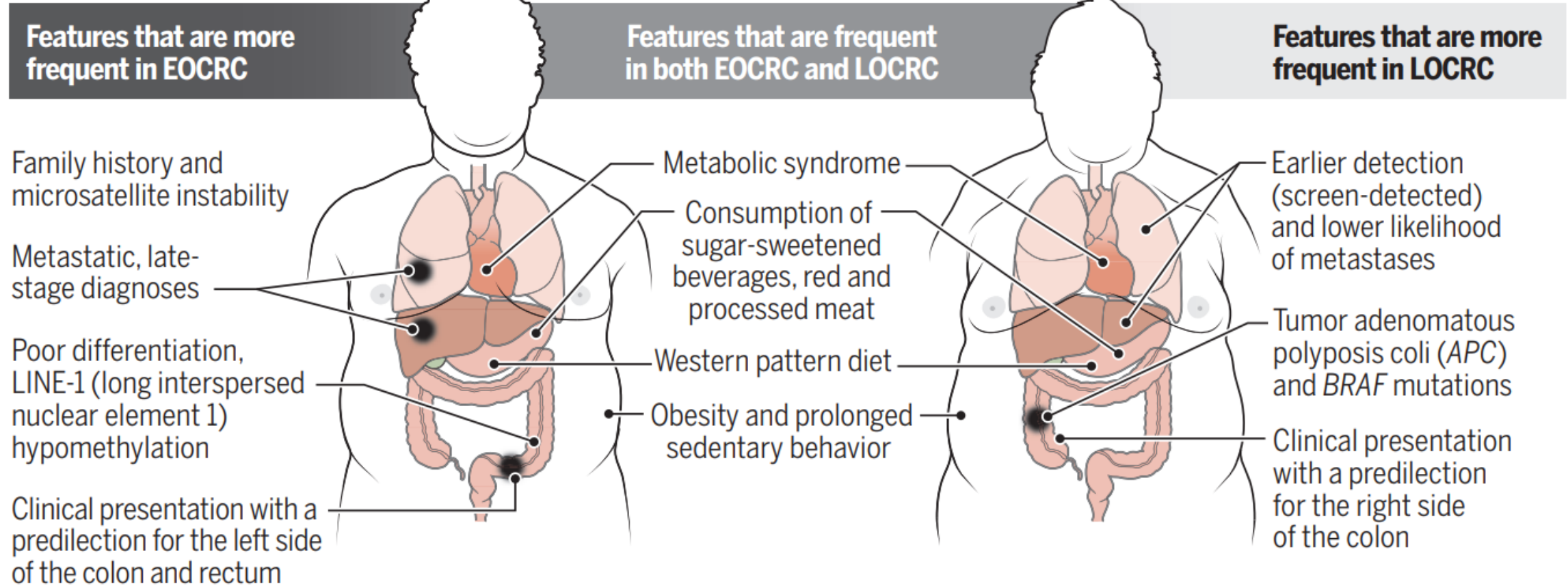
Sources: (44,45,49-54).

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Differences in EOCRC vs. Average-Onset CRC

Early-onset colorectal cancer age <50

Later-onset colorectal cancer age ≥50



Overview

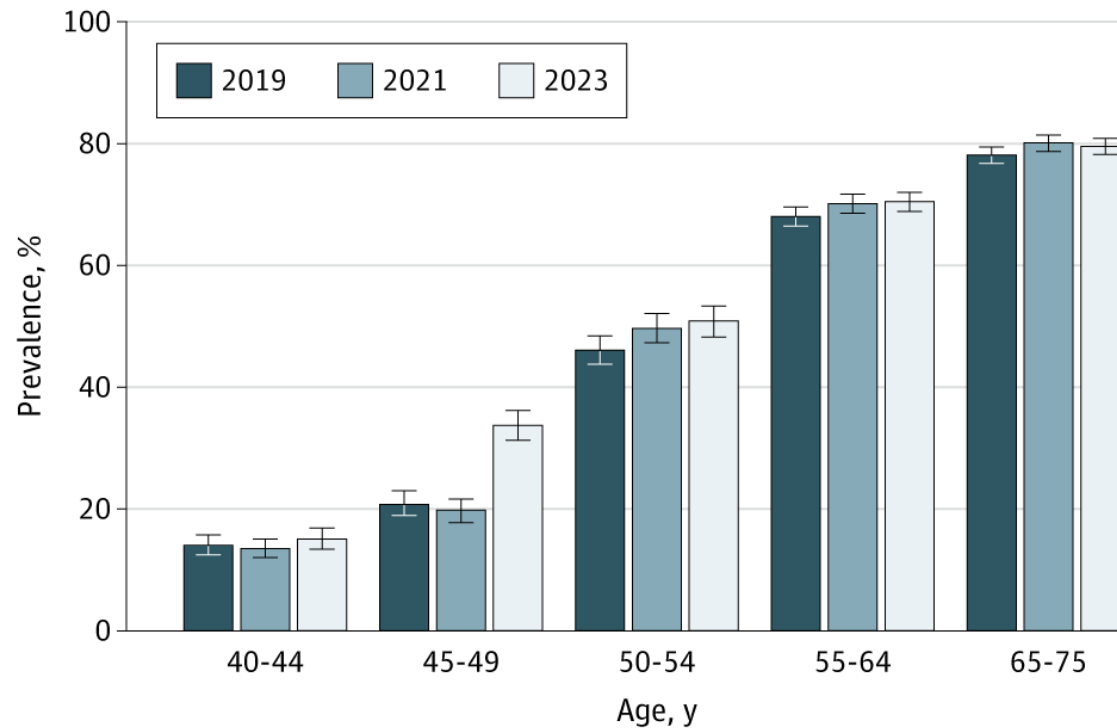
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CRC Patient Demographics (2001-2016)

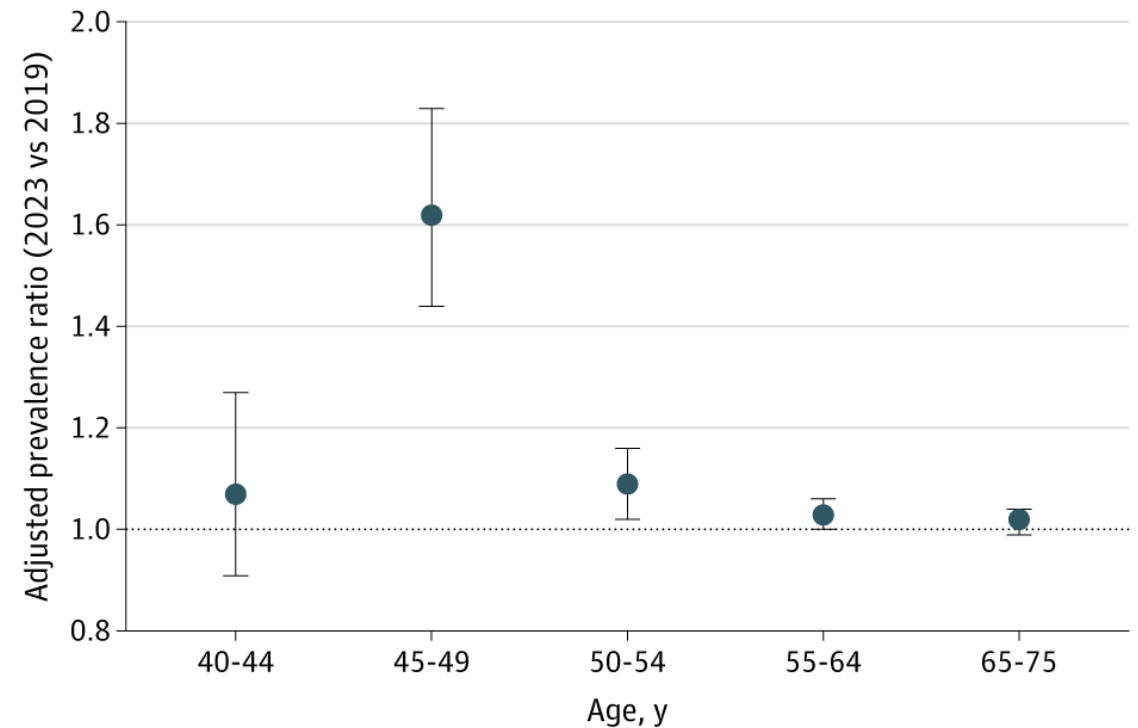
		EOCRC (n=191,659)	LOCRC (n=1,097,765)	P
		n (%)	n (%)	
Sex	Male	101,977 (53)	620,635 (57)	<0.001
	Female	89,682 (47)	477,130 (43)	
Age, years	20-29	8,336 (4)		<0.001
	30-39	38,722 (20)		
	40-44	51,245 (27)		
	45-49	93,356 (49)		
	50-54		169,023 (15)	
	55-59		192,666 (18)	
	60-64		221,169 (20)	
	65-69		254,335 (23)	
	70-74		260,572 (24)	
Race/Ethnicity	White	149,207	902,244	<0.001
	Black	28,536	137,735	
	Asian/Pacific Islander	9,444	39,641	
	Hispanic	23,652	87,049	
Anatomic Site	Proximal Colon	50,802 (27)	411,916 (38)	<0.001
	Distal Colon	59,526 (31)	319,454 (29)	
	Rectum	81,331 (42)	366,395 (33)	
Stage	Localized	60,680 (33)	447,531 (43)	<0.001
	Regional	75,940 (41)	393,426 (38)	
	Distant	46,972 (26)	208,942 (19)	

CRC Screening Prevalence

A Colorectal cancer screening prevalence



B Adjusted colorectal cancer screening prevalence ratios



QUESTION What is the most effective population health strategy to promote colorectal cancer (CRC) screening among average-risk adults aged 45 to 49 years?

CONCLUSION In this trial, unsolicited mailed fecal immunochemical test (FIT) outreach was the most effective population health CRC screening strategy, although overall screening rates were low, underscoring the need for more effective strategies to engage this age group.

POPULATION

20 509
Participants



Primary care patients
aged 45 to 49 years
at average risk for CRC

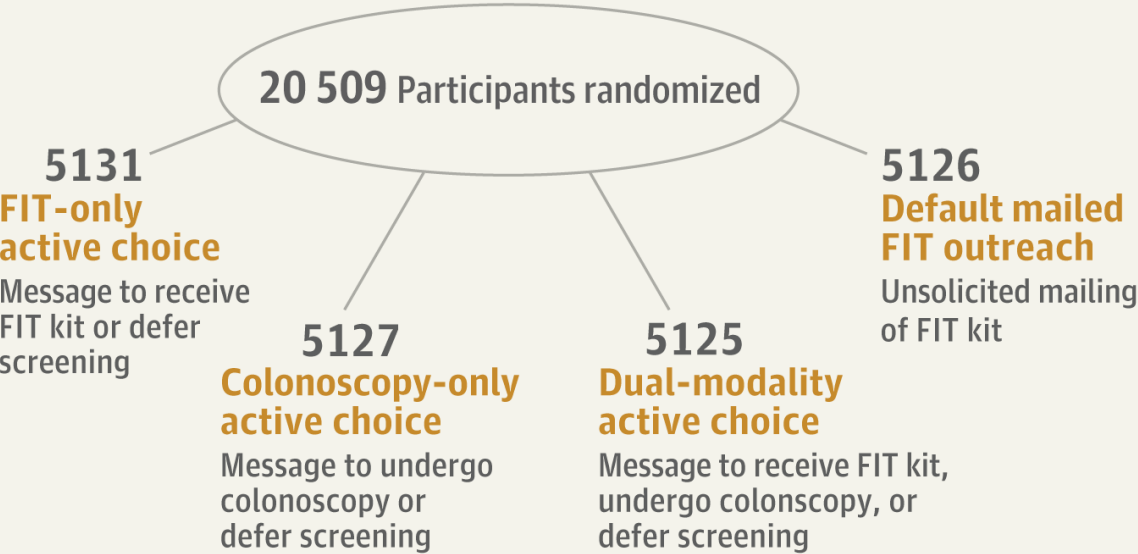
Mean age: 47 years

LOCATION



1 Large
health care system
in California

INTERVENTION



PRIMARY OUTCOME

CRC screening completion (FIT or colonoscopy) at 6 months

FINDINGS

Rate of CRC screening

FIT-only active choice 16.4%
(841 of 5131 participants)

Colonoscopy-only active choice 14.5%
(743 of 5127 participants)

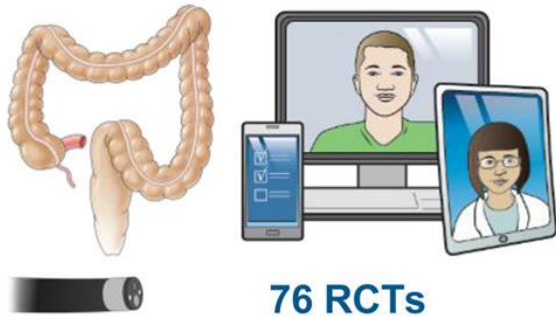
Dual-modality active choice 17.4%
(890 of 5125 participants)

Default mailed FIT outreach 26.2%
(1342 of 5126 participants)

Screening was significantly higher in the default mailed FIT outreach group ($P < .001$ vs each other group).

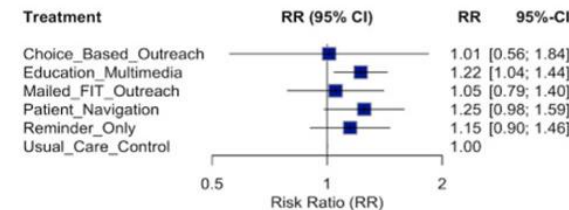
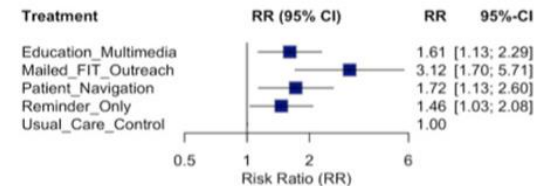
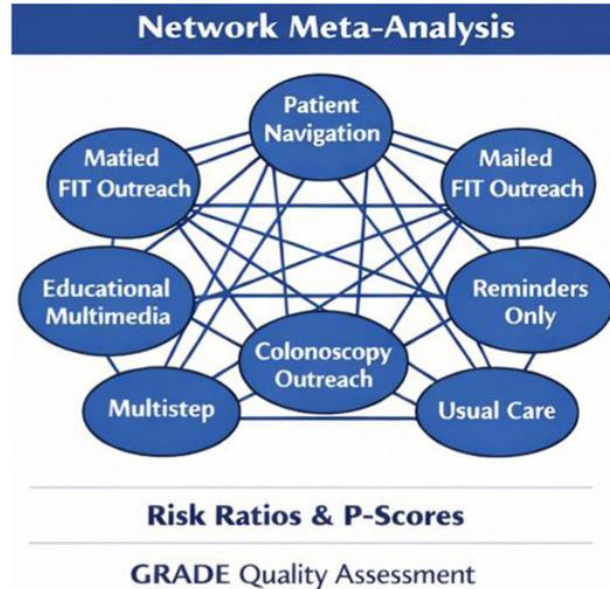
Dual-modality group had a higher screening rate than groups offered single modality only ($P = .004$).

Interventions to Increase CRC Screening Uptake

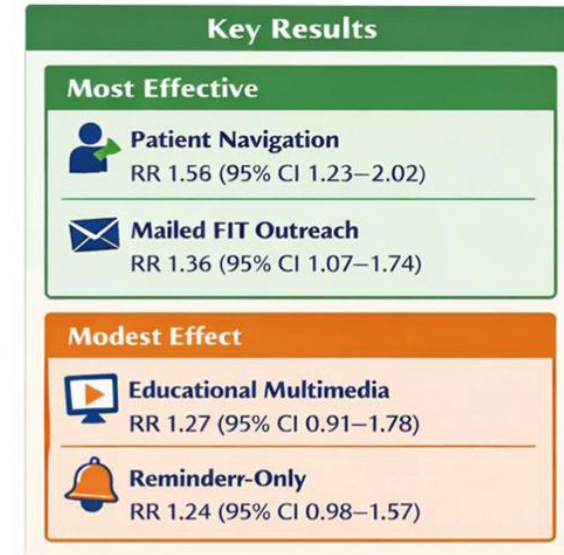


76 RCTs

8 Interventions



Screening outcomes according to baseline uptake levels (A: <30% and B: ≥30%)



Patient Navigation & Mailed FIT – *most effective, especially in low uptake settings*

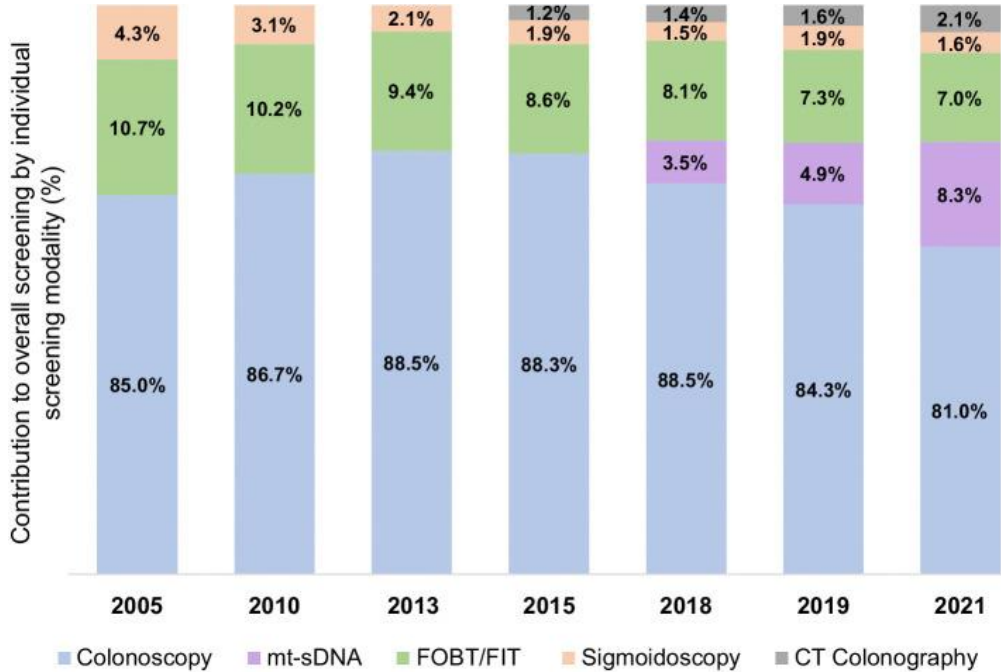
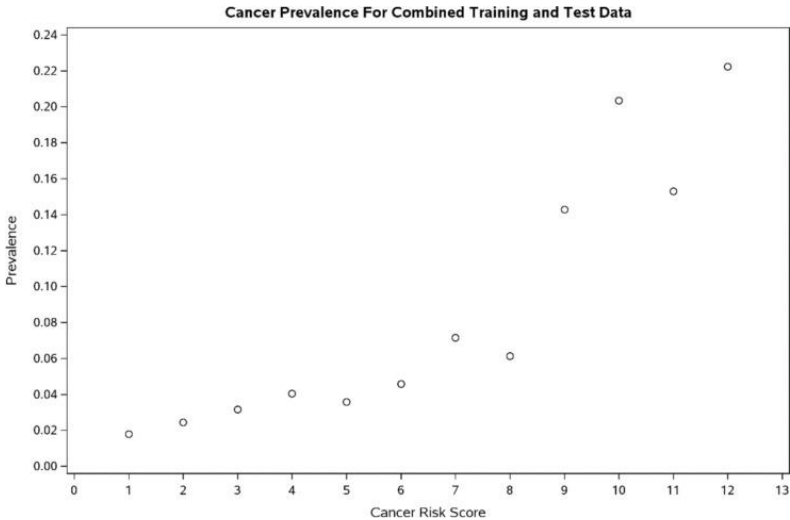
Gastroenterology

Overview

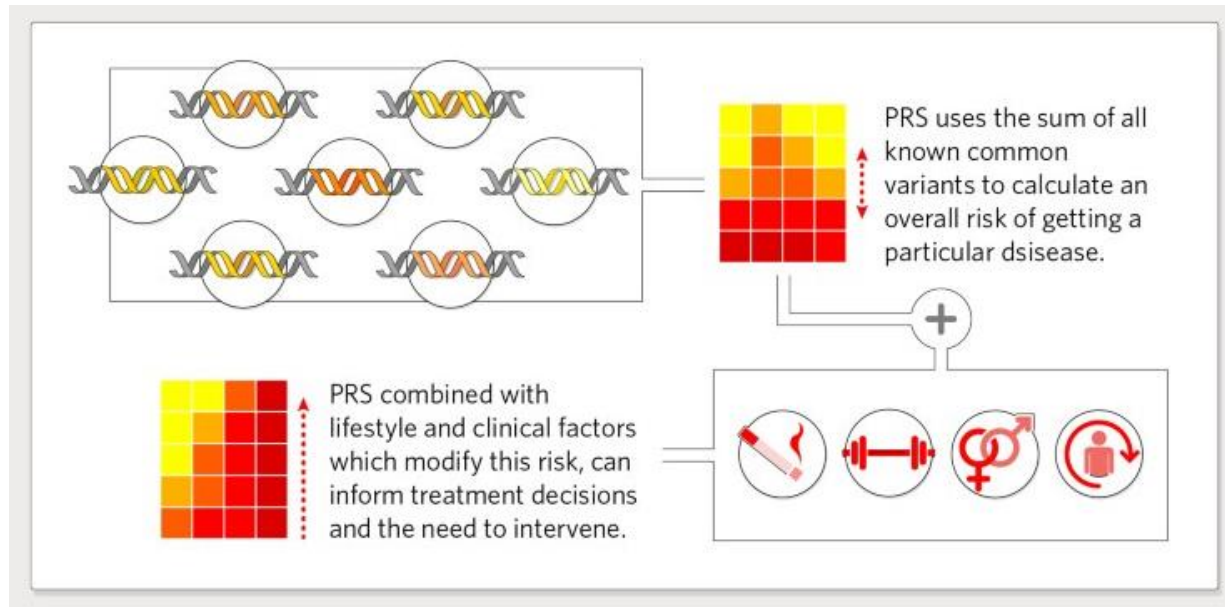
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Risk Stratification + Non-Invasive Screening has Potential to Reduce the EOCRC Burden

Clinical Risk Prediction Score for Early Onset Advanced Colorectal Neoplasia. Min. score = 0. Max score = 12. High risk: ≥ 9.		
Clinical Factor	Category	Points
Sex	Male	1
	Female	0
Tobacco Use	Current	3
	Former	3
	Never	0
Body Mass Index (BMI)	>29	3
	25-29	2
	<25	1
Family History of CRC	1st degree relative with CRC age <60	5
	Any other family history of CRC	4
	None	0

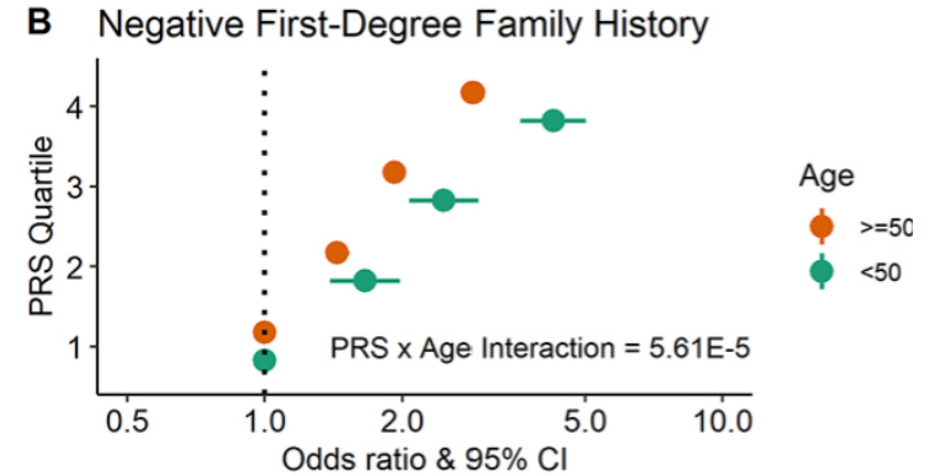
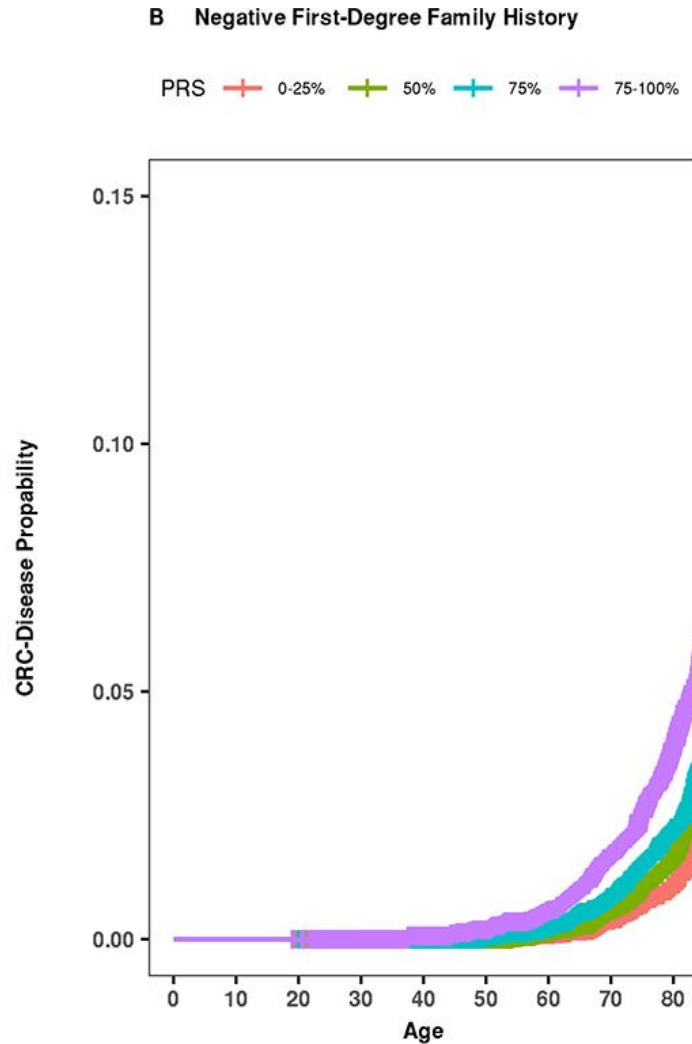


Polygenic Risk Scores (PRS)



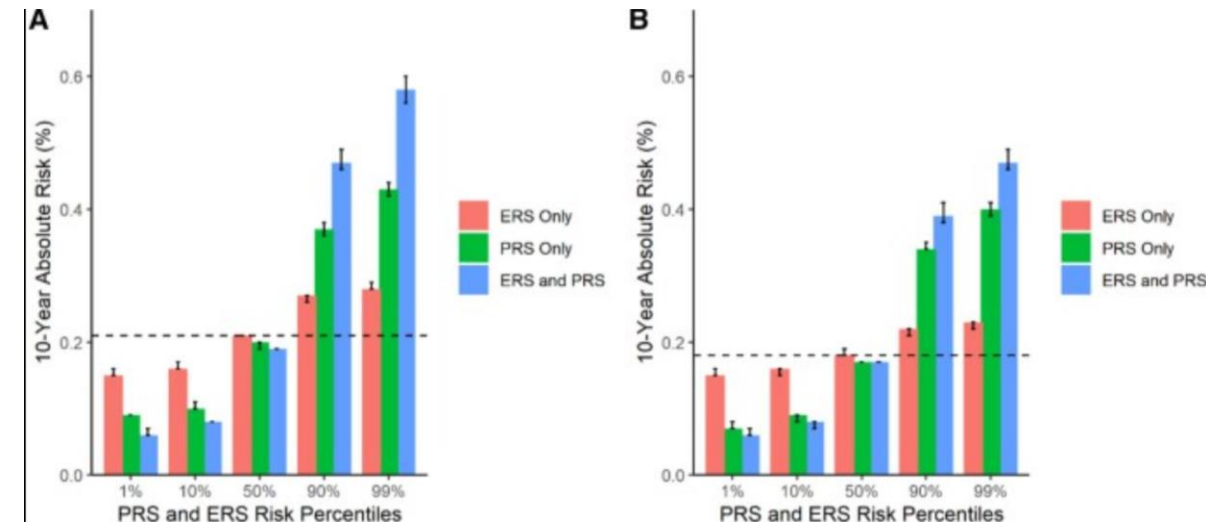
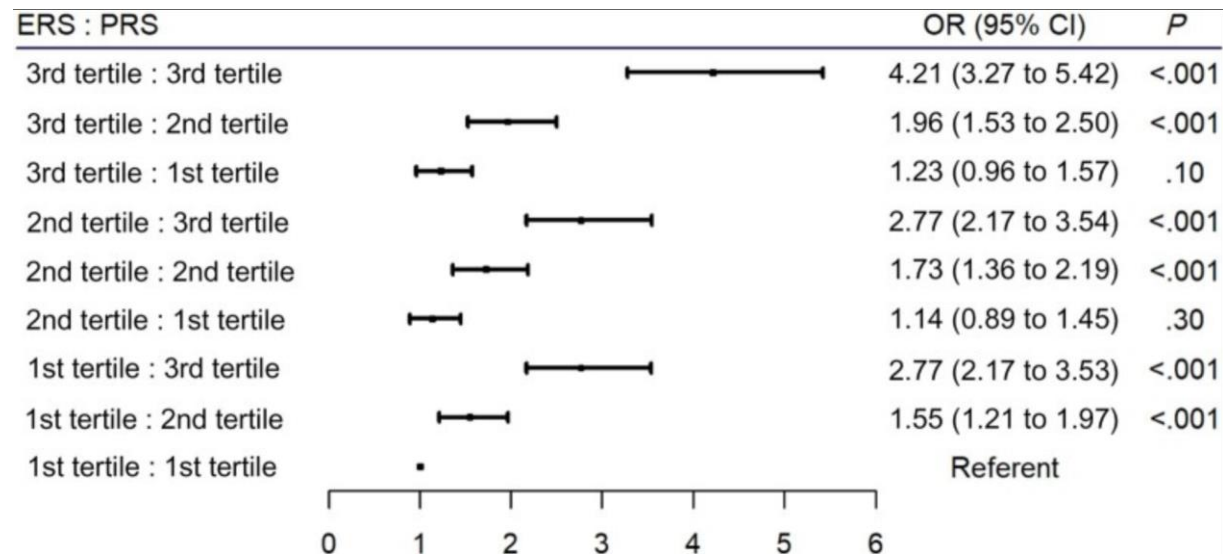
- Weighted sum of genetic risk variants an individual has into a single burden score
- Typically combines hundreds to millions of variants weighted by their effect sizes from genome-wide association studies
- Categorize individuals into percentile groups of risk score
- PRS top decile vs remaining individuals
 - European: Odds Ratio 2.2
 - East Asian: Odds Ratio 1.96

PRS for CRC

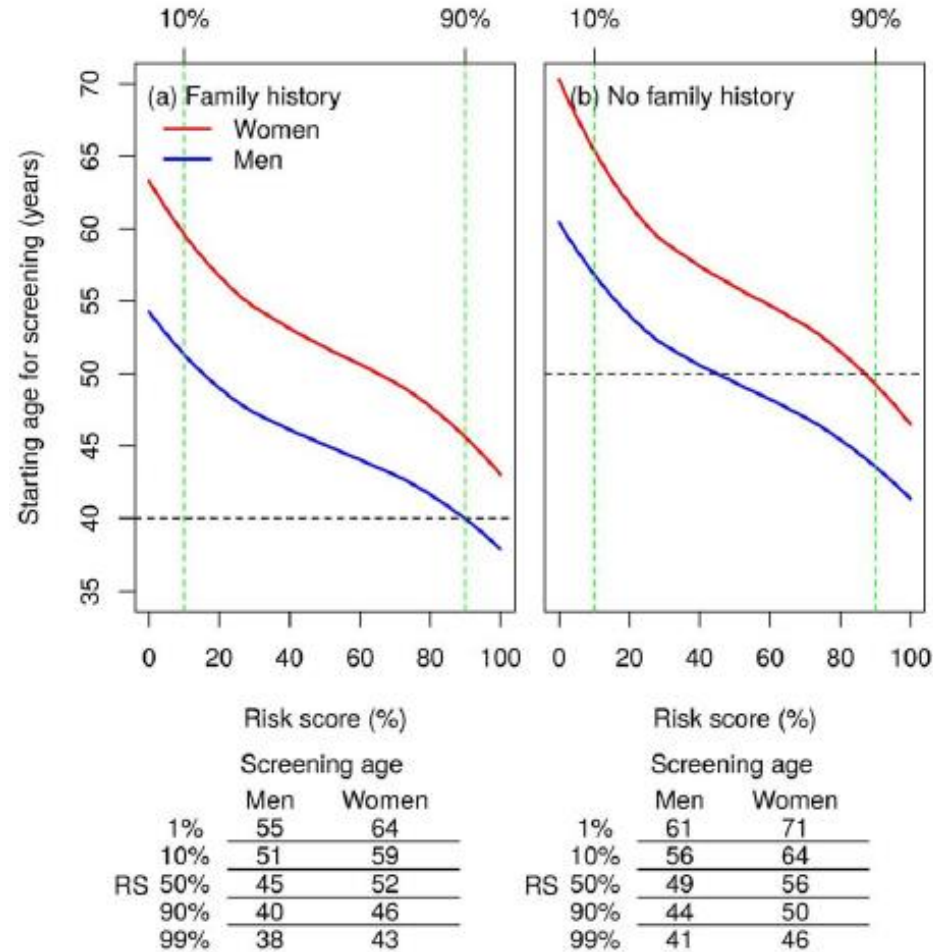


- PRS are more strongly associated with EOCRC than average-onset CRC

PRS + Environmental Risk Score (ERS) for EOCRC



Risk Stratification → Precision Interception



Summary

- EOCRC is on the rise with unclear drivers → primary prevention is challenging
- ~50% of EOCRC occurs among 45-49 year olds → opportunity to improve screening uptake
- Emerging research points to possible risk stratification and early detection strategies for adults < age 45
- What action can we take right now?
 - **Education** about timely follow-up of symptoms and age-appropriate screening
 - Intervening in the **obesity epidemic** → healthier diets, increased physical activity
 - **Scientific discovery**: research into the underlying drivers

Thank you!



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