

Blood-Based Screening for Colorectal Cancer



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Disclosures

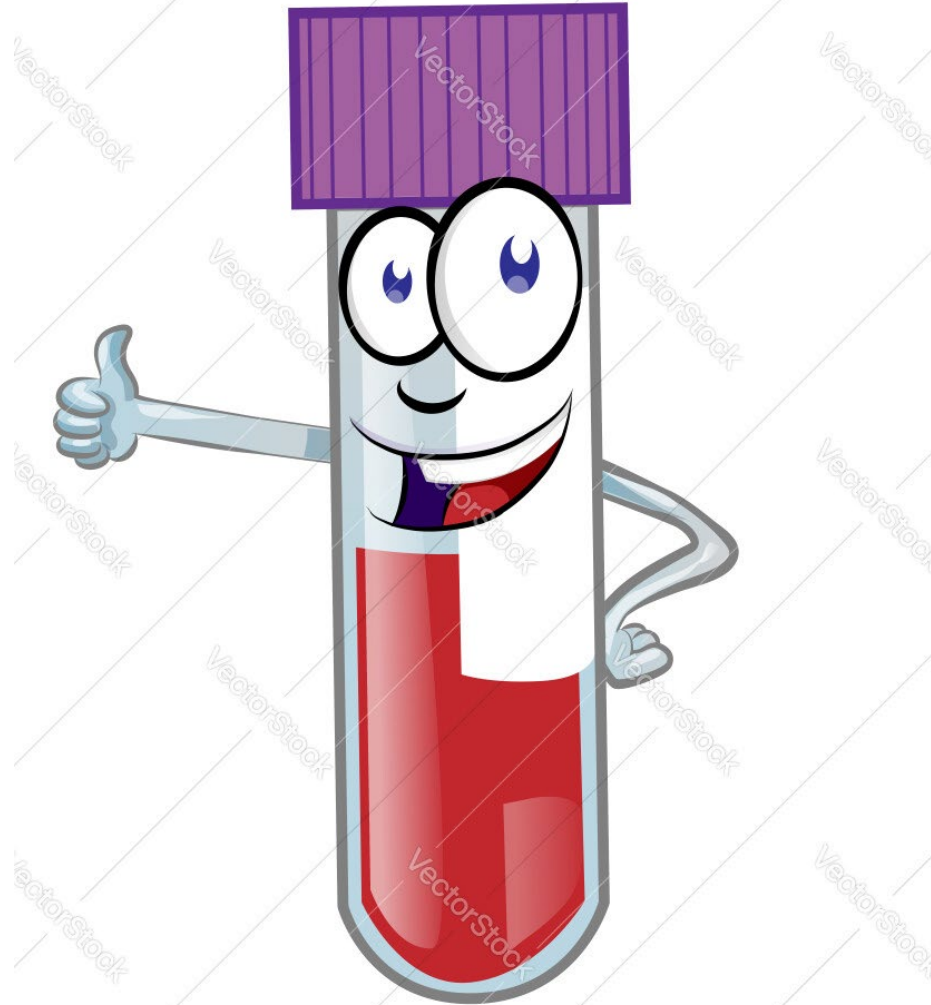
Research Support:

- Freenome
- Immunovia, Inc.
- Exact Sciences

Advisory:

- Guardant

New CRC Screening Blood Tests



Centers for Medicare and Medicaid Services (CMS) Guidance on Blood Tests for CRC

- CMS has issued guidance for reimbursement of blood test for colorectal cancer: 74% sensitivity for cancer (FIT) at 90% specificity (Cologuard)
- Sensitivity only based on CRC – AA detection not considered
- **PROBLEM:** Detecting advanced adenoma contributes significantly to lowering CRC incidence and mortality

How Does Screening Reduce CRC Mortality?

- Early Detection
- Prevention Through Removal of Precursor Lesions

Estimated that about 2/3rd of the reduction in CRC mortality in PLCO trial is attributable to the reduction in incidence

Early Detection vs. Prevention

Case fatality rate (control) X # averted cases in intervention = CRC averted deaths due to prevention

Model	Control case fatality %	Averted Cancers	Averted Deaths to Prevention	% Averted Deaths to Prevention
PLCO	27	283	77	79
Score	27	55	15	83
UK	30	422	335	76



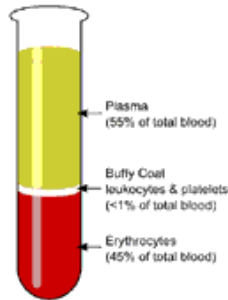
GUARDANT™ - “SHIELD”

ECLIPSE - Evaluation of the ctDNA LUNAR-2 Test In an Average Patient Screening Episode



Inclusion criteria:

- Average risk for CRC
- Age 45-84
- No prior history of cancer or inflammatory bowel disease
- No CRC familial predisposition
- No recent CRC screening



Whole blood collected prior to screening colonoscopy and associated preparation



Screening
Colonoscopy

and

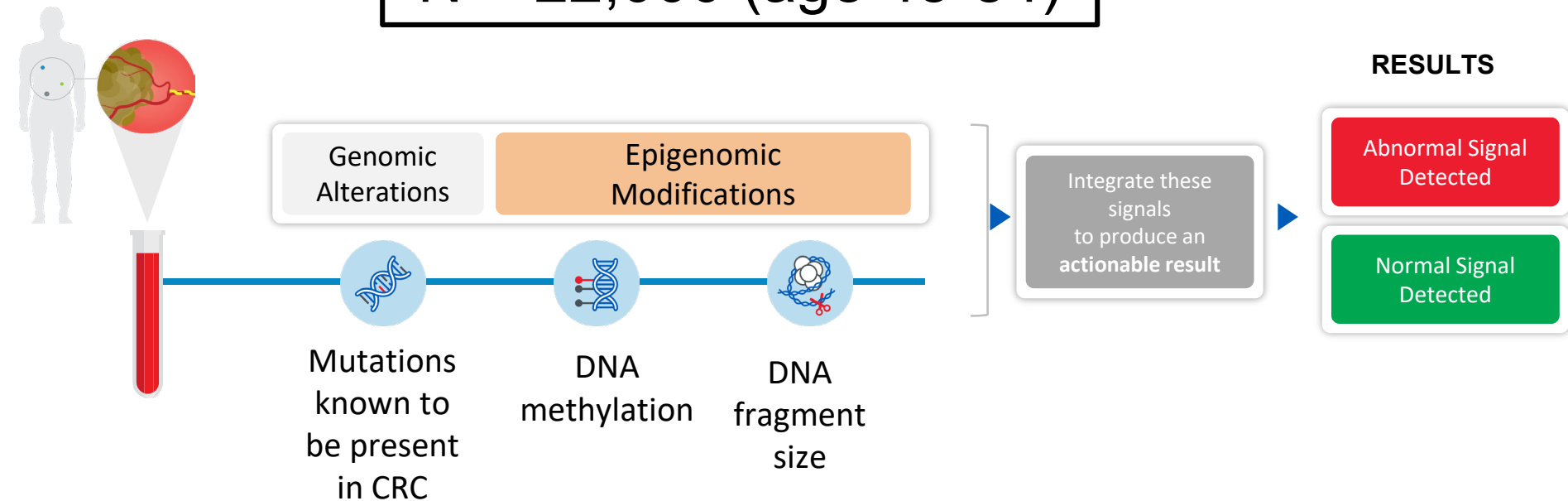
Blood-based
CRC screening
Test

ClinicalTrials.gov: NCT04136002

Chung, *et al.* NEJM 2024

cfDNA blood-based CRC screening test

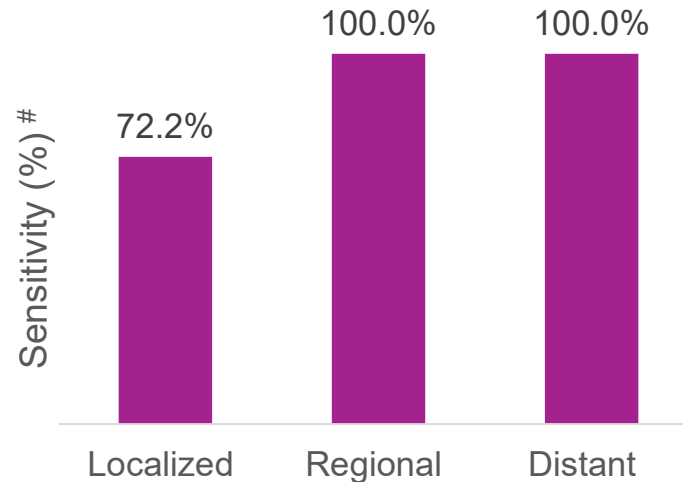
N=>22,000 (age 45-84)



CRC Results

Overall: Sensitivity: 83.1% at 90% Specificity

N=65
CRC



Stage I*	Stage II	Stage III	Stage IV
54.5% (12/22)	100% (14/14)	100% (16/16)	100% (10/10)

Eclipse Study Results

- 83% sensitivity for CRC at 90% specificity
- AA detection rate = 13%

PREEMPT: **P**revention of CRC through **M**ultiomics **B**lood **T**esting

N=49,115 (age 45-85)

Freenome 

NCT: 04369053

Preempt Trial Results

N= 27,010

- Sensitivity for cancer - 79.2%
 - Stage I: 57.1%
 - Stage II: 100%
 - Stage III: 82.4%
- Specificity w/o Advanced Neoplasia - 91.5%
- Sensitivity for AA= 12.5%

Press Release: April 2, 2024

Endpoint	Evaluable Cohort (N=27,010) %, 95% CI, (n/N)	
	Observed	US census sex-age weighted†
Sensitivity for colorectal cancer	79.2%, 68.4%-86.9% (57/72)	81.1%, 71.3%-88.1% (66.43/81.91)
Specificity for advanced colorectal neoplasia*	91.5%, 91.2%-91.9% (22,306/24,371)	90.4%, 90.0%-90.7% (21,938.03/24,280.65)
Negative predictive value for advanced colorectal neoplasia	90.8%, 90.7%-90.9% (22,306/24,567)	90.5%, 90.4%-90.7% (21,938.03/24,238.92)
Positive predictive value for advanced colorectal neoplasia	15.5%, 14.2%-16.8% (378/2443)	15.5%, 14.3%-16.7% (428.46/2771.08)
Sensitivity for advanced precancerous lesions	12.5%, 11.3%-13.8% (321/2567)	13.7%, 12.4%-15.0% (362.03/2647.44)

*Advanced colorectal neoplasia included colorectal cancer and advanced precancerous lesions.

Comparative Effectiveness and Cost-Effectiveness of Colorectal Cancer Screening With Blood-Based Biomarkers (Liquid Biopsy) vs Fecal Tests or Colonoscopy



Uri Ladabaum,^{1,2} Ajitha Mannalithara,^{1,2} Yingjie Weng,^{2,3} Robert E. Schoen,⁴
Jason A. Dominitz,^{5,6} Manisha Desai,^{2,3} and David Lieberman⁷

Annals of Internal Medicine

ORIGINAL RESEARCH

Projected Impact and Cost-Effectiveness of Novel Molecular Blood-Based or Stool-Based Screening Tests for Colorectal Cancer

Uri Ladabaum, MD, MS; Ajitha Mannalithara, PhD; Robert E. Schoen, MD, MPH; Jason A. Dominitz, MD, MHS; and David Lieberman, MD

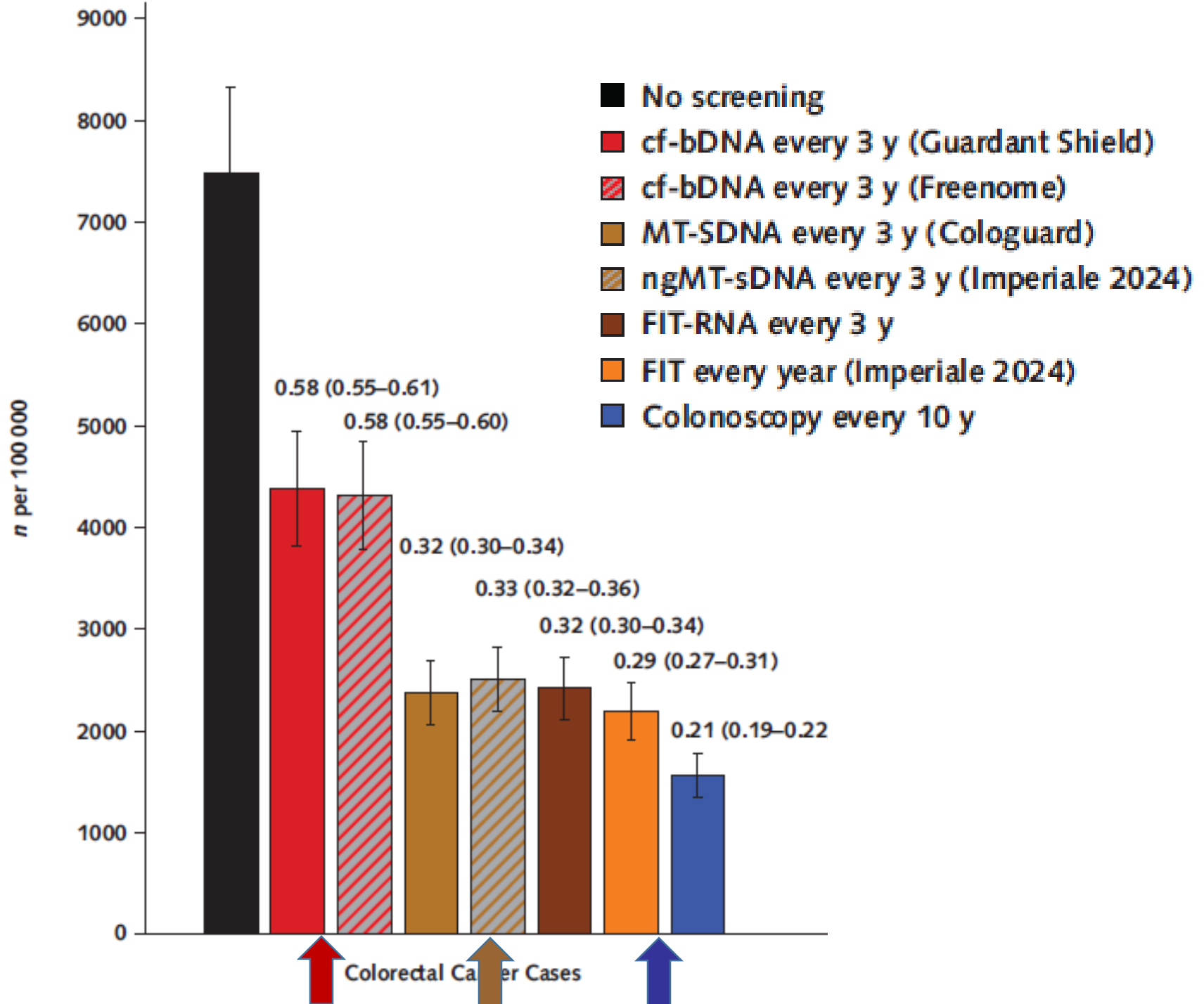
October 2024

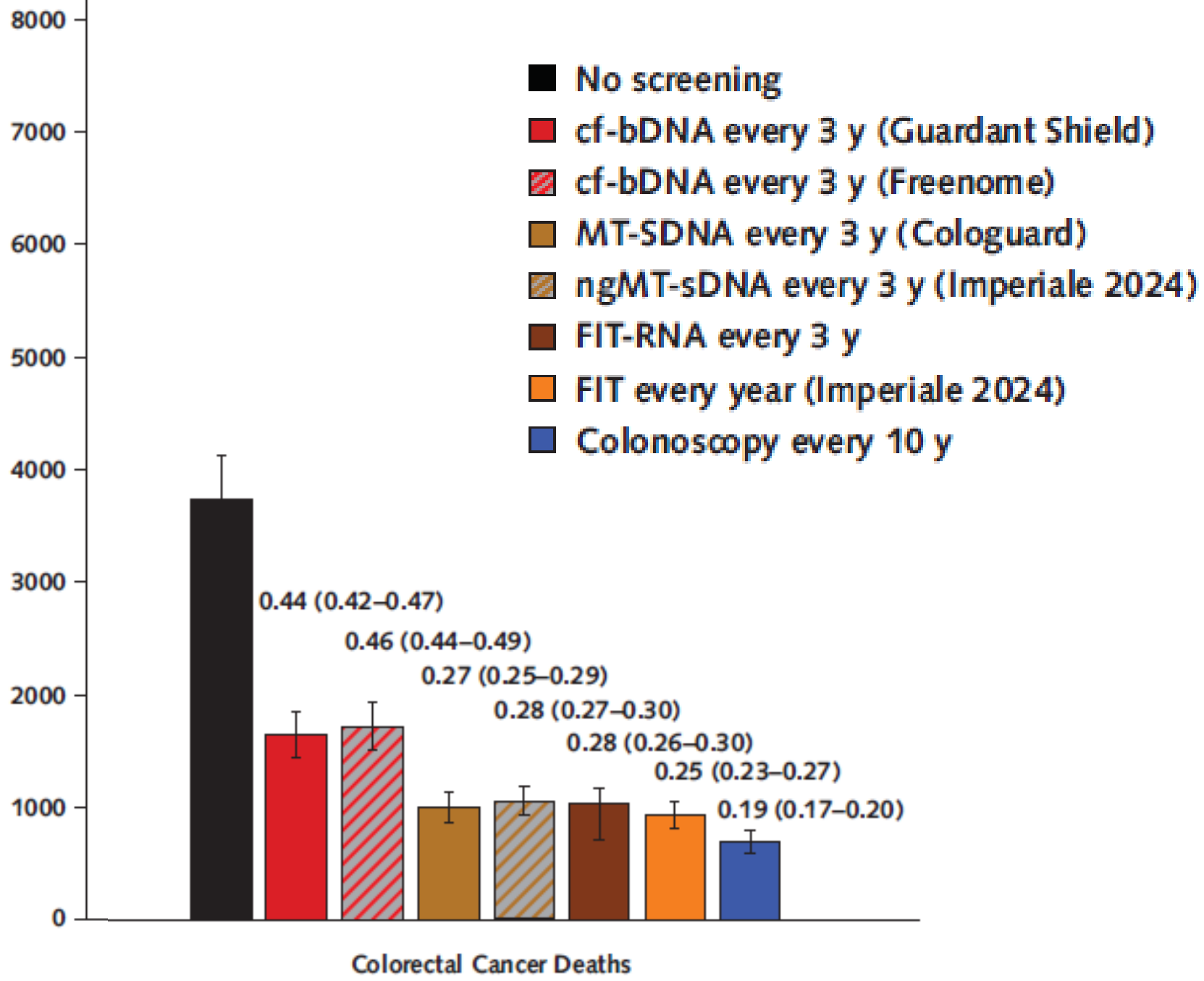
Methods: MOSAIC model

- MOSAIC – **M**odel of **S**creening and surveillance for **CRC** – decision analytic model
- Calibrated to: screening trials, prevalence of CRC/AA, post-polypectomy outcomes, CRC survival

N=100K:
age 45 to age
100 or death

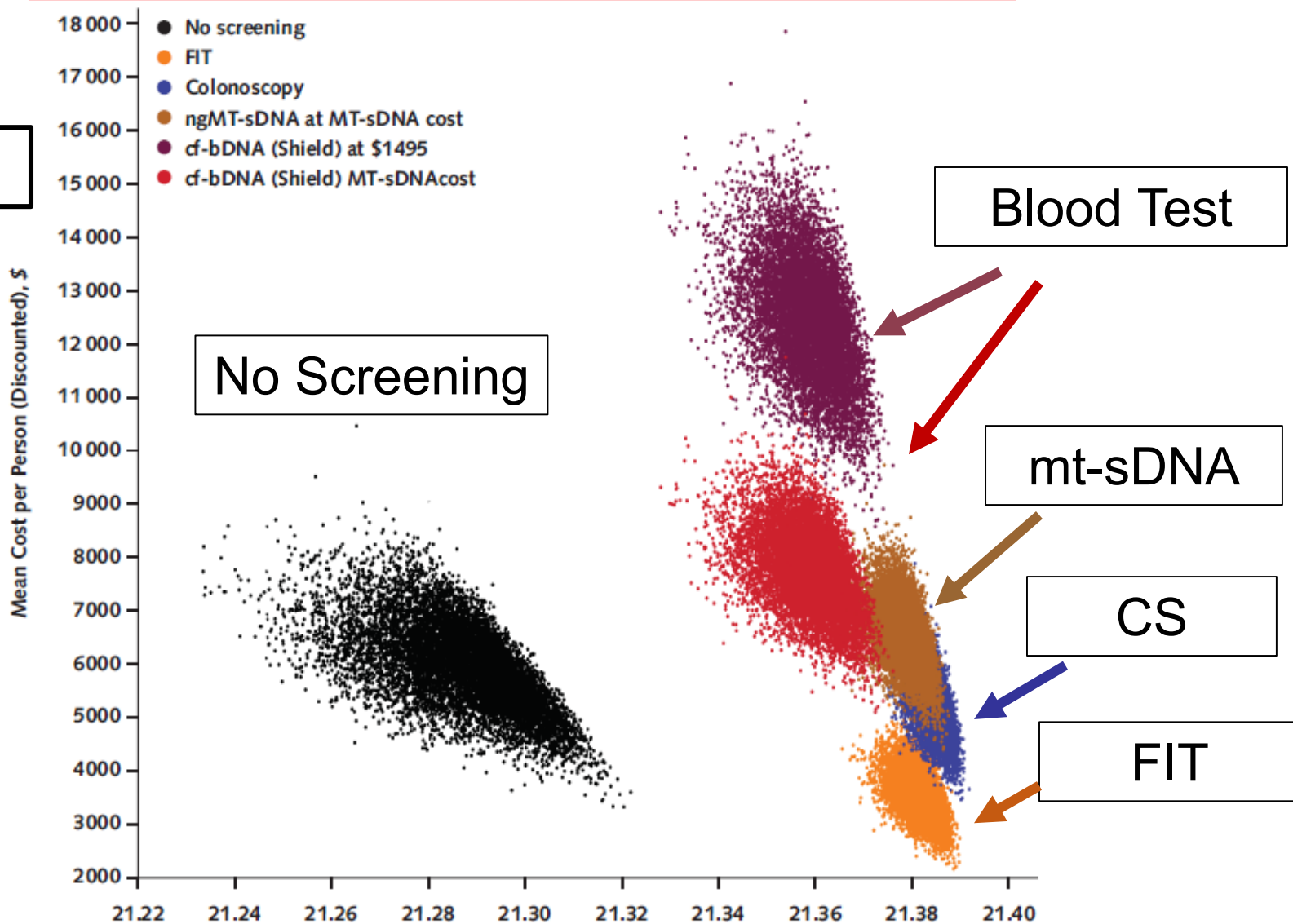
	CRC incidence (n, % reduction vs. no screening)	CRC mortality (n, % reduction vs. no screening)
	CRC Incidence	CRC Deaths
No screen	7,470	3,624
FIT yearly	2,117 (↓72%)	868 (↓76%)
Colonoscopy q10 yr	1,541 (↓79%)	672 (↓81%)
MT-sDNA q3 yr	2,355 (↓68%)	970 (↓73%)
Blood-based test (CMS min q3 years	4,499 (↓40%)	1,754 (↓52%)
Guardant Shield q3 yr	4,146 (↓45%)	1,622 (↓55%)





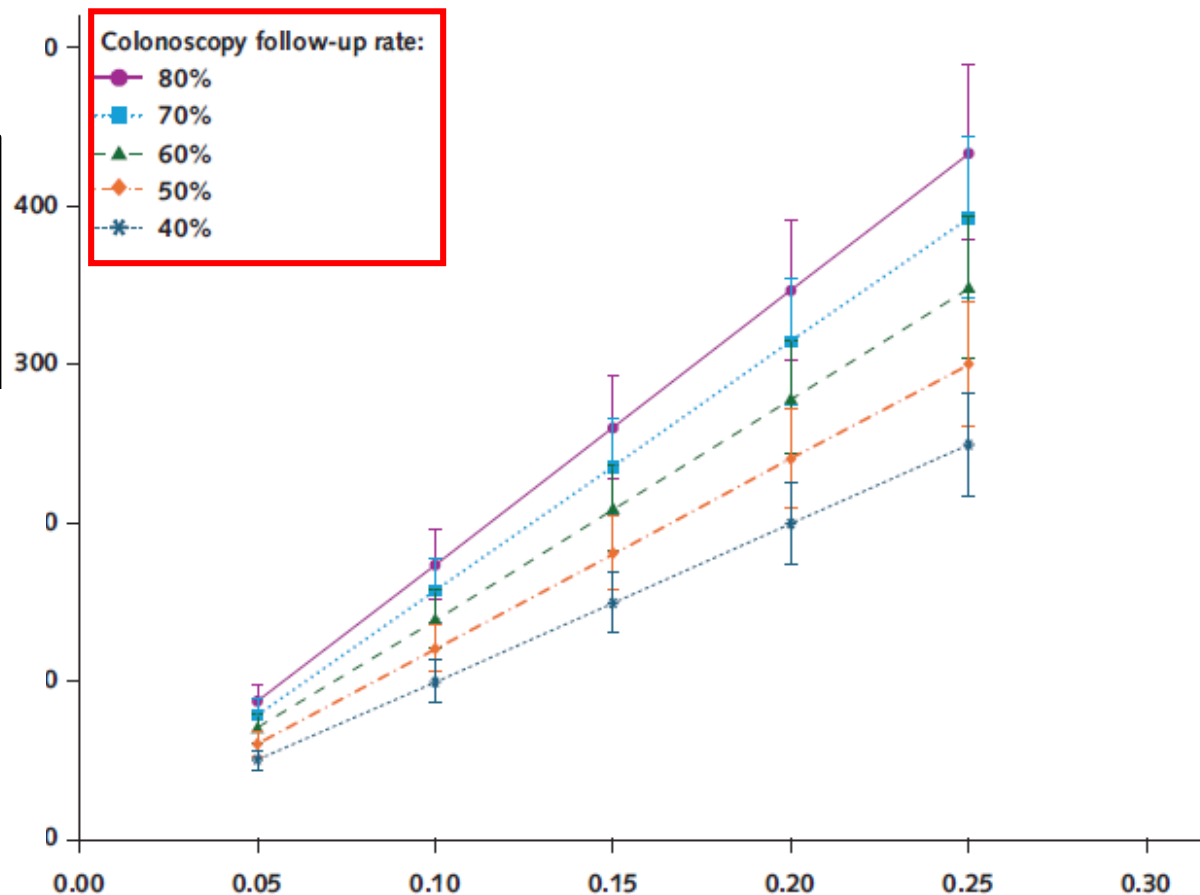
Cost by Quality Adjusted Life Year

COST



QALY

Preventing CRC deaths by Increasing Participation

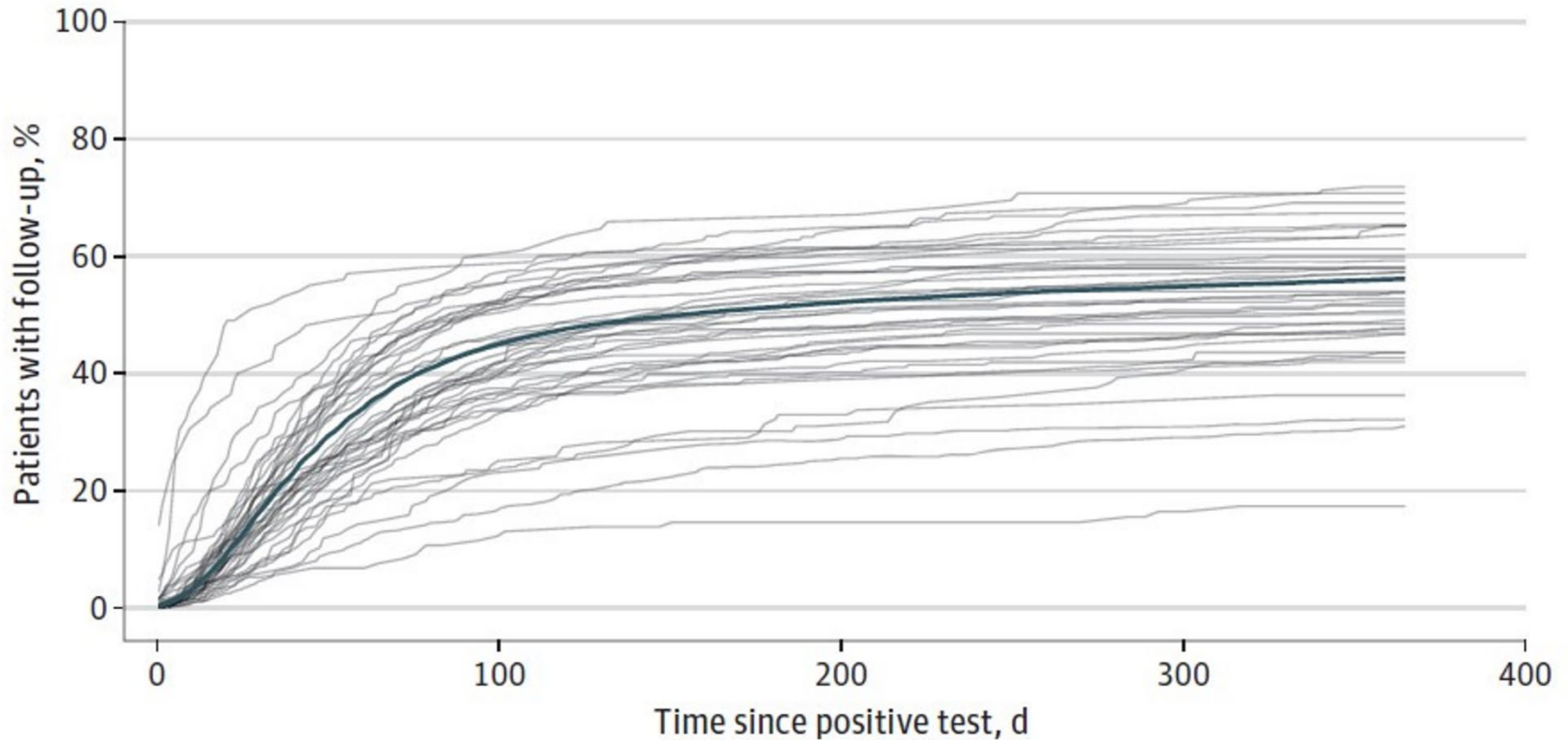


**CRC
Deaths
Prevented**

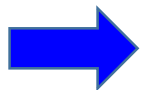
% of Population Moving to Screening

Optum: 33K with Positive Stool Tests

Low Rate of F/U Colonoscopy After Abnormal Stool Test



Mohl JAMA Network Open 2023. PMID 36652246



Only 56% have f/u colonoscopy by 360 days

Blood-test Participation q3 yrs that yields equivalent outcomes to annual FIT

	FIT participatn 10%	FIT participatn 20%	FIT participatn 30%	FIT participatn 40%	FIT participatn 50%	FIT participatn 60%	FIT participatn 70%
CRC cases prevented	18%	36%	54%	72%	90%	Blood test cannot match FIT	Blood test cannot match FIT
CRC deaths prevented	15%	29%	44%	59%	74%	88%	Blood test cannot match FIT
QALYs gained vs. no screening	14%	28%	43%	57%	71%	85%	Blood test cannot match FIT

The blood test must have a 72% compliance to match a FIT compliance rate of 40% for CRC cases prevented

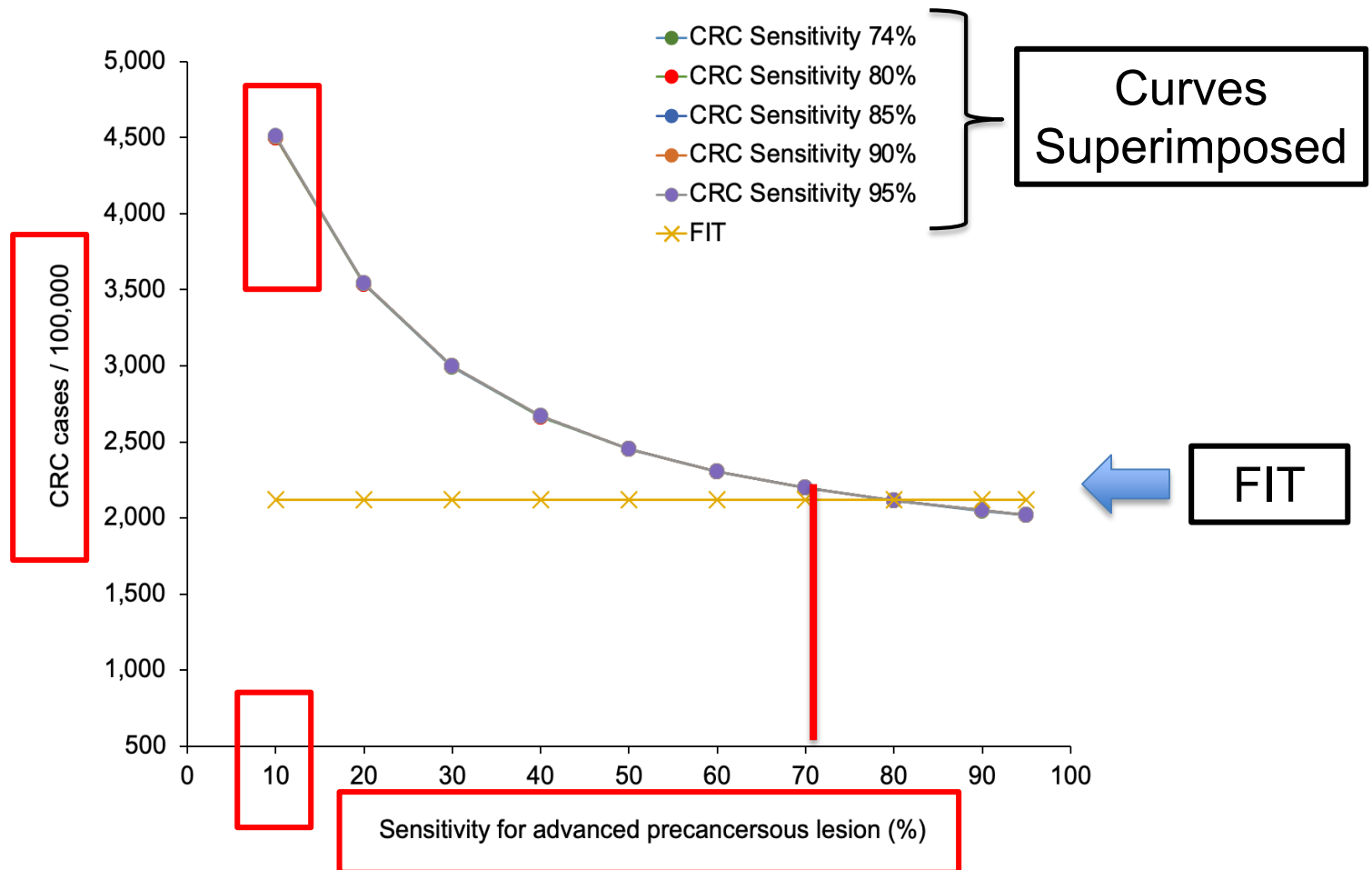
To Match Yearly FIT

- cf-bDNA – **1.7** fold to match incidence reduction of FIT
- cf-bDNA – **1.35** fold to match mortality reduction of FIT

Substitution vs. Addition

- If we offer blood testing, folks who might have otherwise done Stool/CS might opt for cf-bDNA
- Cf-bDNA is LESS effective
- For every 3 substitutions, must get 2 new additions to maintain overall effectiveness

Blood Based Testing: CRC Incidence by Sensitivity for CRC and APL



CRC Incidence Not Affected by CRC Sensitivity

Effectiveness and Cost Effectiveness: Blood-based Screening for CRC

- A blood test that performs at CMS_{\min} is effective BUT less so than current tests
- Blood tests MORE costly than current tests
- Blood tests would have to SIGNIFICANTLY increase participation to match current tests – to levels that are likely unrealistic
- Sensitivity for AA is KEY determinant of effectiveness on incidence and mortality

Conclusions: Blood-based Screening for CRC

- Without substantial detection of advanced adenomas, blood-based screening is inferior to other screening modalities
- Blood testing UNFAVORABLE as a “substitution” test
- Better than nothing - (presuming colonoscopy performed after positive test)
- Useful as non-invasive test for detection of cancer (when detection of precursors not of importance) – such as in very elderly - >80s?

