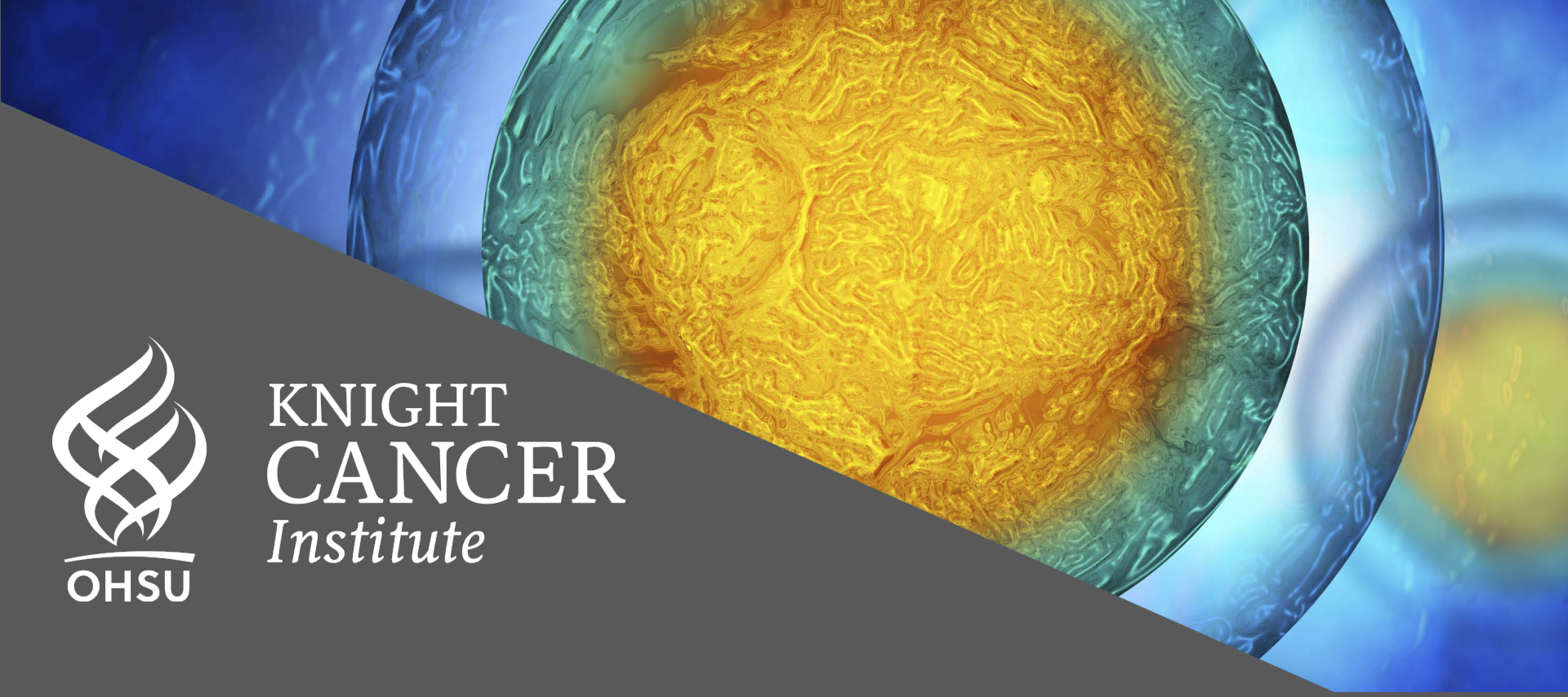

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Emerging Multi-Cancer Early Detection Strategies

Presented by Tomasz M. Beer, MD

Disclosures

- Consultant for Arvinas, Astellas Pharma, AstraZeneca, Bayer, Bristol-Myers Squib, Constellation, Grail Inc., Janssen, Myovant Sciences, Pfizer, Sanofi, Clovis Oncology, Novartis, Tolero
- Stock ownership in Arvinas, and Salarius Pharmaceuticals
- Grant/research support from Alliance Foundation Trials, Astellas Pharma, Bayer, Boehringer Ingelheim, Corcept Therapeutics, Endocyte Inc., Freenome, Grail Inc., Harpoon Therapeutics, Janssen Research & Development, Medivation, Sotio, Theraclone Sciences/OncoResponse, and Zenith Epigenetics

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Learning Objectives

- To review currently available recommended cancer screening strategies
- To compare and contrast single cancer and multiple cancer early detection strategies
- To introduce blood-based multi-cancer early detection technologies
- To review current results from multi-cancer early detection clinical trials

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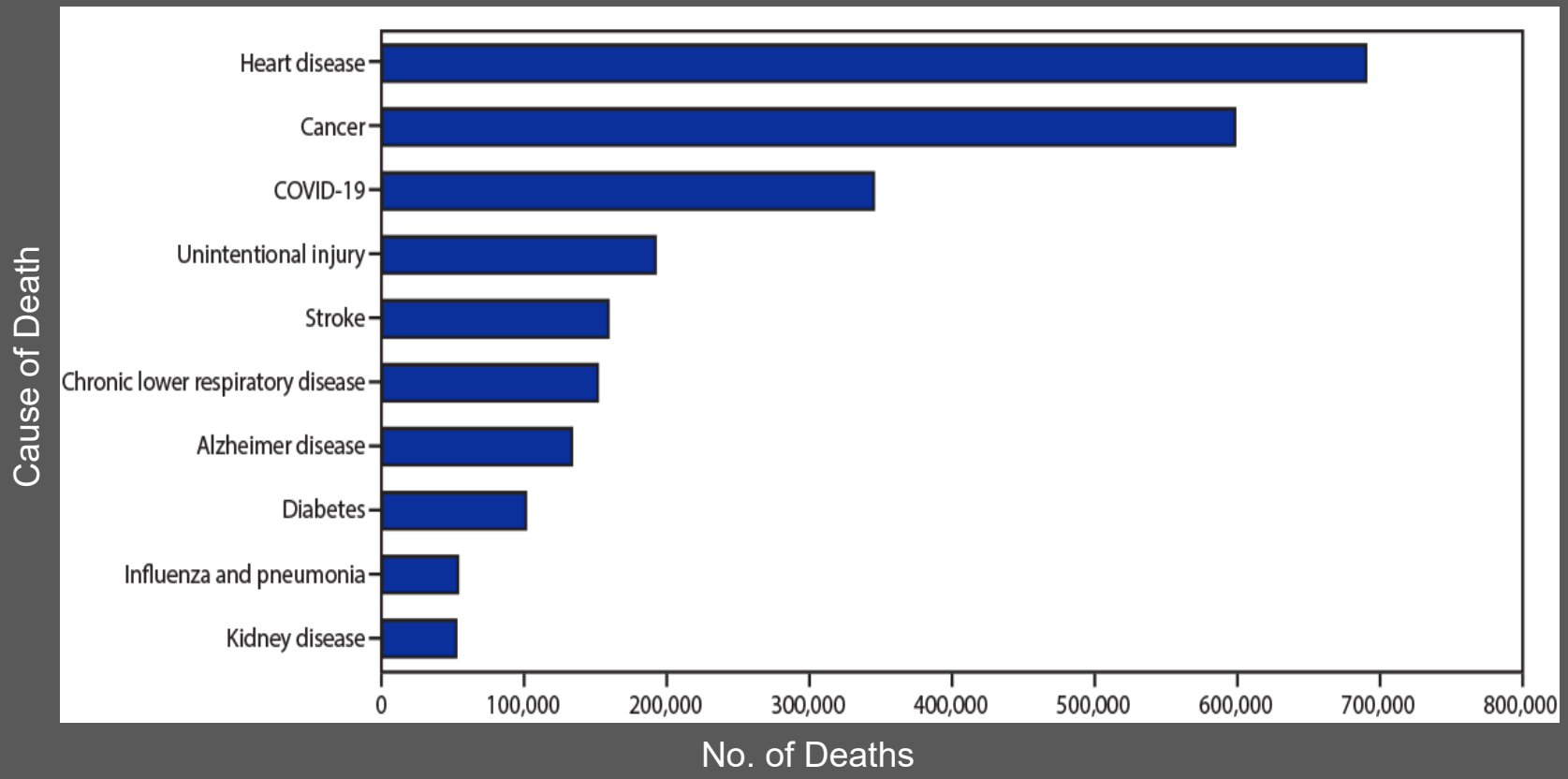
Overall Burden of Cancer in the US

10 leading causes of death in the US in 2020



Ahmad FB et al., *MMWR Morb Mortal Wkly Rep 2021*

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The Staggering Human and Economic Toll From Cancer

UNITED STATES ESTIMATES

8.7M

Years of lost life[1]

One of the leading causes of death in the US[2] with more than 600,000 deaths expected in 2020;[3] $94.4B in lost earnings associated with cancer mortality

$201B

Annual cost of cancer[4]

Total estimated US direct healthcare costs in 2020

$1.3T

Economic burden[1,5]

The majority is due to cancers without recommended screening programs

"Preventing cancer in the first place or detecting it early is the best way to reduce many costs associated with cancer treatment—patient out-of-pocket costs, health care payer costs, and indirect costs."

— AMERICAN CANCER SOCIETY CANCER ACTION NETWORK[6]

US, United States.

[1]Islami F, et al. *JAMA Oncol. 2019*;5:e191460. [2]https://www.cdc.gov/nchs/fastats/leading-causes-of-death.htm [3]https://seer.cancer.gov/statfacts/html/all.html. [4]Mariotto et al. (2020) *Cancer Epi Biom Prev 29:1304*. [5]Based on willingness to pay of $150,000. [5]*American Cancer Society Cancer Action Network*, "The Costs of Cancer: Addressing Patient Costs"

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Current Cancer Screening Guidelines

Cancer	Screening Modality	Age at First Screening	Interval
Lung	Low-dose CT	50 if meets high-risk criteria	Annually
Breast	Mammogram, Ultrasound, MRI	40-50	Every 1-2 years
Colorectal	<u>Stool-based methods</u> -FIT -Stool DNA -High-sensitivity guaiac-based fecal offcut blood test <u>Direct Visualization</u> -CT colonography -Colonoscopy -Flexible sigmoidoscopy	45-50	1-10 years, depending on test
Cervical	Pap test HPV test	21-25	3-5 years
Prostate	PSA Digital rectal exam	50-55	1-4 years

U.S. Preventive Services Task Force and American Cancer Society

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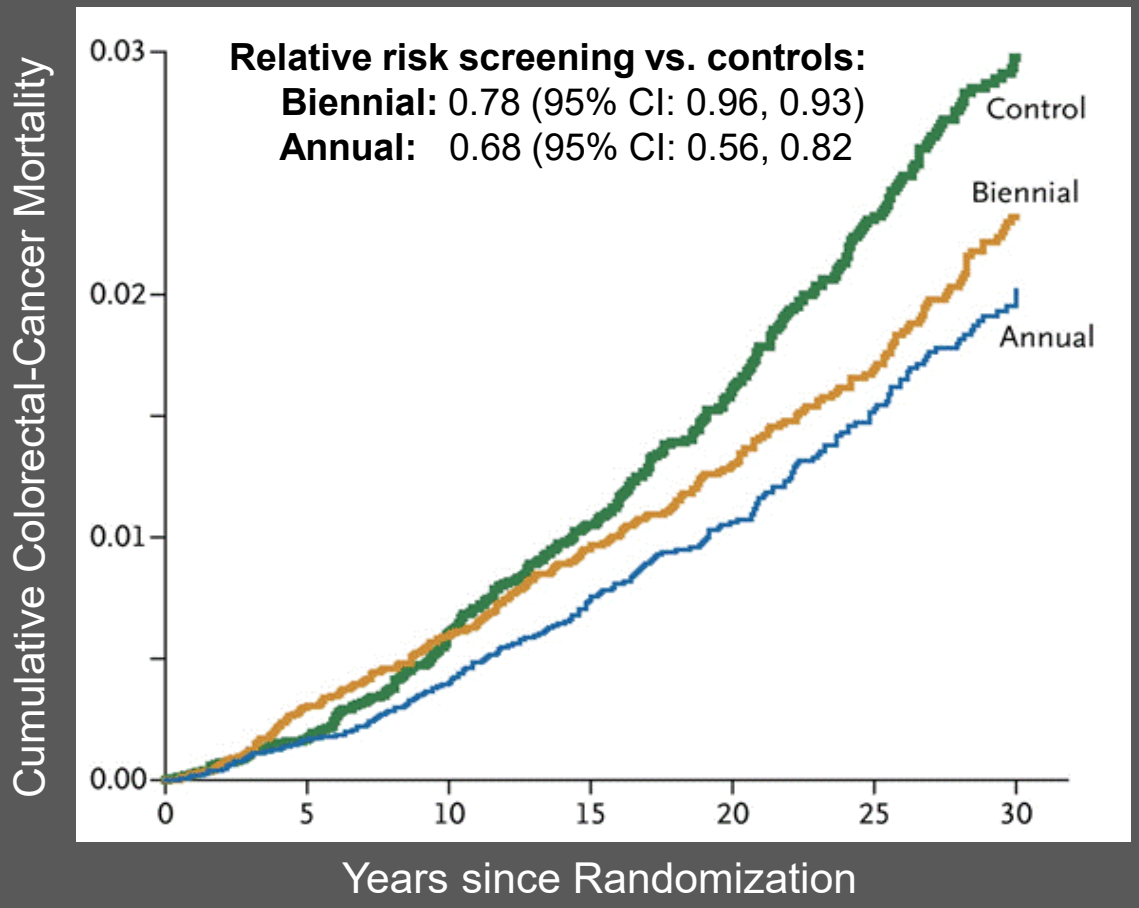
Colorectal Cancer Mortality

Minnesota Colon Cancer Control Study: FOBT vs usual care



Shaukat A et al. *N Engl J Med*. 2013;369(12):1106-1114.

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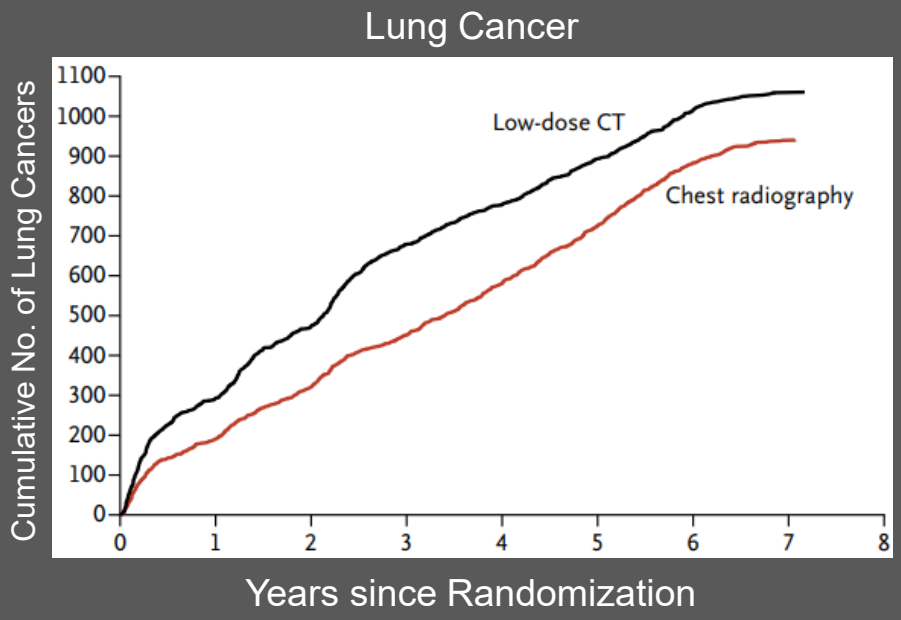
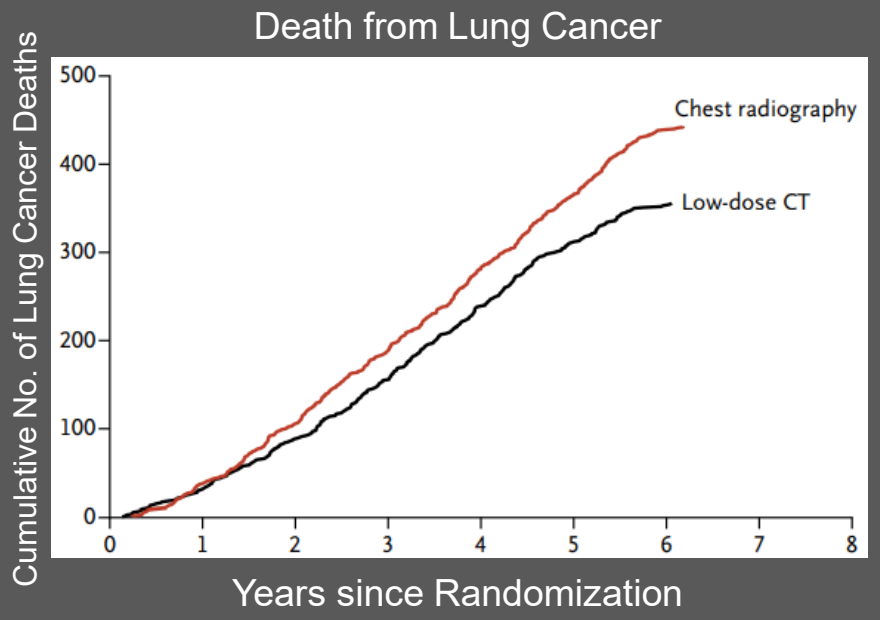
Lung Cancer Diagnosis and Mortality

Randomized trial of low-dose CT vs chest radiography in 53,454 high-risk individuals





The National Lung Screening Trial Research Team. *N Engl J Med*. 2011;365(5):395-409.

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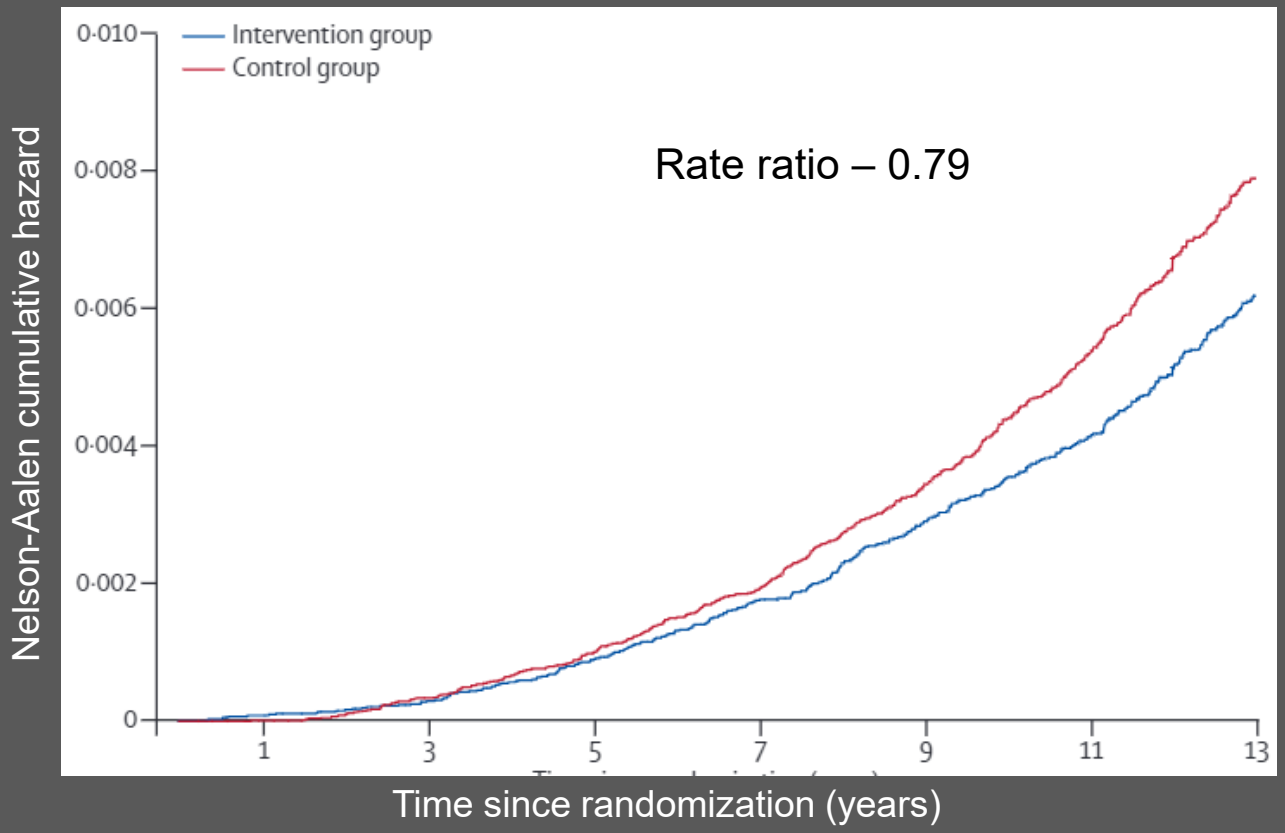
Prostate Cancer Mortality
ERSPC



1 PCa death averted
Per 781 men screened
Per 27 PCa detected

Schroder F, *Lancet*, 2014

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Single Cancer Screening
Test Performance

Cancer	Prevalence (%)	USPSTF Recommended Screening	Sensitivity (%)	Specificity (%)	Positive Predictive Value (%)	Compliance With Recommended Screening (%)[6]
Breast[1]	0.6	Biennial mammography, women ages 55–79	87	89	4.4	78.3
Cervical[2]	<0.1	Triennial cytology or quinquennial cytology/HPV test, women ages 21–65	95	85.5	<1%	80
Colorectal[3]	0.65	Decennial Colonoscopy	*Reference*	*Reference*	*Reference*	69.7
		Triennial Stool-based screening (Cologuard)	92.3	86.6	3.7	
		Annual Stool-based screening (FIT)	73.8	94.9	8.7	
Lung[4]	1.1 (high risk)	Annual low-dose CT for high-risk persons ages 55–80[5]	85	87	6.9	14

CT, computed tomography; FIT, fecal immunochemical test; HPV, human papillomavirus; USPSTF, United States Preventive Services Task Force.
[1]USPSTF. 2016. Lehman, et al. *Radiology.* 2017;283(1):49-58. [2]Kim, et al. *JAMA. 2018;320(7):706-714.* [3]USPSTF. 2017. United States Food and Drug Administration Premarket Approval P130017. Accessed March 26, 2019. Cologuard Test. Available from www.cologuardtest.com/hcp/crc-screening-redefined. Accessed March 26, 2019. [4]Pinsky et al Ann Intern Med. 2015 April 7; 162(7): 485–491. [5]Pinsky. *J Med Screen.* 2012;19(3):154-156. Recommendation for lung screening limited to high-risk smoking population, which accounts for less than 33% of all lung cancers [6] Compliance from BRFSS Prevalence & Trends Data. 2015. [accessed Aug 12, 2020]. URL: https://www.cdc.gov/brfss/brfssprevalence/ except LDCT from Zahnd, et al. *Am J Prev Med* 2019;57(2):250–255.

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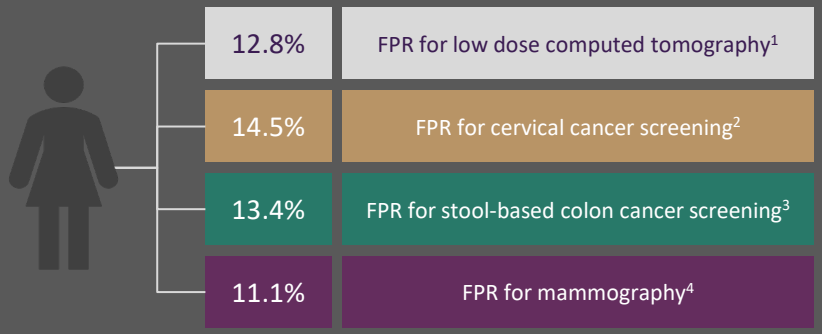
Cumulative False Positive Rate From Single-Cancer Screening

Existing paradigms are associated with a high cumulative false positive rate

- Each false positive from a screening test would require follow-up tests or interventions with attendant risks
- These risks are not well understood at the population level because current paradigms only evaluate one cancer at a time
- An opportunity for a multi-cancer approach to early cancer detection

A 60-year-old female with a history of smoking screened for 4 cancers would have a 43% false positive rate (FPR)*



*Assumes eligibility for all 4 tests.

[1]Pinsky PF, et al. *Ann Intern Med*. 2015;162:485-491. [2]Kim, et al. *JAMA*. 2018;320(7):706-714. [3]US Food and Drug Administration PMA P130017: FDA summary of safety and effectiveness data. August 11, 2014. Accessed March 21, 2020. [4]Lehman CD, et al. *Radiology*. *2017*;283:49-58.

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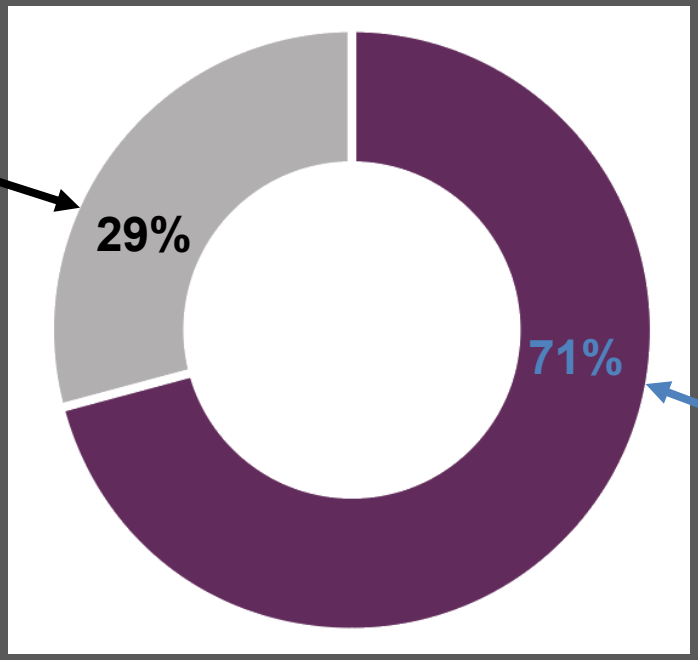
Cancers Without Recommended Screening Tests Account for 71% of Cancer Deaths in the United States in 2020[1,2]

Deaths due to cancers with recommended screening tests (prostate, breast, cervical, colorectal and lung)



Deaths due to cancers without recommended screening tests

https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2020/cancer-facts-and-figures-2020.pdf

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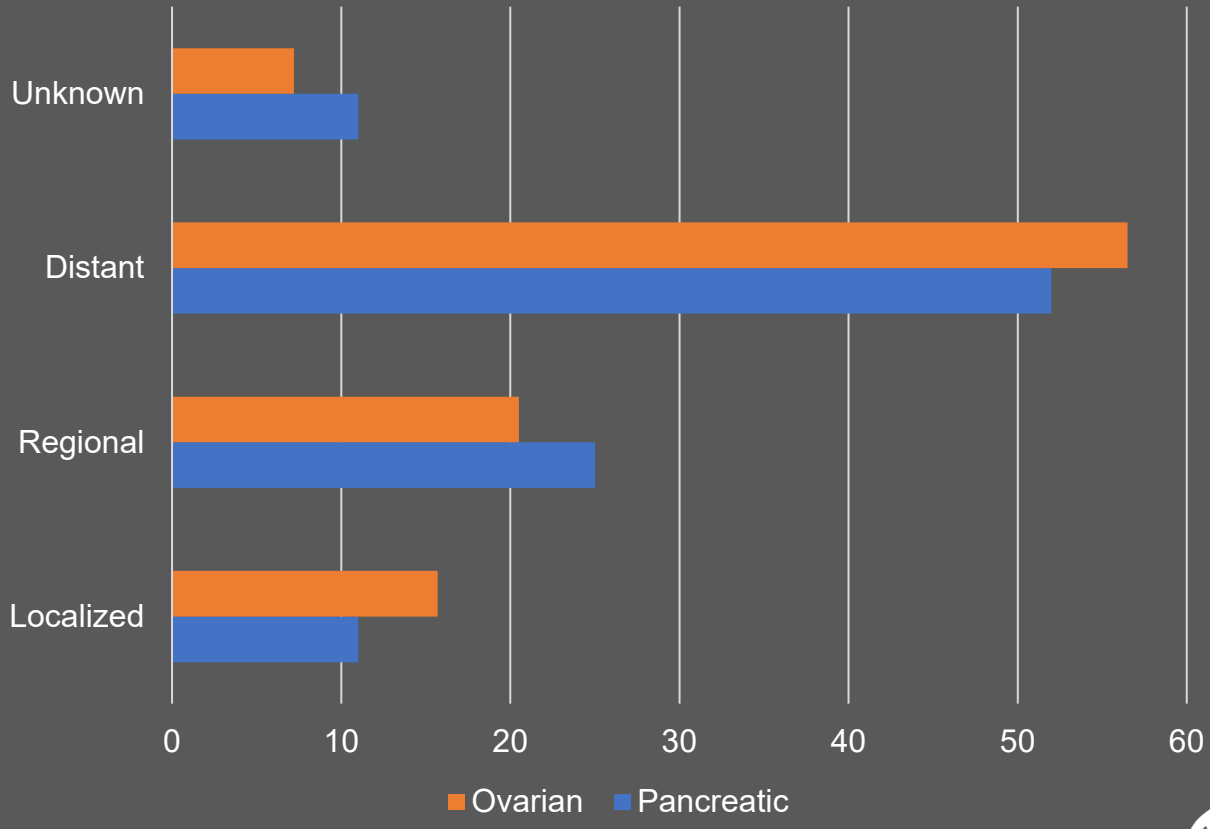
Lethal Cancers Without Effective Screenings Are Often Diagnosed Late

Stage distribution of SEER Incidence Cases



SEER 18 (2008-2017). Available at: *seer.cancer.gov*.

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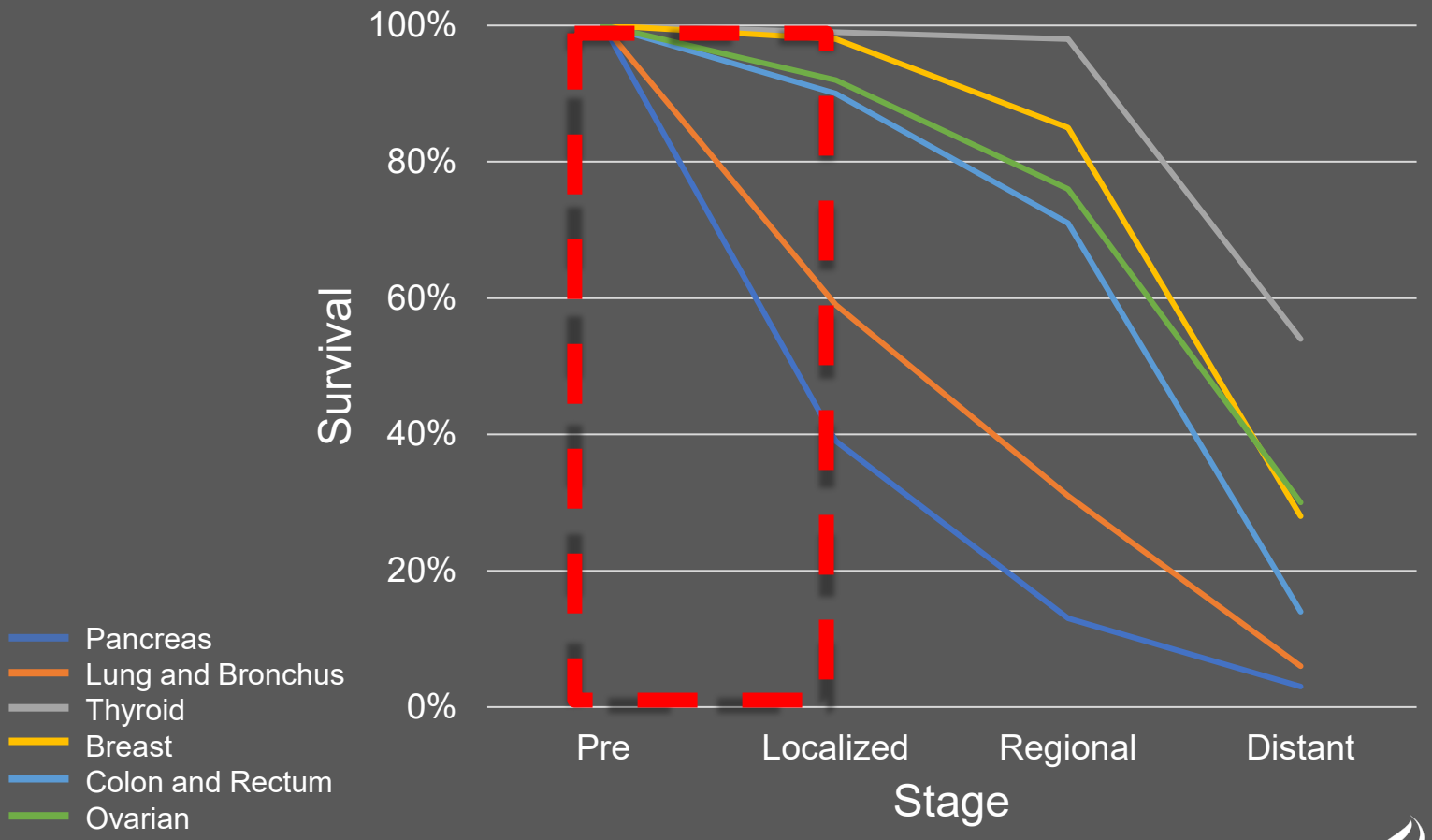
5-year relative survival by stage at diagnosis



SEER 18 (2010-2016). Available at: *seer.cancer.gov*.

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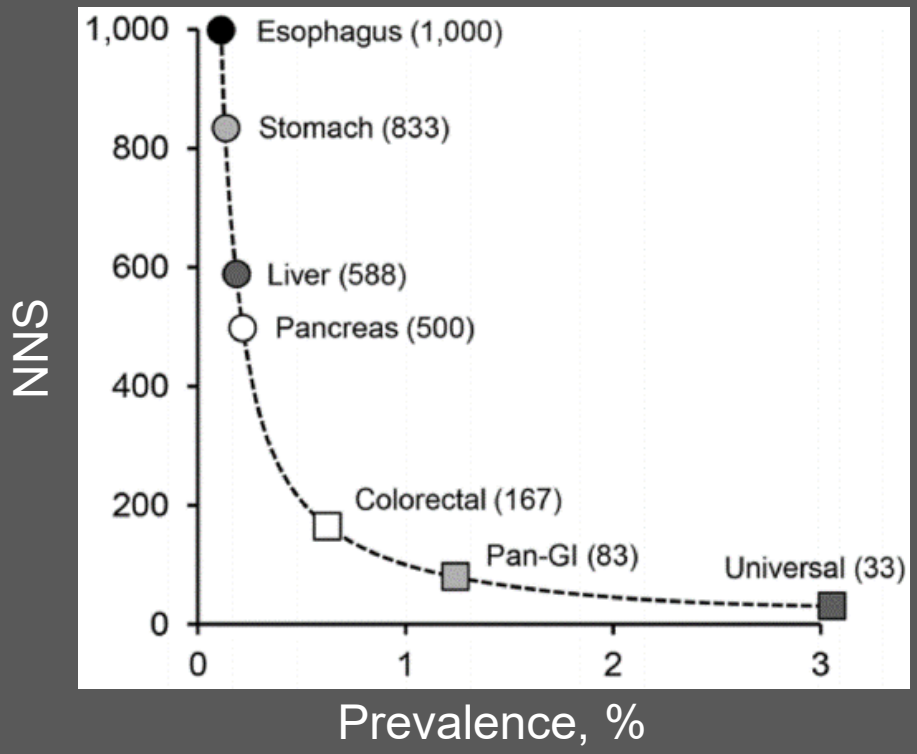
Low Prevalence of Individual Cancers Presents a Challenge to Early Detection



Ahlquist DA. *NPJ Precis Oncol*. 2018;2:23.

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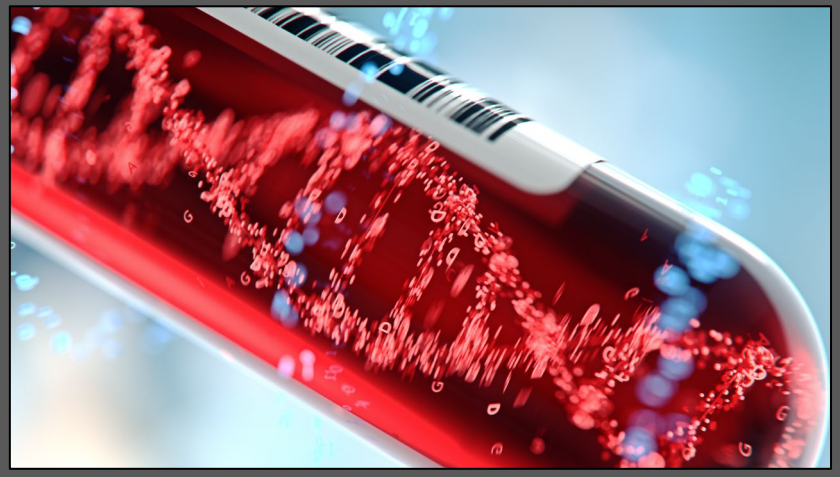
Integrated Multi-omic Analysis of Circulating Cancer Biomarkers Provides a Potential Avenue for Revolutionizing Early Detection of Cancer

- A range of biomarkers can be comprehensively analyzed
  - DNA (mutations, methylation)
  - Proteins
  - Extracellular Vesicles / Exosomes
  - CTCs and CTC clusters
  - RNA, tumor educated platelets, etc.
- Tissue of origin identification is possible
  - DNA methylation patterns



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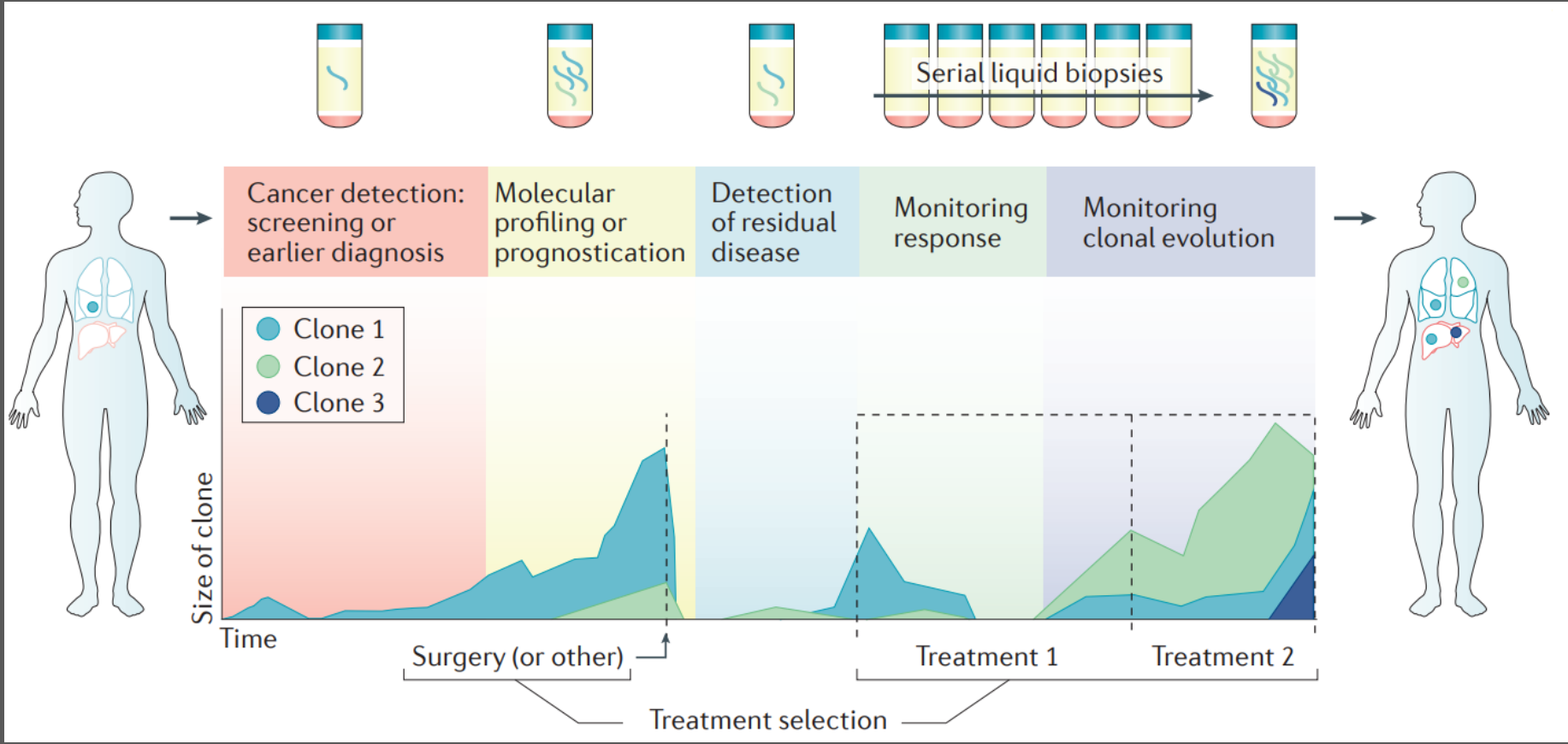
Promise and Applications of Circulating Tumor-derived Material



Wan JCM et al. *Nat Rev Cancer*. 2017;17(4):223-238.

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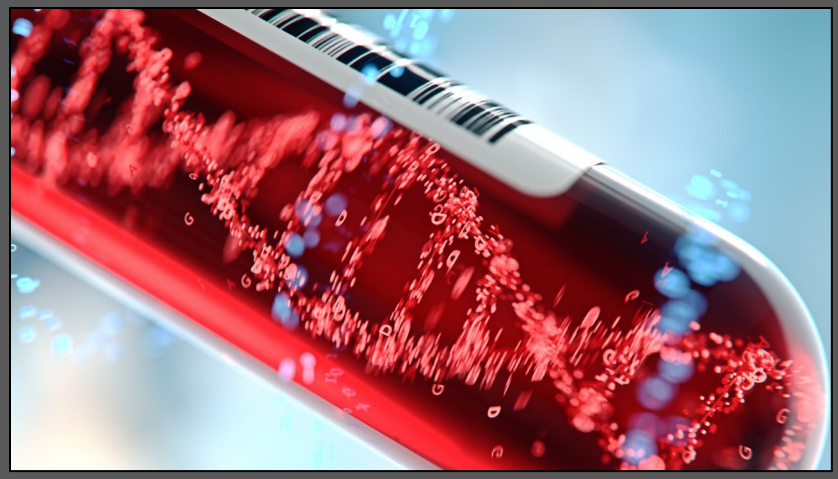
Development Of Blood-Based Cancer Early Detection Tests

- Assay development
- Test development and initial validation
  - Case control design
- Prospective studies measured against current SOC tests
  - Testing simultaneously with a standard screening procedure
  - Focus on single cancer
  - No return of results
- Prospective studies with return of results
  - Multi-cancer application



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Requirements for Multi-Cancer Screening

- Specific and sensitive detection of clinically relevant malignancies at the earliest state possible
- Detect early stage cancer across all major tumor types
- Identify those cancers that will impact survival
- Avoid detection of premalignant and benign “tumors”
- Determine tissue of origin

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Cancer Detection Trial Overview

	Test name	Company	Biomarker	Cancer types	Inclusion criteria	n	Findings
AI-EMERGE[1,2]	—	Freenome	Multi-omic	1 (CRC)	Ages 18-84, recent dx or undergoing routine screening colonoscopy	3275	SE 94% for stage I/II, SP 94%
ECLIPSE[3,4]	LUNAR-2	Guardant	ctDNA genomic, epigenomic alterations	1 (CRC)	Ages 45-84, non high-risk, undergoing routine CRC screening	~10,000	—
PREEMPT CRC[5]	—	Freenome	Multi-omic	1 (CRC)	Ages 45-85 scheduled for standard screening colonoscopy	~14,000	—

SE, sensitivity. SP, specificity. ctDNA, circulating tumor DNA. CCGA, Circulating Cell-free Genome Atlas Study. cfDNA, cell-free DNA.

1. Lin CJ et al. *Journal of Clinical Oncology*. 2021; 39(3 supp). 2. AI-EMERGE. NCT03688906. Updated May 1, 2020. Accessed April 21, 2021. https://clinicaltrials.gov/ct2/show/NCT03688906?term=ai-emerge&draw=2&rank=1. 3. Dean J et al. Digestive Disease Week 2020. Abstract Sa1651. 4. ECLIPSE. NCT04136002. Updated April 13, 2021. Accessed April 21, 2021. https://clinicaltrials.gov/ct2/show/NCT04136002?term=eclipse+AND+guardant&draw=2&rank=1. 5. PREEMPT CRC. NCT04369053. Updated March 19, 2021. Accessed April 21, 2021. https://clinicaltrials.gov/ct2/show/NCT04369053?term=preempt+crc&draw=2&rank=1.

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Cancer Detection Trial Overview, (*cont.*)

	Test	Company	Biomarker	Cancer types	Inclusion criteria	n	Findings
ASCEND[6,7]	Thrive	Cancer SEEK	ctDNA protein	Multiple	Age 50+, healthy controls & cancer cohorts	6399	—
CCGA[8,9]	Galleri	GRAIL	cfDNA methylation	>50	Age 20+, non-cancer and cancer arms	15,254	Substudy: Stage I-III SE 40.7%, SP 99.5%
DETECT-A[10]	Thrive	Cancer SEEK	cfDNA protein	10 types detected	Females age 65-75, no cancer hx	9911	SE 27.1%, SP 98.9%
PATHFINDER[11]	Galleri	GRAIL	cfDNA methylation	>50	Ages 50+, elevated & non-elevated risk groups	~6600	—
STRIVE[12]	Galleri	GRAIL	cfDNA methylation	Breast + other	Females undergoing screening mammography, ages 18+	99,481	—
SUMMIT[13]	Galleri	GRAIL	cfDNA methylation	Lung + other	Ages 55-77 at high risk of lung cancer	~25,000	—

6. ASCEND. NCT04213326. Updated February 16, 2021. Accessed April 21, 2021. https://clinicaltrials.gov/ct2/show/NCT04213326?term=cancerseek&draw=2&rank=1. 7. Cohen JD et al. *Science*. 2018;359(6738):926-930. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6080308/. 8. CCGA. NCT02889978. Updated August 31, 2020. Accessed April 21, 2021. https://clinicaltrials.gov/ct2/show/NCT02889978?term=ccga&draw=2&rank=1. 9. Klein EA et al. AACR Annual Meeting 2021. Abstract LB013. 10. Lennon AM et al. *Science*. 2020;369(6499). 11. Assessment of the Implementation of an Investigational Multi-Cancer Early Detection Test Into Clinical Practice. NCT04241796. Updated January 14, 2021. Accessed April 21, 2021. https://clinicaltrials.gov/ct2/show/NCT04241796?term=GRAIL&draw=2. 12. The STRIVE Study. NCT03085888. Updated July 31. 2020. Accessed April 14, 2021. https://clinicaltrials.gov/ct2/show/NCT03085888?term=strive+AND+grail&draw=2&rank=1. 13. The SUMMIT study. NCT03934866. Updated January 29, 2021. Accessed April 21, 2021. https://clinicaltrials.gov/ct2/show/NCT03934866?term=summit+AND+grail&draw=2&rank=1

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Key Clinical Studies

CancerSEEK Test:

- Evaluates the levels of 8 cancer proteins and the presence of cancer gene mutations

Galleri Test:

- Targeted methylation assay

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CANCER-SEEK

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DETECT-A Study

Multicenter prospective trial in 10,006 women ages 65-75 women not known to have cancer to examine the feasibility and safety of CancerSEEK coupled with PET-C imaging

Science

RESEARCH ARTICLES

Cite as: A. M. Lennon *et al.*, *Science* 10.1126/science.abb9601 (2020).

Feasibility of blood testing combined with PET-CT to screen for cancer and guide intervention

Anne Marie Lennon[1,4,10*], Adam H. Buchanan[11*], Isaac Kinde[12*], Andrew Warren[12,13*], Ashley Honushefsky[11*], Ariella T. Cohain[12], David H. Ledbetter[11], Fred Sanfilippo[14], Kathleen Sheridan[11], Dillenia Rosica[11], Christian S. Adonizio[11,16], Hee Jung Hwang[12], Kamel Lahouel[1,6], Joshua D. Cohen[1,2,3,4,5], Christopher Douville[1,3], Aalpen A. Patel[11], Leonardo N. Hagmann[12], David D. Rolston[11], Nirav Malani[12], Shibin Zhou[1,3,4], Chetan Bettegowda[1,3,8], David L. Diehl[11], Bobbi Urban[12], Christopher D. Still[11], Lisa Kann[12], Julie I. Woods[11], Zachary M. Salvati[11], Joseph Vadakara[11], Rosemary Leeming[11], Prianka Bhattacharya[11], Carroll Walter[11], Alex Parker[12], Christoph Lengauer[12,13], Alison Klein[1,4,15], Cristian Tomasetti[1,6,7], Elliot K. Fishman[1,4,10], Ralph H. Hruban[1,4,9], Kenneth W. Kinzler[1,3,4†], Bert Vogelstein[1,2,3,4†], Nickolas Papadopoulos[1,3,4,9†]

Lennon AM et al. Science. 2020;369(6499):eabb9601.

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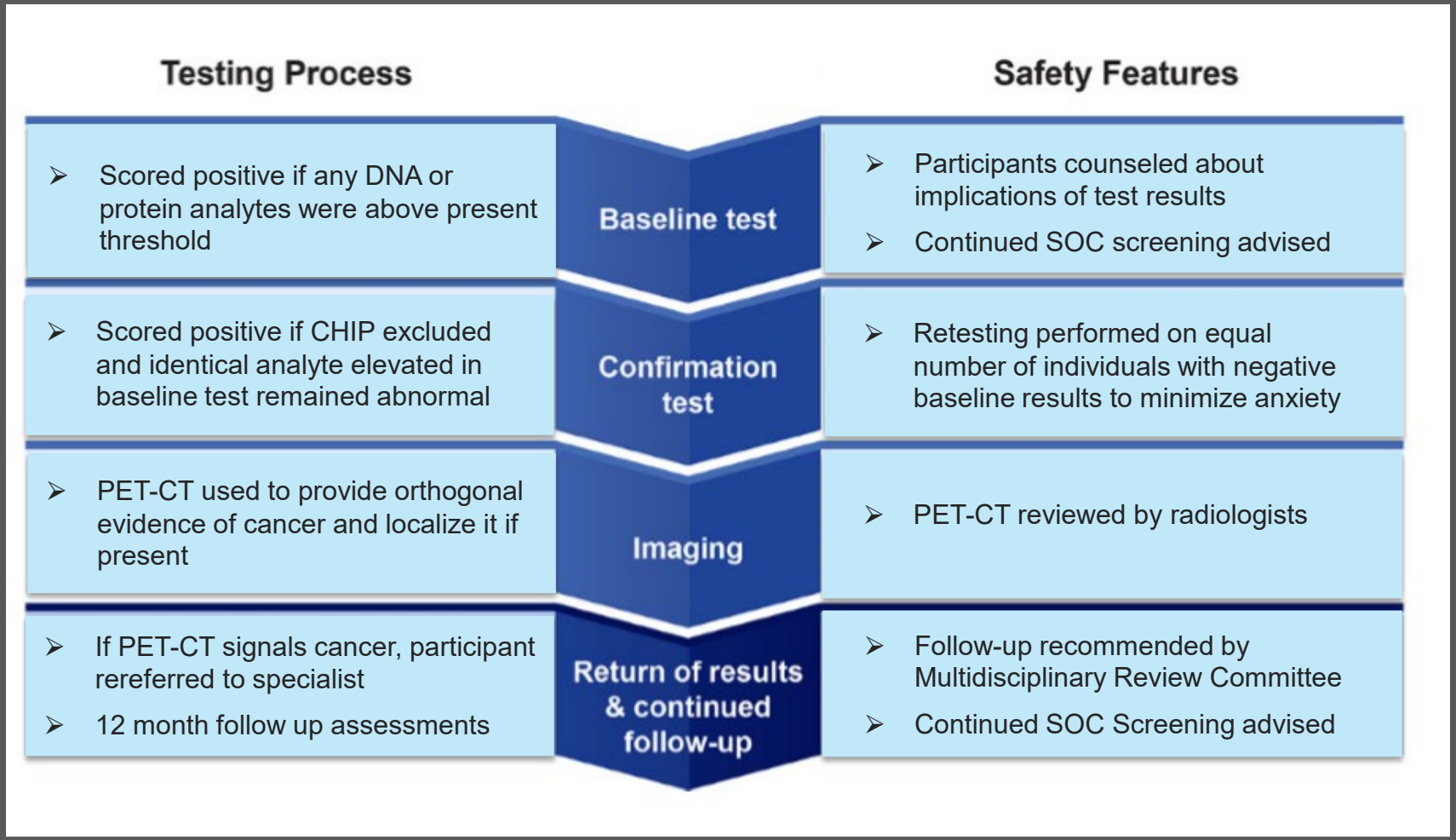
DETECT-A Testing Process



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DETECT-A Results

- 9911 women screened
- 490 positive on baseline test
- 127 positive on both tests
- 26 cancers detected

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DETECT-A Results

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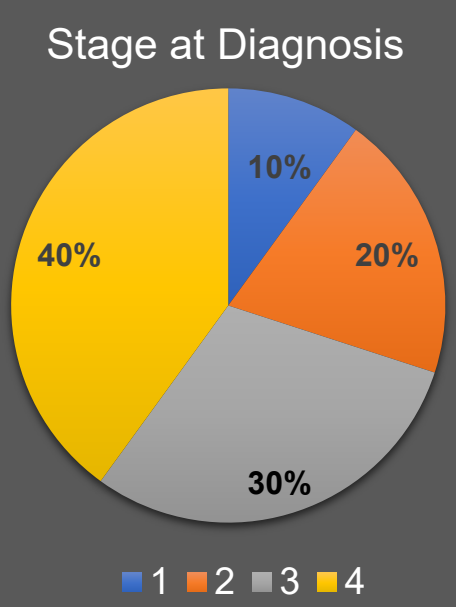

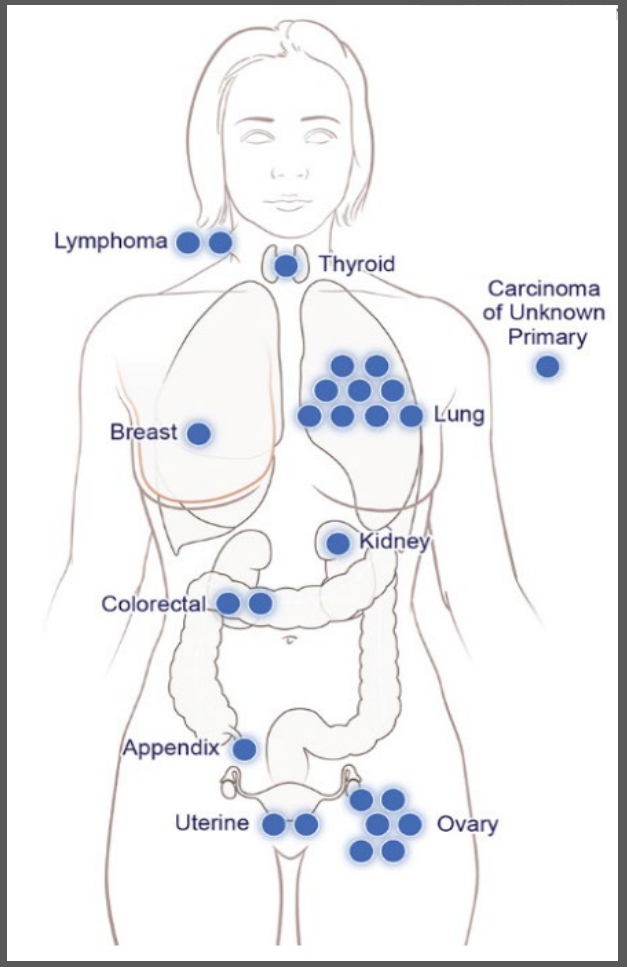

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DETECT-A Results (cont.)

- 9911 women screened
- 490 positive on baseline test
- 127 positive on both tests
- 26 cancers detected

- 101 participants had imaging based on false-positive test
- 22 invasive diagnostic procedures after false-positive test

- 24 cancers detected with routine screening
- 46 cancers detected with neither approach

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Test Performance

Performance with and without confirmation test and 95% confidence intervals

	Blood Test Without Confirmation	Blood Test With Confirmation
Positive Predictive Value	5.9% (4.0-8.4)	19.4% (13.1-27.1)
Specificity	95.3% (94.9-95.7)	98.9% (98.7-99.1)
Negative Predictive Value	99.3% (99.1-99.4)	99.3% (99.1-99.4)
# Needed to Screen to Detect 1 Cancer	342 (238-510)	381 (260-583)
Sensitivity		
All Cancers	30.2 (21.3-40.3)	27.1% (18.5-37.1)
Cancers with SOC Screening	27.5% (15.9-41.7)	23.5% (12.8-37.5)
Cancers with no SOC Screening	33.3% (20.0-49.0)	31.1% (18.2-46.6)

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GALLERI

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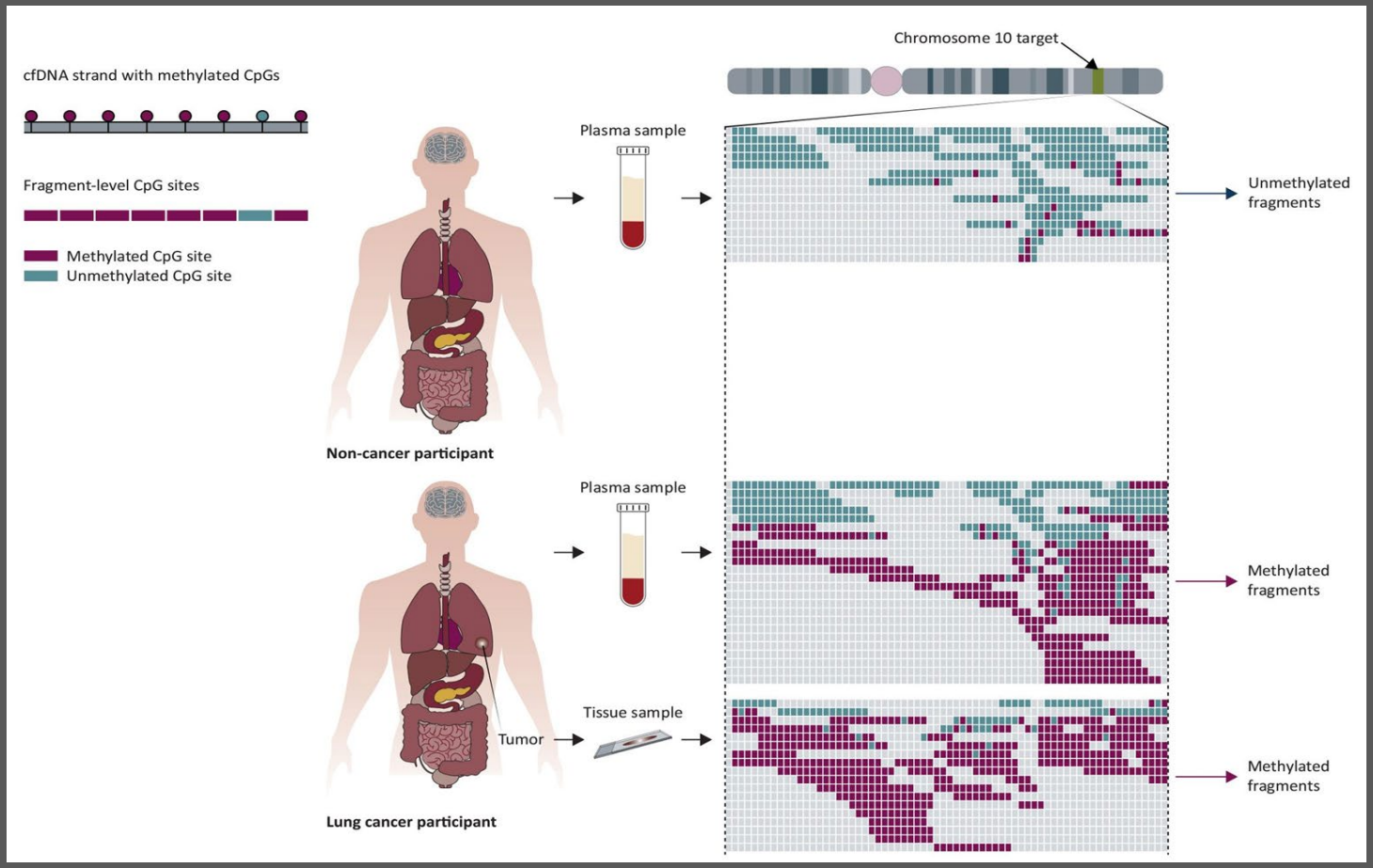
Methylation Biology Differentiates Cancer From Non-Cancer



cfDNA, cell-free DNA. Figure from Liu MC, et al. *Ann Oncol*. 2020;31(6):745-759. DOI: 10.1016/j.annonc.2020.02.011.

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Grail MCED Clinical Trials

CCGA[1]	STRIVE	PATHFINDER	SUMMIT
NCT02889978	NCT03085888	NCT04241796	NCT03934866
15,254 participants ♂♀	99,308 participants ♀	~6,200 participants ♂♀	~25,000 participants ♂♀
Demonstrate feasibility of detecting cancer and predicting tissue of origin with minimal false positives	Confirm performance in a population with no known active cancer diagnosis	Evaluate implementation of test in clinical practice	Additional performance in a population with no known active cancer diagnosis and clinical utility in a high-risk population

[1]Circulating Cell-Free Genome Atlas study.

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Multi-Cancer Early Detection Test

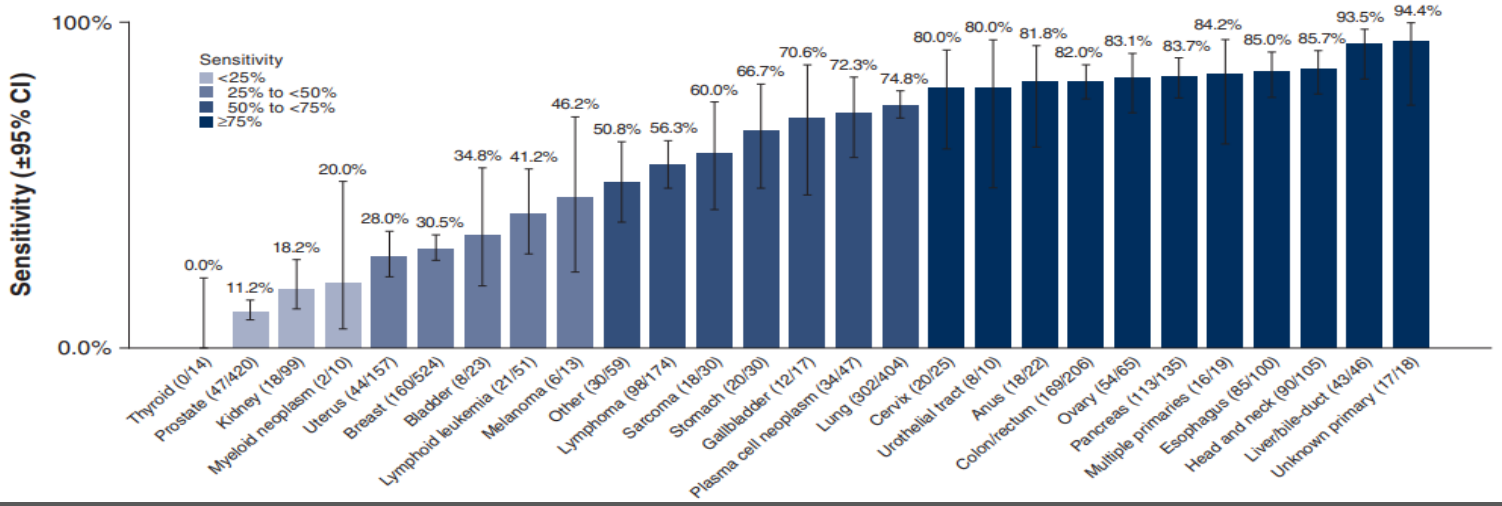
Sensitivity and Specificity

Overall sensitivity and specificity

	Cancer	Non-cancer	Total
	2823	1254	4077
Test positive	1453	6	1459
Test negative	1370	1248	2618
	Sensitivity = 1453/2823 51.5% (49.6%-53.3%)	Specificity = 1248/1254 99.5% (99.0%-99.8%)	

Two-sided 95% Wilson confidence intervals were calculated.

Sensitivity by cancer class



Klein EA et al. Ann Oncol. 2021; S0923-7534(21)02046-9.

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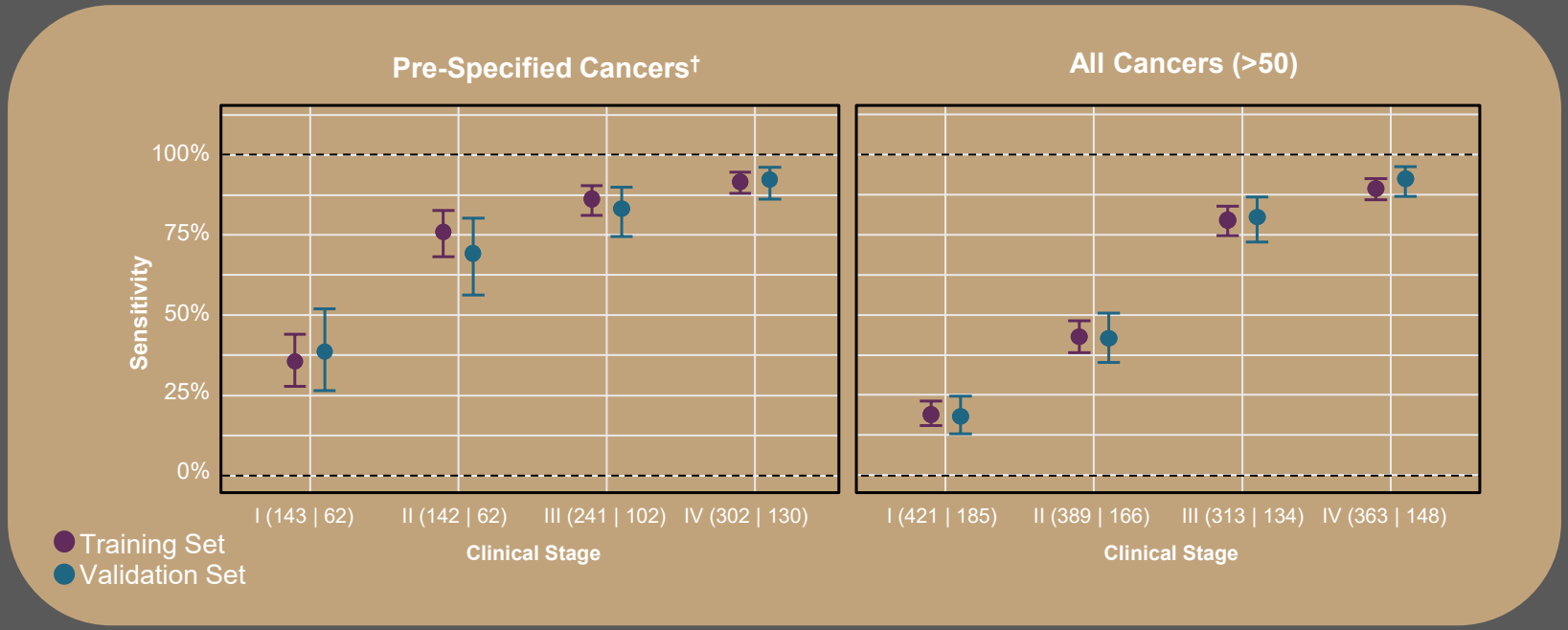
Circulating Cell-free Genome Atlas (CCGA) Sub-Study 2

- 76.4% (71.6-80.7%) sensitivity in pre-specified† cancers (validation set)
- 54.9% (51.0-58.8%) overall sensitivity in >50 cancers (validation set)
- Single fixed false positive rate (0.7%) across all cancers



†Anus, bladder, colon/rectum, esophagus, head and neck, liver/bile-duct, lung, lymphoma, ovary, pancreas, plasma cell neoplasm, stomach.
Plot excludes unstaged cancers.
Liu MC, et al. *Ann Oncol*. 2020;31(6):745-759. DOI: 10.1016/j.annonc.2020.02.011.

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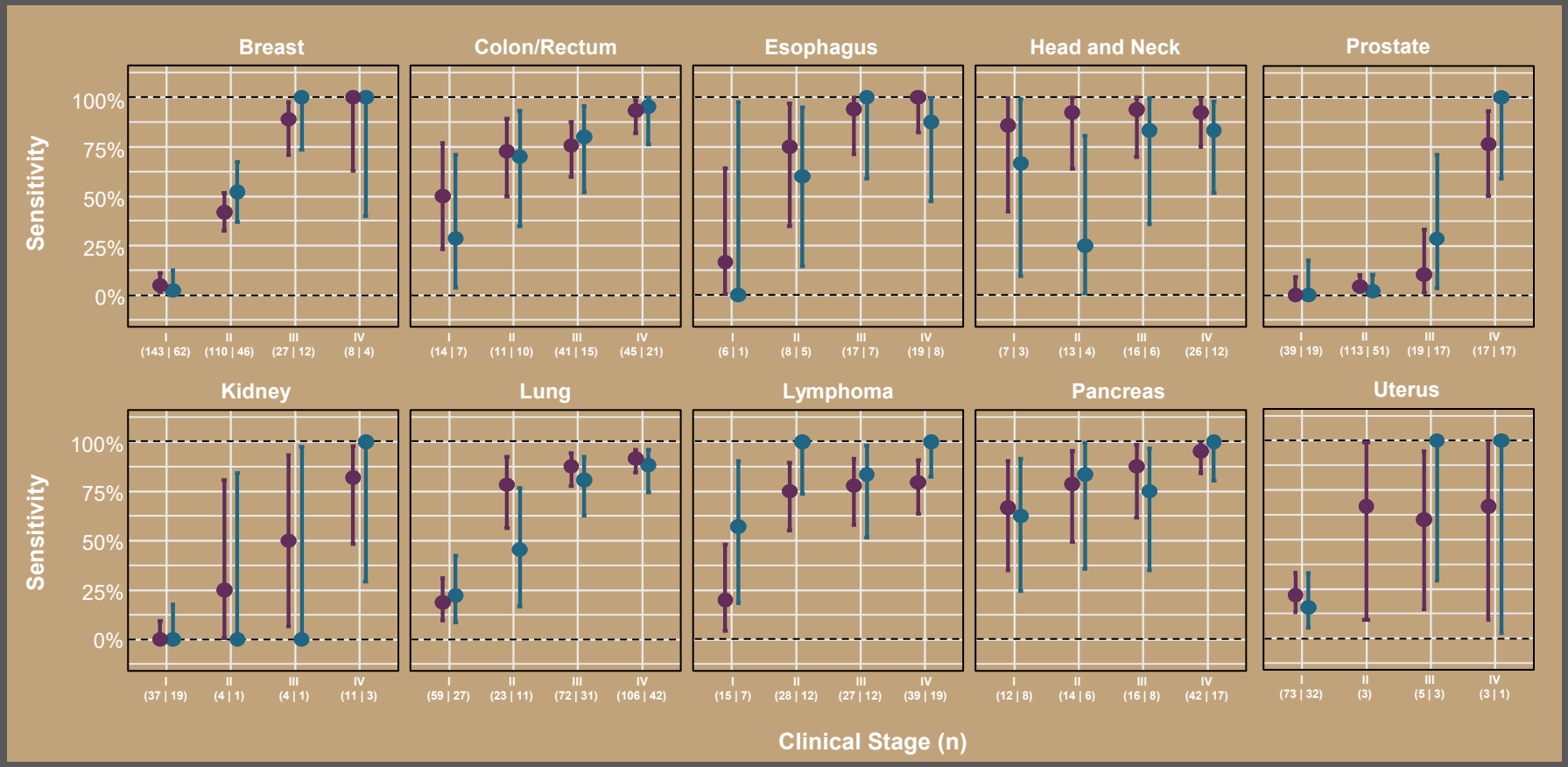
Circulating Cell-free Genome Atlas (CCGA) Sub-Study 2



[a]Includes cancers with >50 samples.

Liu MC, et al. Ann Oncol. 2020;31(6):745-759. DOI: 10.1016/j.annonc.2020.02.011.

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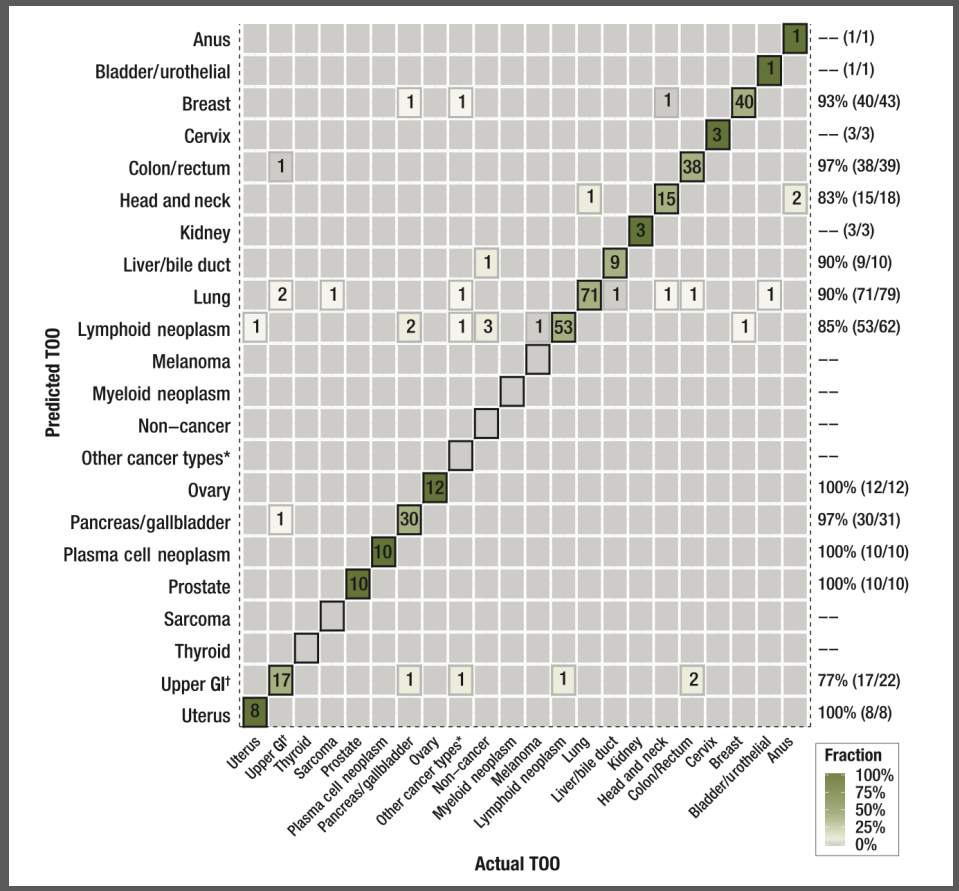
Circulating Cell-free Genome Atlas (CCGA) Study –Tissue of Origin (TOO)

- >95% of samples with assigned TOO
- >93% of those calls were correct



Liu MC et al. *Ann Oncol.* 2020;31(6):745-759.

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Key Performance Features of Galleri Test

Demonstrated in CCGA Case Control Study

> 50	Cancers detected
43%	Positive predictive value (modeled)
0.7%	False-positive rate
44%	Sensitivity stages I-III for all cancer
67%	Sensitivity stages I-III for prespecified cancers representing ⅔ of cancer mortality in US
93%	Rate tissue of origin predicted correctly[1]

> 50 cancers, including unscreened cancers

- Anorectal
- Bladder/urothelial
- Esophageal
- Gastric
- Head and neck
- Liver/bile-duct
- Lymphoid neoplasm[2]
- Melanoma
- Myeloid neoplasm
- Ovarian
- Pancreas/gallbladder
- Plasma cell neoplasm
- Renal
- Sarcoma
- Seminoma
- Skin
- Testicular
- Thyroid
- Uterine
- Vaginal
- Vulva

Recommended screening programs*

- Breast
- Cervical
- Colorectal
- Lung
- Prostate

CCGA, Circulating Cell-free Genome Atlas.

Liu MC, et al. *Ann Oncol*. 2020;31(6):745-759. DOI: 10.1016/j.annonc.2020.02.011.

[1]Based on tissue of origin class assigned in 96% of cases where cancer was detected.

[2]Lymphoid neoplasm includes lymphoma and leukemia. Leukemia includes chronic lymphocytic leukemia and hairy cell leukemia

*USPSTF A, B, or C rating.

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The Pathfinder Study: Assessment of A Multi-Cancer Early Detection Test In Clinical Practice

Prospective, multicenter, interventional, return-of-results study (NCT04241796)

Study Objectives

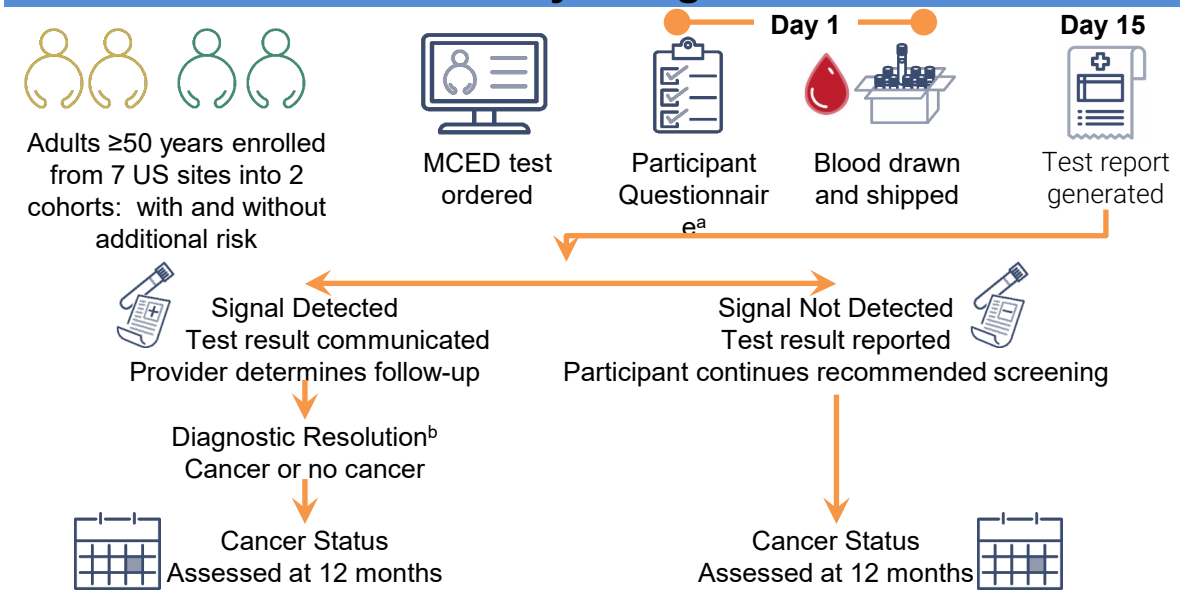
Primary

- Assess extent of diagnostic testing required to achieve diagnostic resolution following a "signal detected" test result

Secondary

- Evaluate test performance
- Assess participant-reported outcomes and perceptions of the MCED test

Study Design



[a]Also collected at other timepoints during the study.
[b]Defined as date when study team determines to end diagnostic evaluation triggered by a "signal detected" test result.
MCED, multi-cancer early detection.

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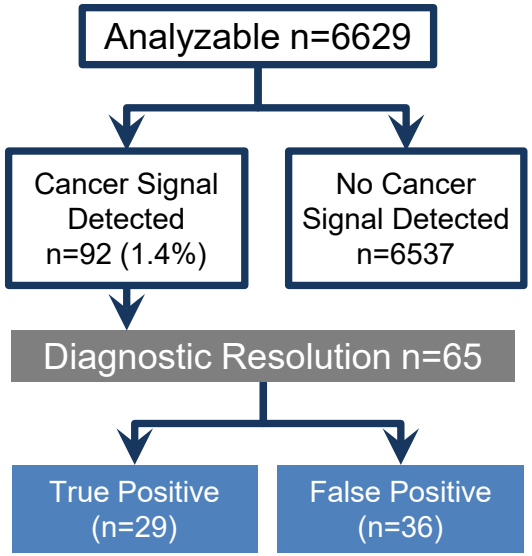
Interim Primary Outcome: Extent of Diagnostic Testing



	True Positive n=27*	False Positive n=36	
All Imaging/Invasive Procedures	2.0 (1.5, 3.0)	1.5 (1.0, 2.2)	2.0 (1.0, 3.0)
All Imaging Tests	1.0 (1.0, 1.5)	1.0 (1.0, 2.0)	1.0 (1.0, 2.0)
Functional	1.0 (0, 1.0)	1.0 (0, 1.0)	1.0 (0, 1.0)
Anatomic	1.0 (0, 1.0)	1.0 (0, 1.0)	1.0 (0, 1.0)
All Invasive Procedures*	1.0 (1.0, 1.0)	0 (0, 0.2)	0 (0, 1.0)
Minimally Invasive	1.0 (0.5, 1.0)	0	0 (0, 1.0)
Surgical	0	0	0
Clinical Lab Tests	3.0 (1.0, 5.5)	3.0 (1.0, 6.0)	3.0 (1.0, 6.0)
Days to Resolution	50.0 (27.0, 76.5)	49.0 (30.2, 153.8)	50.0 (28.0, 91.0)

Most participants with diagnostic resolution had at least 1 imaging test (57/63; 90%)
More true positives (21/27; 78%) than false positives (9/36; 25%) had at least 1 invasive procedure
Most invasive procedures were minimally invasive (88%)

*2 participants with 'signal detected' MCED test result (true positives) were excluded from the diagnostic workup analysis because diagnostic testing was initiated before MCED test results were returned.
As of March 2021, 30 participants had ≥1 invasive procedure (26 minimally invasive, 2 surgical, 2 both).

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Interim Secondary Outcome: Test Performance

	With Additional Risk	Without Additional Risk	Total
Cancer Signal Detection, No.	n=3695	n=2934	N=6629
Detected, No. (%)	**56 (1.5)**	**36 (1.2)**	**92 (1.4)**
True Positive	20 (0.5)	9 (0.3)	29 (0.4)
False Positive	15 (0.4)	21 (0.7)	36 (0.5)
No Current Diagnostic Resolution	21 (0.6)	6 (0.2)	27 (0.4)
Not Detected	3639 (98.5)	2898 (98.8)	6537 (98.6)
PPV for Cancer Signal Detection, No.	n=35	n=30	n=65
% (95% CI)	**57.1 (40.9–72.0)**	**30.0 (16.7–47.9)**	**44.6 (33.2–56.7)**
CSO Prediction Accuracy	n=19[a]	n=8[a]	n=27[a]
First CSO, % (95% CI)	**84.2 (62.4–94.5)**	**87.5 (52.9–99.4)**	**85.2 (67.5–94.1)**
First/Second CSO	100 (83.2–100.0)	87.5 (52.9–99.4)	96.3 (81.7–99.8)

Cancer signal was detected in 1.4% of all analyzable participants

Nearly half with diagnostic resolution had confirmed cancer, for an estimated 45% PPV

Cancer signal origin was predicted with high accuracy

Data as of March 2021. CSO, cancer signal origin; PPV, positive predictive value. [a]Excludes 1 participant with unknown cancer type and 1 with indeterminate CSO from the true positive set.

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Cancer Characteristics of True Positive Set (n=28)

Cancer Type Diagnosed	Clinical AJCC Stage of New Cancers					Recurrent Cancers		First Predicted Cancer Signal Origin
	I	II	III	IV	Other	Local	Distant	
Colon or rectum				1	1 Unknown			Upper GI Tract (SIV pt); Colon/Rectum (unk pt)
Head and Neck		1		1				Head and Neck
Liver, bile duct	1		1					Liver, bile-duct
Lung			1					Lung
Lymphoid leukemia					2 NA			Lymphoid Neoplasm
Lymphoma	2	3	1	2				Lymphoid Neoplasm
Ovary, peritoneum/FT			1					Uterus (ovary second CSO)
Pancreas		1						Pancreas/Gallbladder
Plasma cell neoplasm					1 NA			Plasma Cell Neoplasm
Prostate				1				Indeterminate
Small intestine	1							Colon/Rectum (upper GI second CSO)
Waldenstrom macroglobulinemia					1 NA			Lymphoid Neoplasm
Breast cancer							4	3 Breast 1 Breast (first CSO), lymphoid (second)
Prostate cancer						1		Lymphoid (first CSO), prostate (second)
Total	**4**	**5**	**4**	**5**	**5**	**1**	**4**	

AJCC, the American Joint Committee on Cancer version 8; CSO, cancer signal origin; FT, fallopian tube; GI, gastrointestinal; NA, not applicable; pt, participant; SIV, stage IV; unk, unknown.

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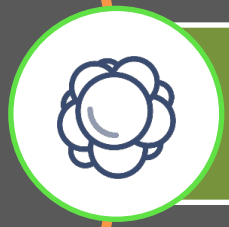
Pathfinder Interim Analysis Conclusions

In this prespecified interim analysis, the MCED test was safely administered and detected cancer signal in a broad range of cancer types



More than half of new cancers were detected at early stages (clinical stages I–III)

Follow-up of PATHFINDER participants continues and will identify the incidence of cancer diagnoses for all participants within 12 months of their initial blood draw, at which time the specificity and negative predictive value of the MCED test will be evaluated

MCED, multi-cancer early detection.

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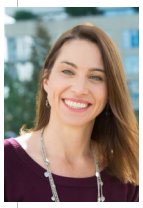
Tom Beer, MD

Tiffani Howard



Diana Potts

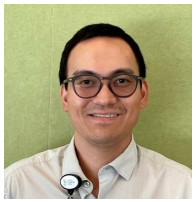
Thank you.

The CEDAR Clinical Trials Team

Mason McLellan

Grace Curran

Mitchell Yep



Francis de Asis

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