Multicancer Early Detection Tests (MCED)

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March 27 – 30, 2025

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Memorial Cancer Institute

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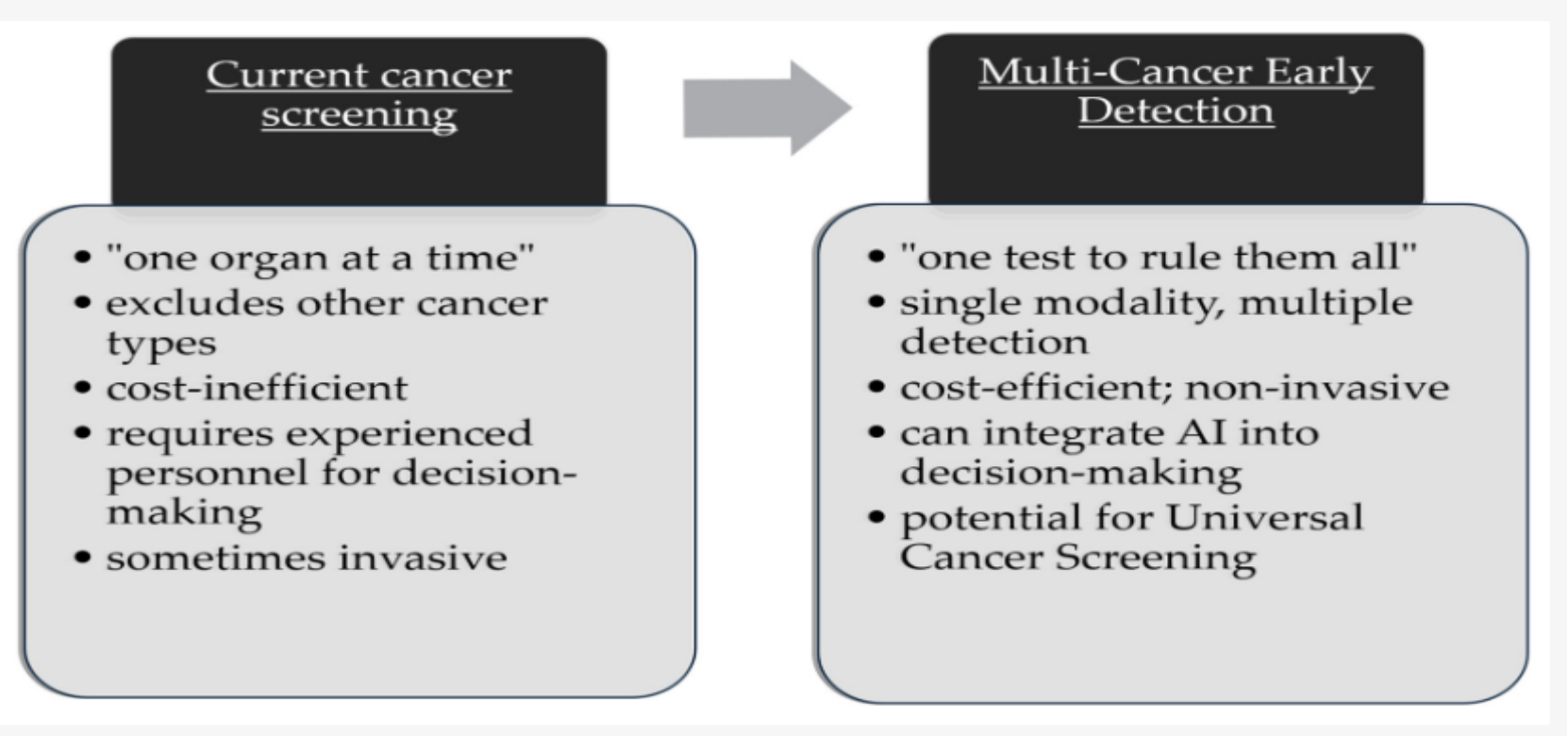


Data from the PLCO)Cancer Screening Trial with 68,436 participants, showed that after 14 screening intervention in 3 years, the cumulative risk of having at least 1 false-positive screening test is 60.4% for men, and 48.8% for women.

The cumulative risk after 14 tests of undergoing an invasive diagnostic procedure prompted by a false-positive test is 28.5% for men and 22.1% for women

Croswell, J.M. Ann. Fam. Med. 7, 212–222

- (NCCN) recommends screening for a single cancer type, and there are no recommended methods for most cancers (MCED)

- MCED needs to simultaneously meet the following conditions:

  (1) High specificity, avoiding overdiagnosis and overtreatment, and reducing the unnecessary mental anxiety and follow up burden of the examinees.

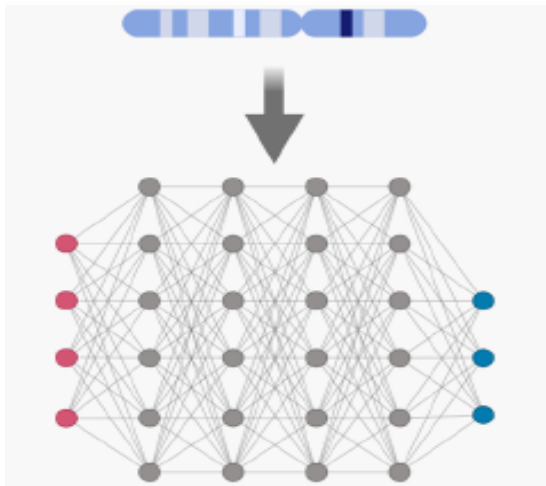
  (2) High sensitivity, lowering the rate of missed detections, and decreasing the number of patients who have progressed to an advanced stage.

  (3) Tissue-traceable accuracy, accurately informing the specific organ where the tumor occurs, and accurately guide the subsequent clinical examination program.

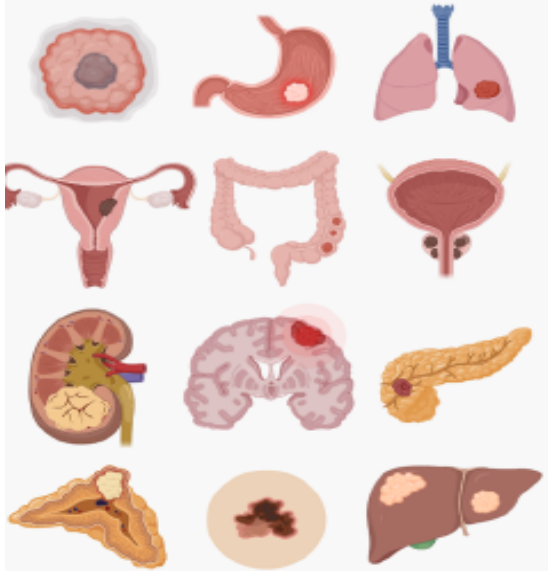
  (4) High cost/effectiveness,

  (5) Less invasive, easy to operate, thus can improve the adherence of the population screening, easy to promote.

MCE+A1:G10D test	Company	Sensitivity	Specificity	Detection method	Detectable cancer types
Aurora	AnchorDx	84% (Lung)	99% (Lung)	Targeted methylation sequencing	Lung, breast, colorectal, gastric, esophageal cancers
CancerRadar	Early Diagnostics	85.60%	99%	cfDNA fragmentation, methylation, CNVs, microbial composition	Lung, colon, gastric, liver cancers
CancerSEEK	Exact Sciences	62%	>99%	Multiplex PCR and single immunoassay	Lung, breast, colorectal, pancreatic, gastric, hepatic, esophageal, ovarian cancers
cfMeDIP-seq	Adela Inc.	AUC 0.92–0.98	–	5mC enrichment and sequencing	Acute myeloid leukemia, pancreatic, lung cancers
DEEPGENTM	Quantgene	43%	99%	Next-generation sequencing (NGS)	Lung, breast, colorectal, prostate, bladder, pancreatic, liver cancers
DELFI	Delfi Diagnostics	73%	98%	cfDNA fragmentation profiles and machine learning	Lung, breast, colorectal, pancreatic, gastric, bile duct, ovarian cancers
EDIM-TKTL1/Apo10	Zyagnum AG	95.80%	97.30%	Epitope detection in monocytes (EDIM)	Oral squamous cell carcinoma, breast, prostate cancers
EpiPanGI Dx	–	85–95% (AUC 0.88)	–	Bisulfite sequencing and machine learning	Gastrointestinal cancers (colorectal, pancreatic, liver, gastric, esophageal)
Galleri®	GRAIL	51.50%	99.50%	Targeted methylation sequencing	More than 50 cancer types
IvyGeneCORE® Test	Laboratory for Advanced Medicine	84%	90%	Methylation analysis	Lung, breast, colorectal, liver cancers
Omni1	Avida Biomed	65% (Stage I)	89%	Targeted methylation sequencing	Lung, breast, colorectal, pancreatic, liver, ovarian cancers
PanSeer	Singlera Genomics	87.60%	96.10%	Semi-targeted PCR libraries and sequencing	Lung, colorectal, gastric, liver, esophageal cancers
PanTum Detect®	Zyagnum AG	100%	96.20%	EDIM-TKTL1 and EDIM-Apo10 tests	Cholangiocellular, pancreatic, colorectal cancers



Machine analysis algorithms and organizational traceability



Type of technology and types of cancer covered	Model effectiveness
CCGA3 • cfDNA methylation sequencing technology • >50 types of cancer	• Sensitivity: 51.5% • Specificity: 99.5% • Organizational traceability accuracy: 88.7%
CancerSEEK • cfDNA mutation and protein biomarker detection technology • Ovarian, liver, stomach, pancreatic, esophageal, colorectal, lung and breast cancers	• Sensitivity: 70% • Specificity: > 99% • Organizational traceability accuracy: 63%
THUNDER • cfDNA methylation sequencing technology • Lung, esophageal, liver, pancreatic, ovarian and colorectal cancers	• Sensitivity: 80.6% • Specificity: 98.3% • Organizational traceability accuracy: 82%
DETECT-A • cfDNA mutations, protein biomarkers, PET-CT/imaging detection techniques	• Sensitivity: 27.1% • Specificity: 99.6% • PPV: 40.6% • NPV: 99.3%
PATHFINDER • cfDNA methylation sequencing technology	• PPV: 44.6% (High-risk group: 57.1%; General-risk group: 30.0%) • Organizational traceability accuracy: 85.2% (High-risk group: 84.2%; General-risk group: 87.5%)

Case-control study: CCGA3, CancerSEEK, THUNDER

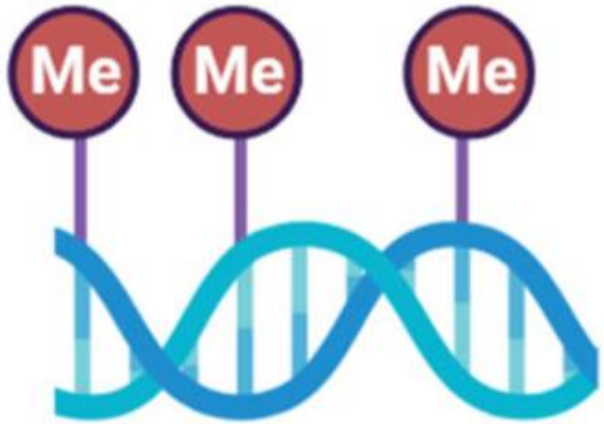
Prospective study: DETECT-A, PATHFINDER

Song J. Critical Reviews in Oncology/Hematology 207 (2025) 104613

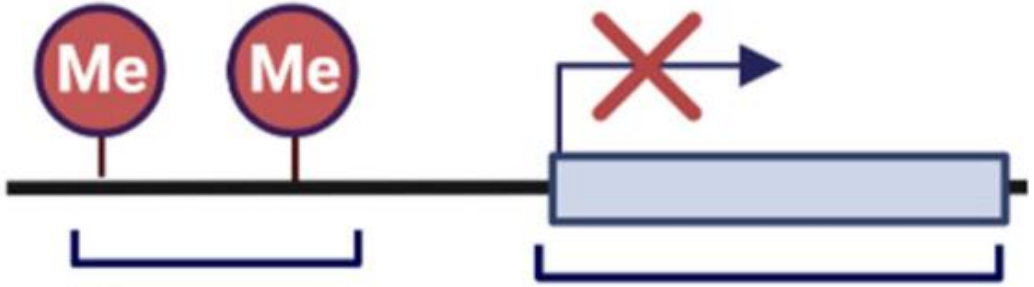
DNA Methylation

a) DNA methylation

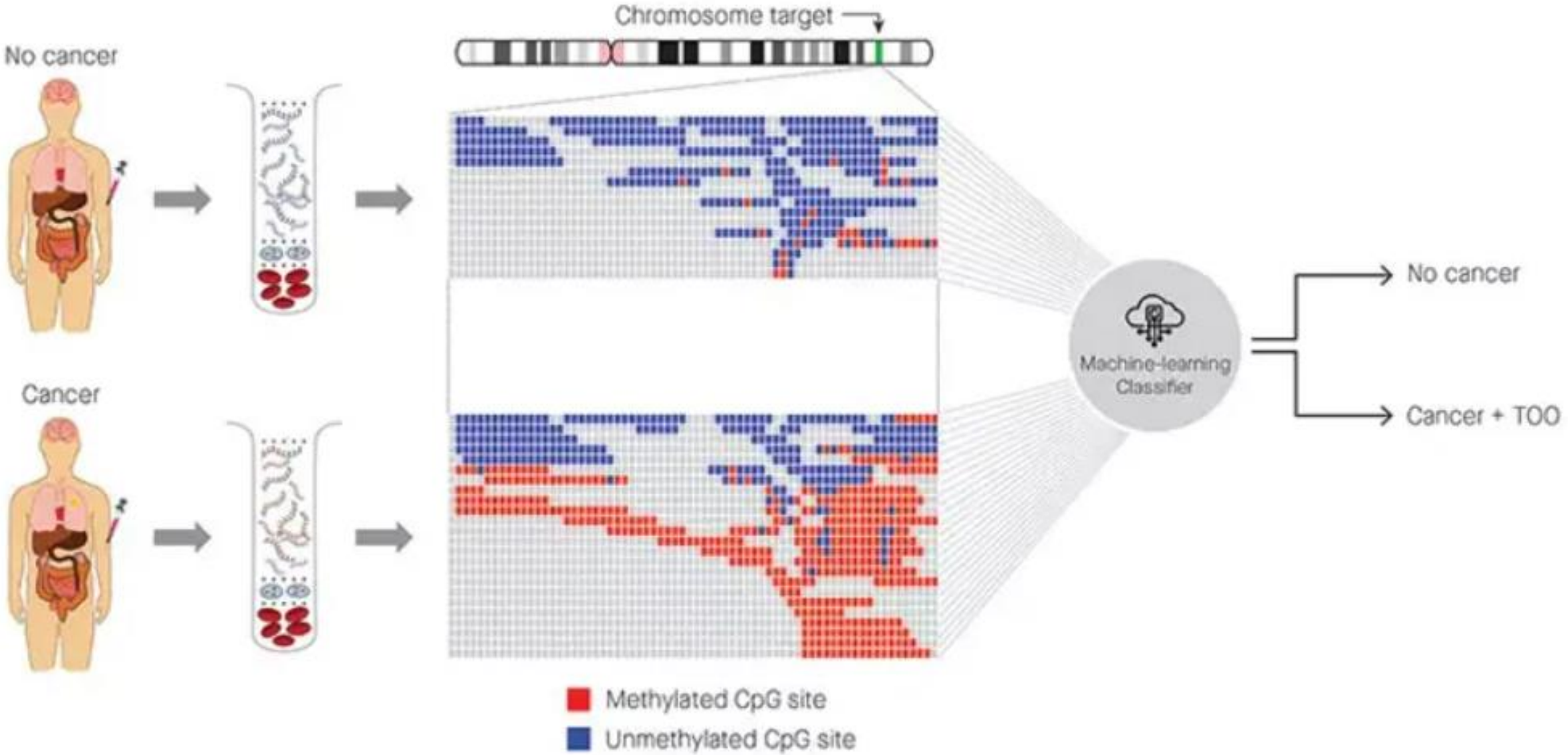
DNA methylation enzymes:
- DNMTs
- TETs



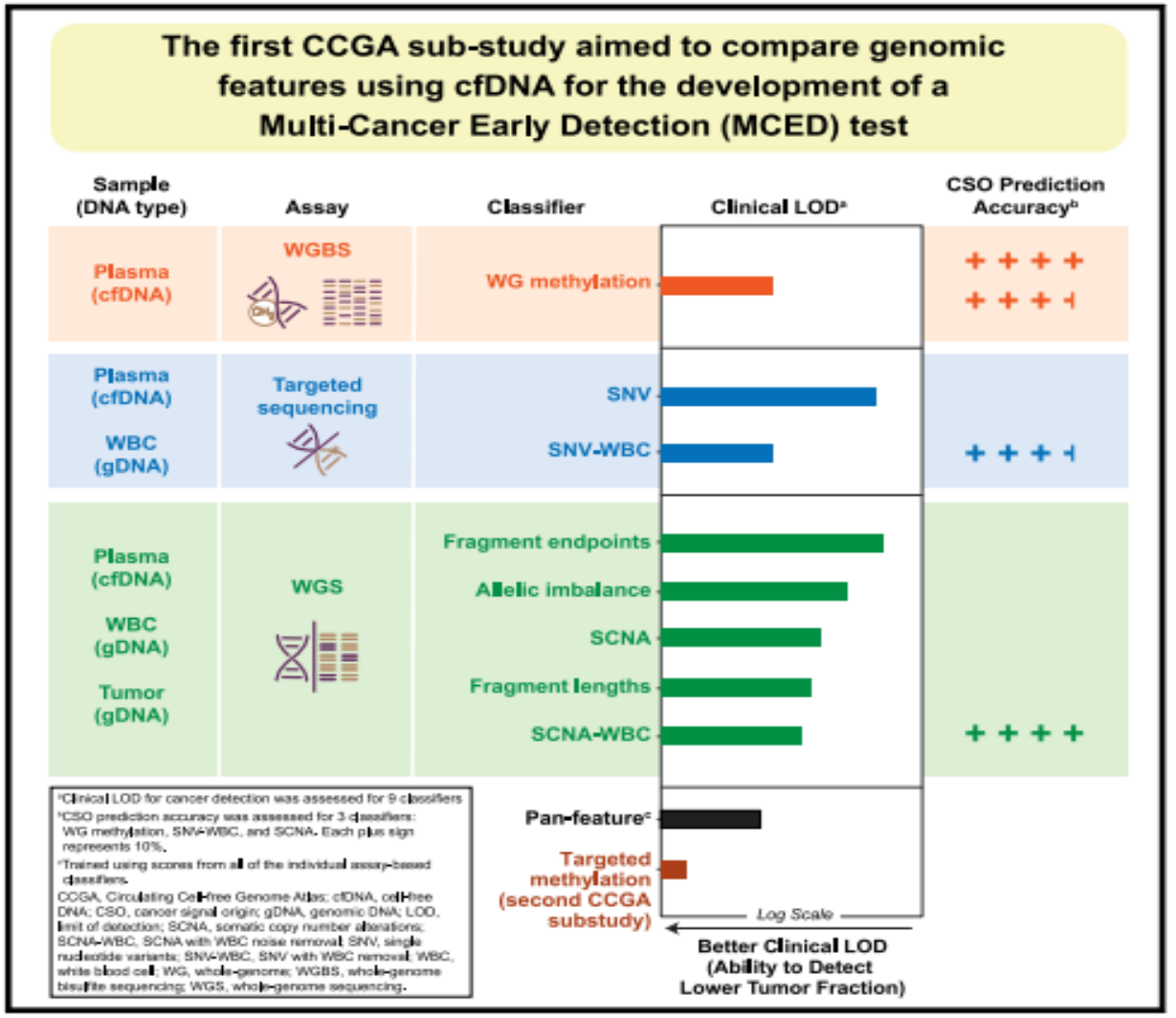
Global DNA methylation



DNA Methylation in a gene's promoter region


No cancer
Cancer
Chromosome target
Machine-learning Classifier
No cancer
Cancer + TOO
Methylated CpG site
Unmethylated CpG site

- Clinical limit of detection (LOD) is a useful benchmark to assess cfDNA-based test performance
- Circulating tumor allel fraction (cTAF) accounts for cfDNA cancer signal variation across cancer types and stages
- cfDNA methylation was the most promising genomic feature for cancer signal detection (whole genome methylation) and cancer signal origin.
- The results informed the development of a cfDNA-based multi-cancer early detection test



Jamshidi, A et a. Cancer Cell 40, 1537–1549.e12.

The Circulating Cell-Free Genome Atlas Study (CCGA Study; NCT02889978)

Prospective, multicenter, case-control, observational study

Study Goals

- Develop and validate a blood-based MCED test analyzing plasma cell-free DNA (cfDNA)
- Detect cancer signals across multiple cancer types & simultaneously predict their signal origin

Study Design

15,254 participants with/without cancer

Fully Enrolled (142 sites)

Blood samples
all participants

Tissue samples
cancer only

Follow-up for 5 years
(vital status, cancer status)

cfDNA, cell-free DNA; MCED, multi-cancer early detection test.

Klein E, et al. *Ann Oncol*. 2021;32(9):1167-1177. DOI: 10.1016/j.annonc.2021.05.806.

CCGA3: Cancer Signal Detection: Specificity and Overall Sensitivity

	Cancer (n=2823)	Non-cancer (n=1254)	Total (n=4077)
Test Positive	1453	6	1459
Test Negative	1370	1248	2618

Specificity:
99.5%
(95% CI: 99.0–99.8%)

↓

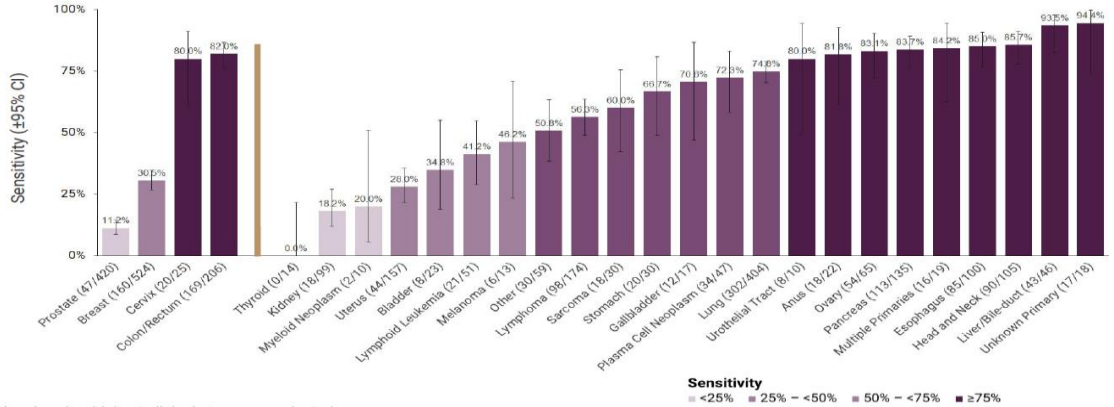
0.5%
false-positive rate

Sensitivity:
51.5%
(95% CI: 49.6–53.3%)

CCGA3: Sensitivity of Cancer Signal Detection in Cancers With and Without Common Screening

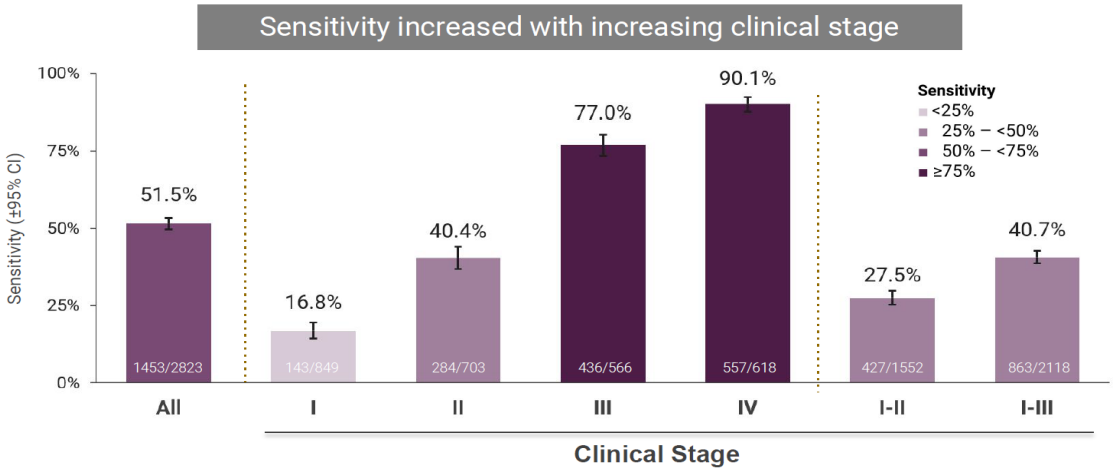
With Common Screening Options:
33.7% (95% CI: 31.1–36.5%)

Without Common Screening Options:
63.8% (95% CI: 61.4–66.1%)



For multiple primaries, highest clinical stage was selected.
CI, confidence interval.
Klein E, et al. *Ann Oncol*. 2021;32(9):1167-1177. DOI: 10.1016/j.annonc.2021.05.806.

CCGA3: Sensitivity of Cancer Signal Detection by Clinical Stage



CCGA3: Projected PPV and NPV

Estimated values were adjusted to SEER cancer incidence and stage distribution in the 50–79 years age group

Positive Predictive Value

44.4%
(95% CI: 28.6–79.9%)

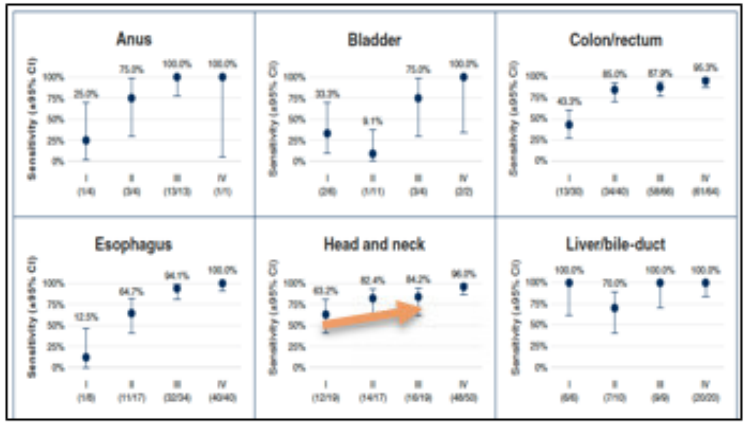
Probability a person with a positive test result has cancer

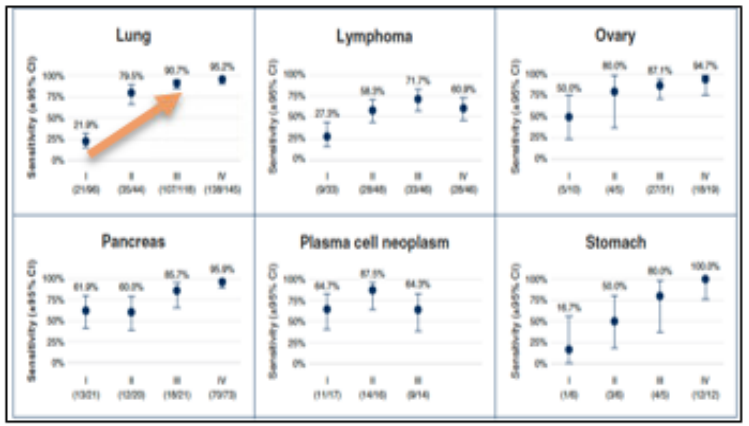
Negative Predictive Value

99.4%
(95% CI: 99.4–99.5%)

Probability a person with a negative test result does not have cancer

CI, confidence interval; MCED, multi-cancer early detection; NPV, negative predictive value; PPV, positive predictive value; SEER, Surveillance, Epidemiology, and End Results.
Klein E, et al. *Ann Oncol*. 2021;32(9):1167-1177. DOI: 10.1016/j.annonc.2021.05.806.

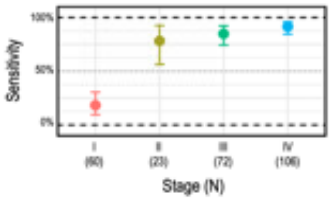




Clinical stage	Total *N*	Test positive	Sensitivity % (95% CI)[a]
All	2823	1453	51.5 (49.6% to 53.3%)
I	849	143	16.8 (14.5% to 19.5%)
II	703	284	40.4 (36.8% to 44.1%)
III	566	436	77.0 (73.4% to 80.3%)
IV	618	557	90.1 (87.5% to 92.2%)
I-II	1552	427	27.5 (25.3% to 29.8%)
I-III	2118	862	40.7 (38.7% to 42.9%)
I-IV	2736	1420	51.9 (50.0% to 53.8%)
III-IV	1184	993	83.9 (81.7% to 85.9%)
Not expected to be staged	67	23	34.3 (24.1% to 46.3%)
Missing	20	10	50.0 (29.9% to 70.1%)

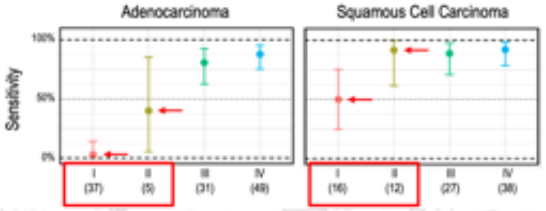
MCED: All subtypes have the same sensitivity?

Lung Cancer Detection Varies by Subtype at 99.4% Specificity

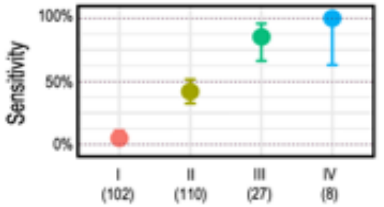


- Overall lung cancer sensitivity: 71.6% (95% CI: 65.8-77.0%)

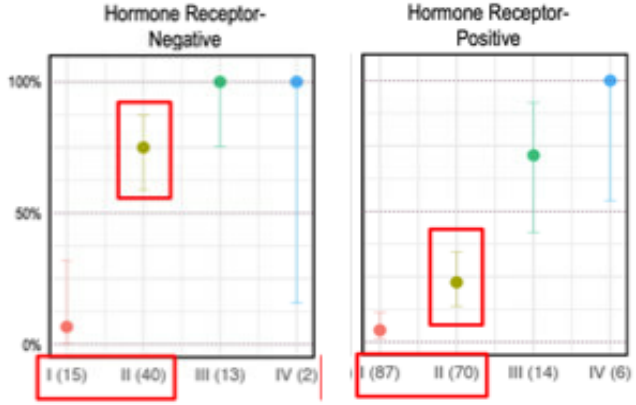
- Detection rate affected by early-stage adenocarcinomas
  - Detection higher in squamous cell carcinoma
- Consistent with prior report showing ctDNA detection was higher in squamous cell carcinoma than adenocarcinoma[1]



Breast Cancer Detection Varies by Subtype at 99.4% Specificity



- Overall breast cancer sensitivity: 33.2% (95% CI: 27.4-39.4%)



The James

THE OHIO STATE UNIVERSITY COMPREHENSIVE CANCER CENTER

Oxnard et al, ESMO 2019, Klein EA, et al. Ann Oncol 2021

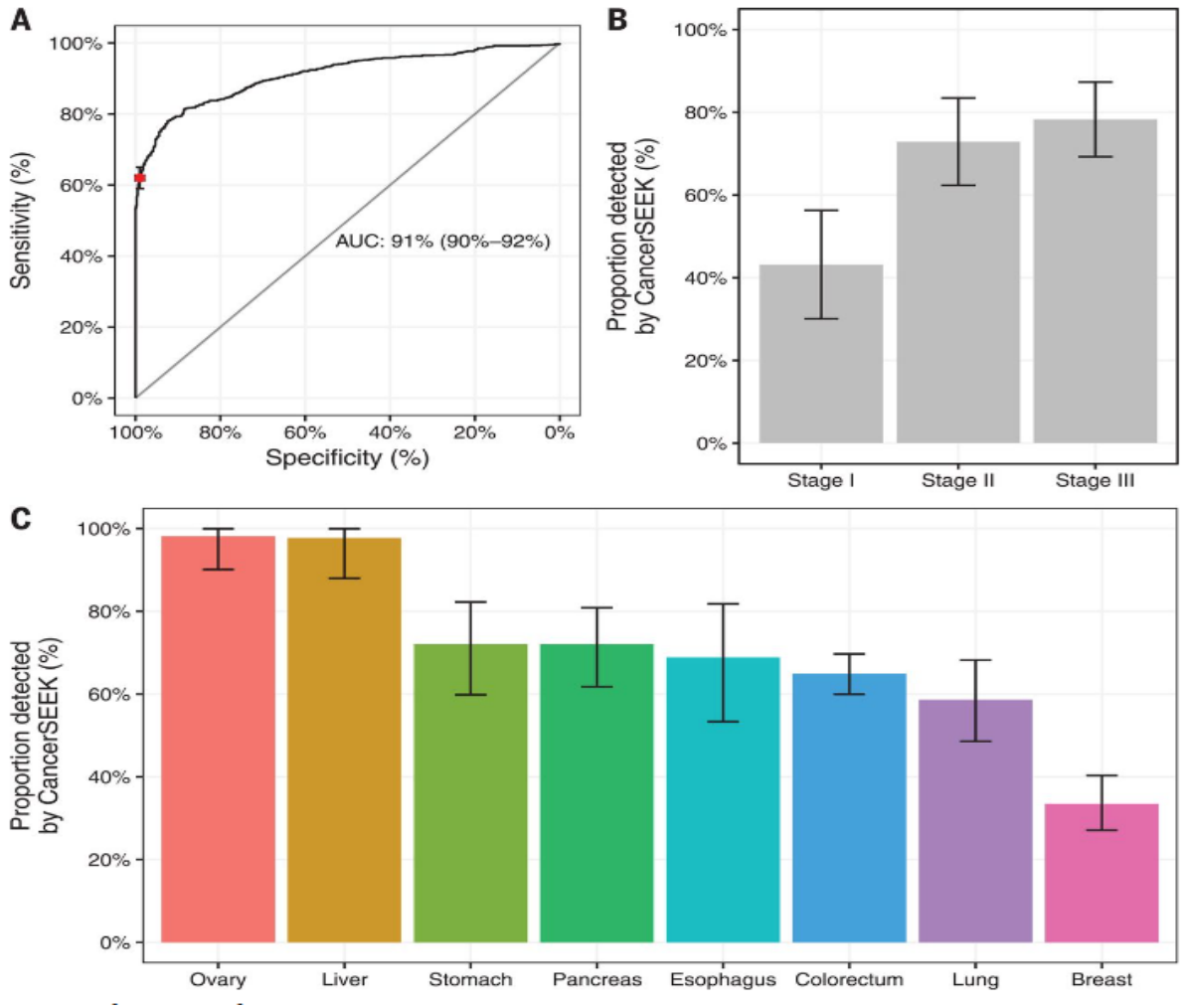
Cancer Seek

Multiplex PCR analysis of circulating cell-free tumour DNA (ctDNA) enables the detection of mutations at 2,001 genomic positions across 16 genes, whereas levels of the protein biomarkers are assessed using immunoassays.

The eight proteins are:

cancer antigen 125, carcinoembryonic antigen, cancer antigen 19-9, prolactin, hepatocyte growth factor, osteopontin, myeloperoxidase, and tissue inhibitor of metalloproteinases 1.

1817 subjects Specificity 99% and Sensitivity 70%



Steven J. Cohen et al. JCO 26, 3213-3221(2008).

MCED Test Performance Outcomes from DETECT-A Study

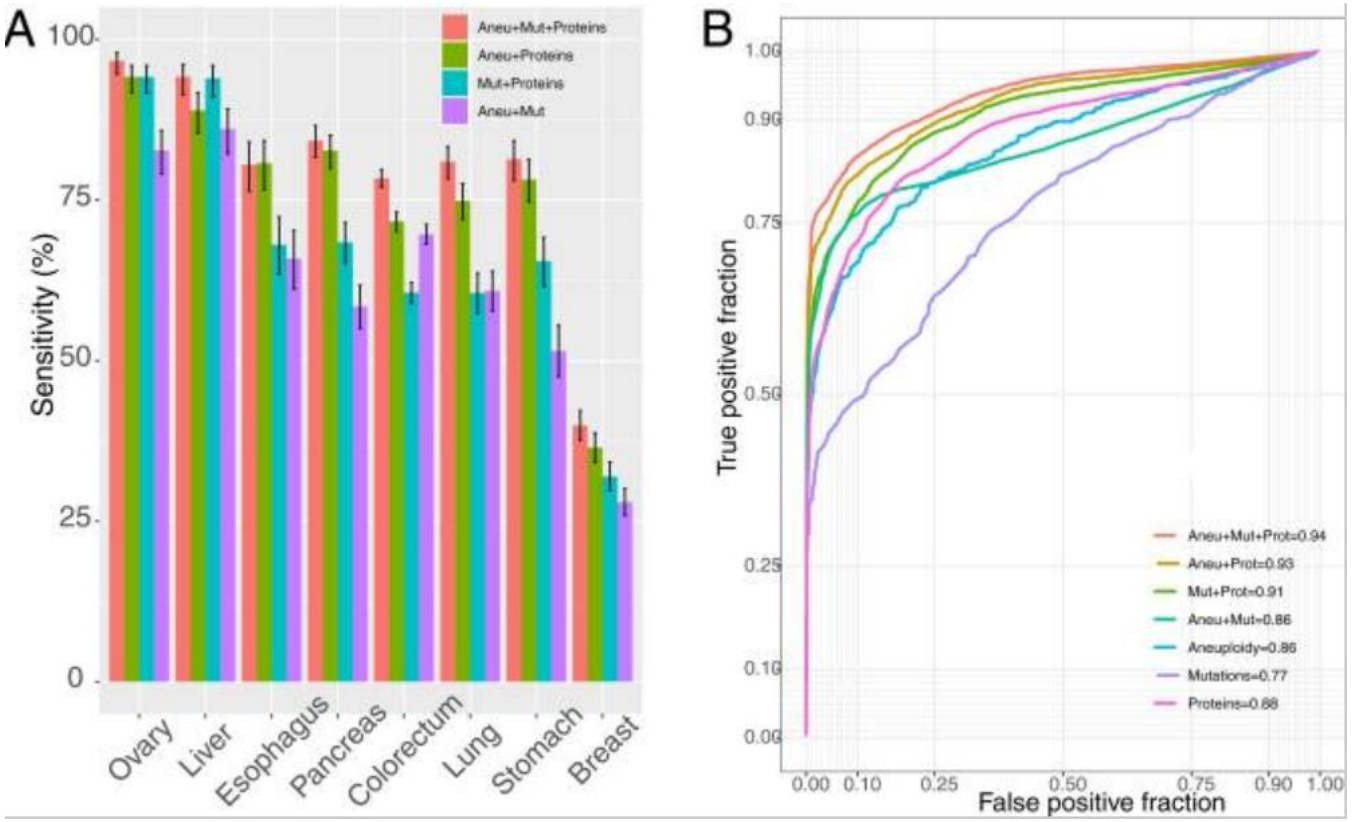
Calculated in the basis of a one-year follow-up

Metric	Specifications	DETECT-A Results
Sensitivity TP/(TP+FN)	Cancers found by CancerSEEK alone	**27.1%** 26/(26+70)
	Cancer found by CancerSEEK or SOC screening	**52.1%** 50/(50+46)
Specificity TN/(TN+FP)	CancerSEEK + PET-CT	**99.6%** 9777/(9777+38)
	CancerSEEK alone	**98.9%** 9707/(9707+108)
Positive Predictive Value (PPV) TP/(TP+FP)	CancerSEEK + any form of imaging	**40.6%** 26/(26+38)
	CancerSEEK alone	**19.4%** 26/(26+108)

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

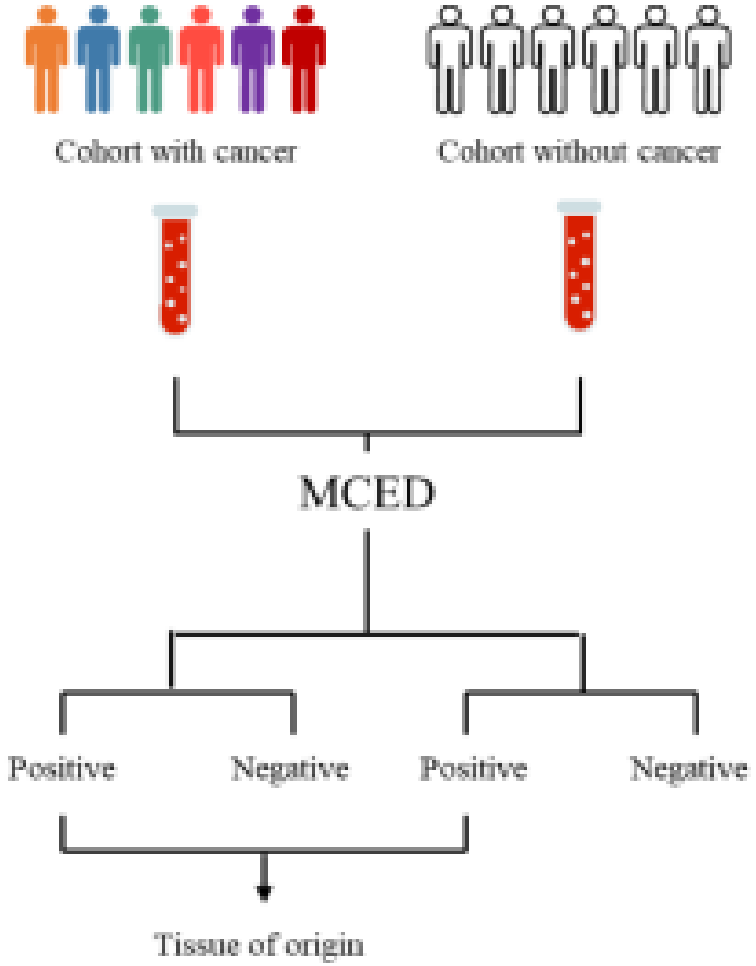
More Analytes to improve sensitivity

PCR-based approach to detect the presence of aneuploidy in liquid biopsies, even when only small amounts of blood are available for assay. This approach detected cancers in 49% of 883 non-metastatic patients with cancer but in less than 1% of 812 healthy controls.

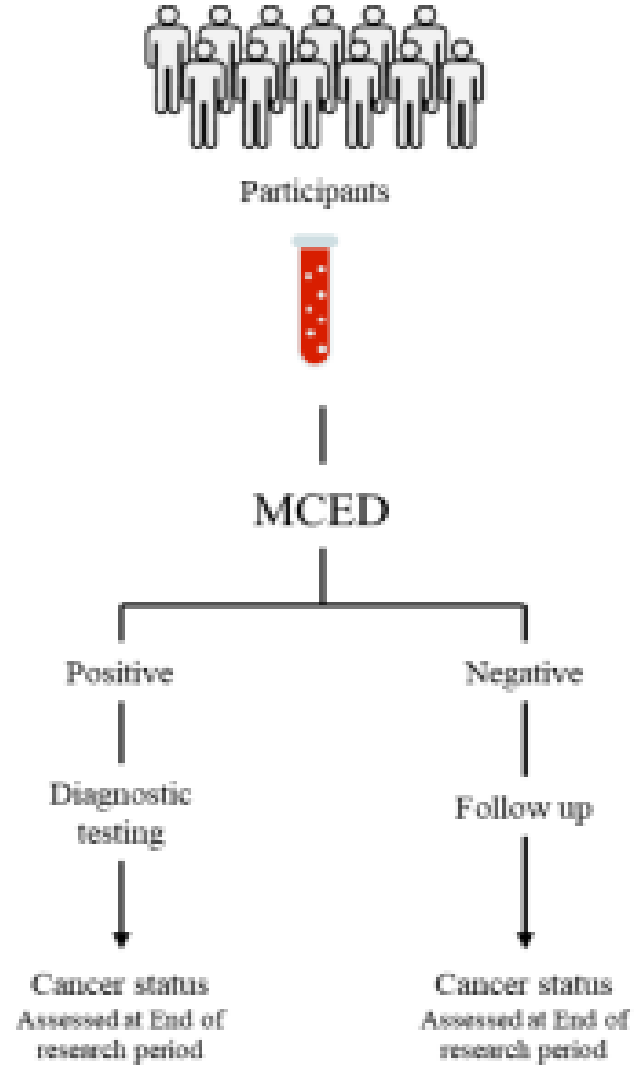


Douville, 2020 Feb 19;117(9):4858–4863

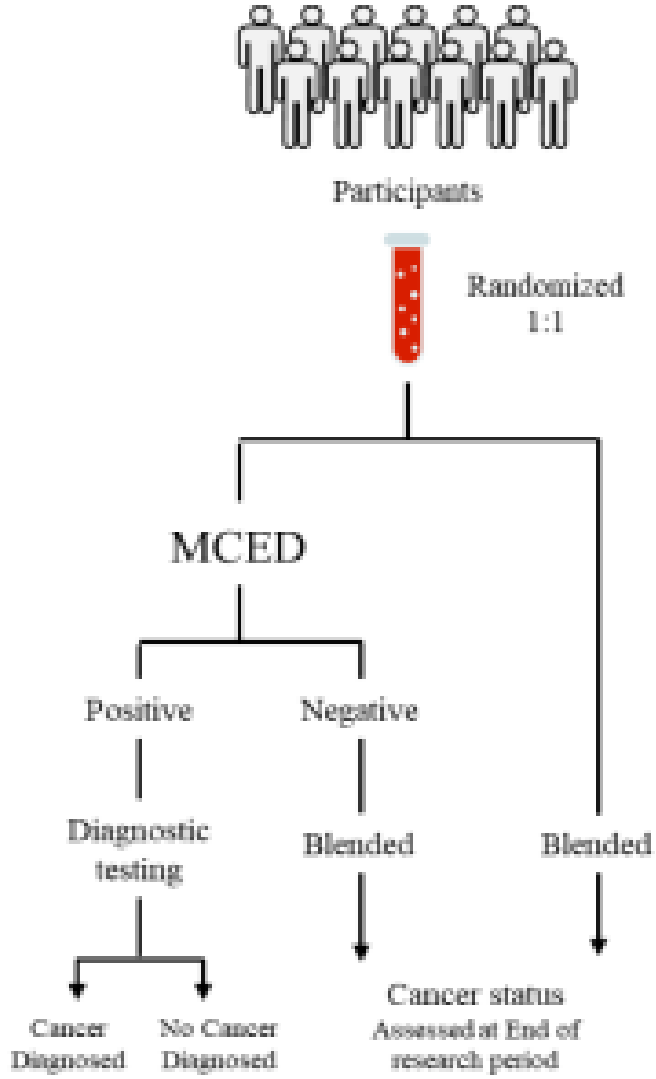
a) Case control study



b) Single arm trial



c) Randomized controlled trial



H.R. 842: Nancy Gardner Sewell Medicare Multi-Cancer Early Detection Screening Coverage Act

Sponsor and status

Jodey Arrington

Sponsor. Representative for Texas's 19th congressional district. Republican.

H. R. 842

IN THE HOUSE OF REPRESENTATIVES

A BILL

Read Text »

Last Updated: Jan 31, 2025

Length: 7 pages

Introduced Jan 31, 2025
119th Congress (2025–2027)

Status **Introduced** on **Jan 31, 2025**

This bill is in the first stage of the legislative process. It was introduced into Congress on January 31, 2025. It will typically be considered by committee next before it is possibly sent on to the House or Senate as a whole.

Other activity may have occurred on another bill with identical or similar provisions.

Cosponsors 150 Cosponsors (75 Republicans, 75 Democrats)

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