

**The future of cancer screening, validated
today.**

Lara Bagby, MS, CGC
Field Medical Director



Important Safety Information

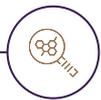
The Galleri test is recommended for use in adults with an elevated risk for cancer, such as those aged 50 or older. The Galleri test does not detect all cancers and should be used in addition to routine cancer screening tests recommended by a healthcare provider. Galleri is intended to detect cancer signals and predict where in the body the cancer signal is located. Use of Galleri is not recommended in individuals who are pregnant, 21 years old or younger, or undergoing active cancer treatment.

Results should be interpreted by a healthcare provider in the context of medical history, clinical signs and symptoms. A test result of No Cancer Signal Detected does not rule out cancer. A test result of Cancer Signal Detected requires confirmatory diagnostic evaluation by medically established procedures (e.g. imaging) to confirm cancer.

If cancer is not confirmed with further testing, it could mean that cancer is not present or testing was insufficient to detect cancer, including due to the cancer being located in a different part of the body. False-positive (a cancer signal detected when cancer is not present) and false-negative (a cancer signal not detected when cancer is present) test results do occur. **Rx only.**

Laboratory / Test Information

GRAIL's clinical laboratory is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) and accredited by the College of American Pathologists. The Galleri test was developed, and its performance characteristics were determined by GRAIL. The Galleri test has not been cleared or approved by the Food and Drug Administration. The GRAIL clinical laboratory is regulated under CLIA to perform high-complexity testing. The Galleri test is intended for clinical purposes.



Current state of cancer screening



Blood-based multi-cancer early detection (MCED)



Clinical validation, feasibility and real world experience

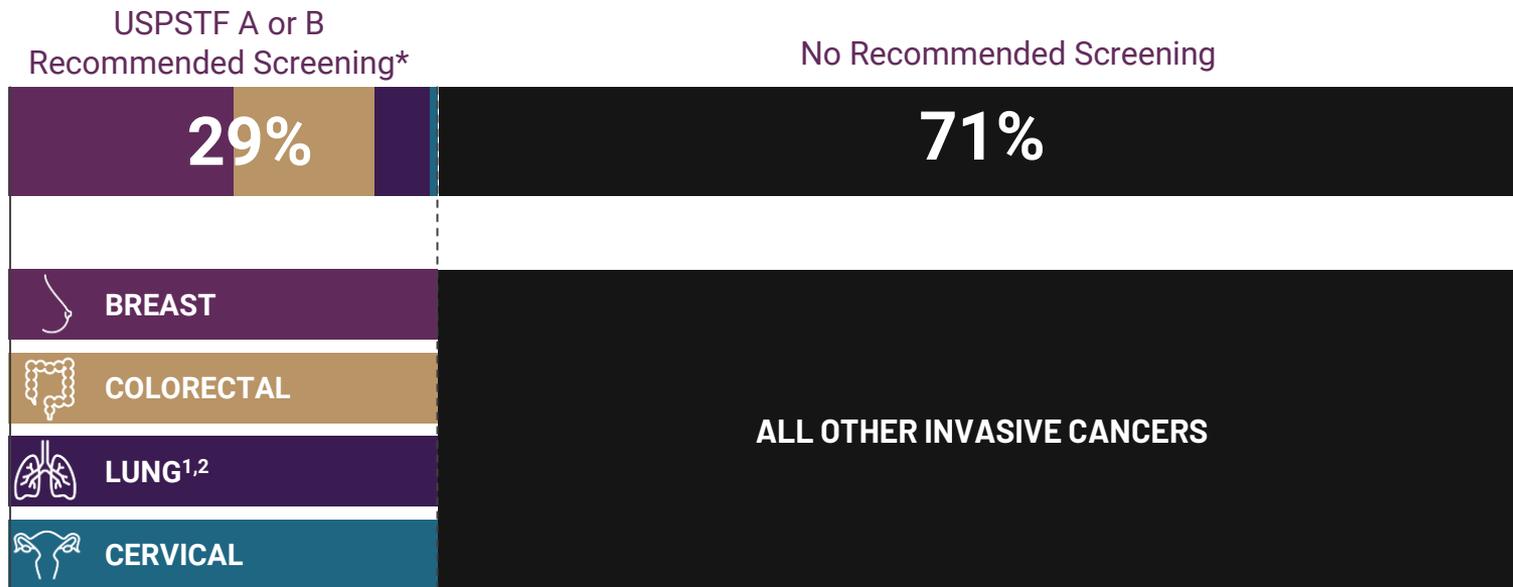


Implementing MCED into practice



Less Than a Third of Cancers Have Screening Options Today

1.2% Cancer Incidence in a Population Aged 50-79



*Prostate cancer screening is recommended on an individual basis[§]

[§]Calculated using rates per 100,000 person years in a population with same age/sex distribution as outlined by SEER18 2011-15. USPSTF, United States Preventive Services Task Force. *Assumes screening is available for all breast, cervical, and colorectal cancer cases and 43% of lung cancer cases (based on estimated proportion of lung cancers that occur in screen-eligible individuals older than 40 years). Source: SEER Stat Database: Incidence - SEER 18 Regs Research Data, Nov 2017 Sub. Includes persons aged 50+ diagnosed 2006-2015. Data on file GA2021-0065. 1. Meza R, et al. JAMA. 2021;325(10):988-997. 2. Pinsky PF, et al. J Med Screen. 2012;19(3):154-156. 2. Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence - SEER Research Data, 17 Registries, Nov 2024 Sub (2000-2022) - Linked To County Attributes - Time Dependent (1990-2023) Income/Rurality, 1969-2023 Counties, National Cancer Institute, DCCPS, Surveillance Research Program, released April 2025, based on the November 2024 submission. Data on File GR-2025-0249

Recommended Single-Cancer Screening

Optimize Sensitivity Over Specificity

CANCER	USPSTF RECOMMENDED SCREENING	SENSITIVITY (%)	SPECIFICITY (%)	POSITIVE PREDICTIVE VALUE (%)
BREAST ¹	Mammography	87 [‡]	89 [‡]	4.4 [‡]
COLORECTAL ^{2,3}	Decennial colonoscopy	<i>Reference Standard</i>	<i>Reference Standard</i>	<i>Reference Standard</i>
	Stool-based screening (sDNA)	92.3	86.6	3.7*
	Stool-based screening (FIT)	73.8	94.9	6.9
LUNG ^{4,5}	Low-dose CT	85 [‡]	87 [‡]	6.9 [‡]
CERVICAL ⁶	Cytology / HPV Test	95	85.5	<1*

CT, computed tomography; FIT, fecal immunochemical test; HPV, human papillomavirus; USPSTF, United States Preventive Services Task Force. *Pre-cancerous lesions were excluded. †Based on previous USPSTF recommendations of adults 55–80 years with a 30 pack/year smoking history. ‡Based on previous recommendation age range 50–74.1. USPSTF. 2016. Lehman, et al. Radiology. 2017;283(1):49-58. 2. USPSTF. 2017. United States Food and Drug Administration Premarket Approval P130017. 3. Imperiale T, et al. N Engl J Med 2014;370:1287-1297 4.Pinsky PF, et al. J Med Screen. 2012;19(3):154-156. 5. Meza R, et al. JAMA. 2021;325(10):988–997. Recommendation for lung screening limited to high-risk smoking population, which accounts for less than 33% of all lung cancers. 6. Kim, et al. JAMA. 2018;320(7):706-714

Criteria for an Effective Multi-Cancer Early Detection (MCED) Test



Detect **many deadly cancers**, including unscreened cancers, using a single blood sample



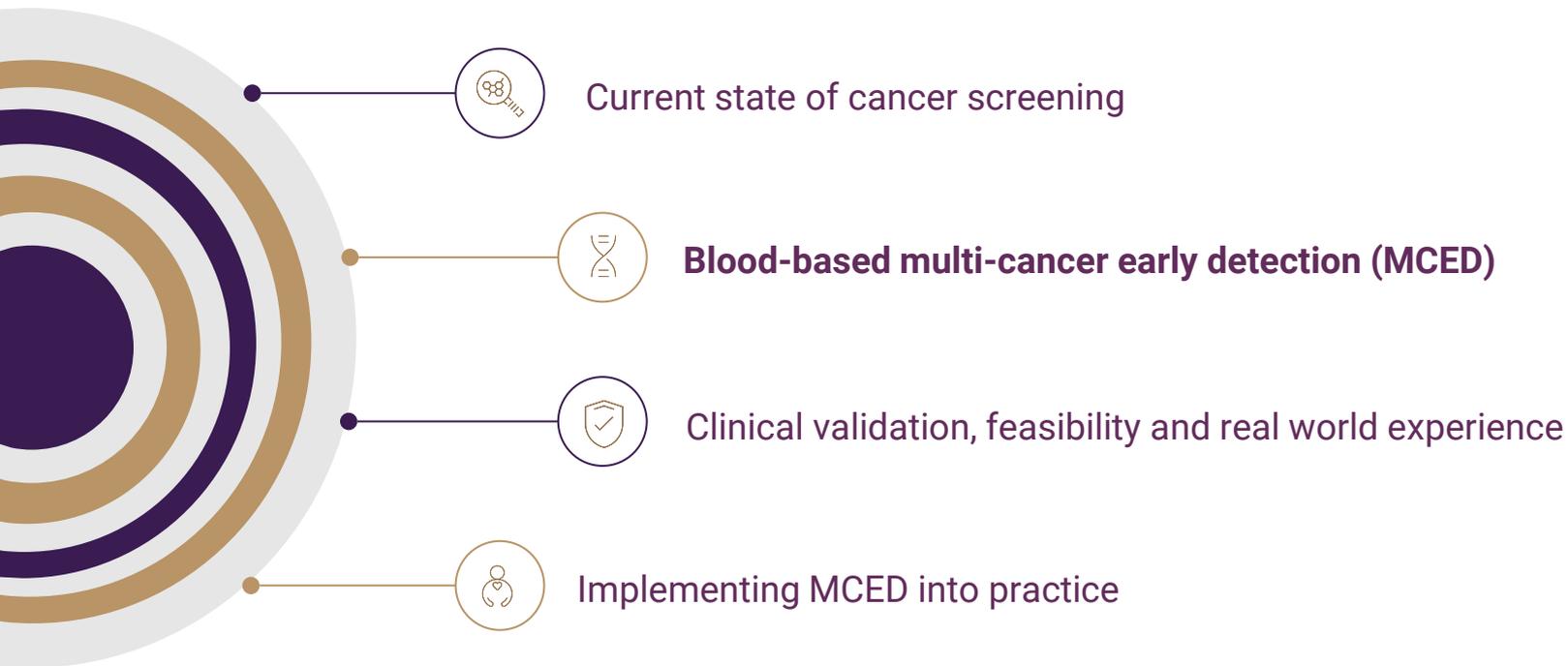
Predict **signal origin** to assist with diagnostic workup



High **positive predictive value** and a low **false-positive rate** to limit unnecessary workups

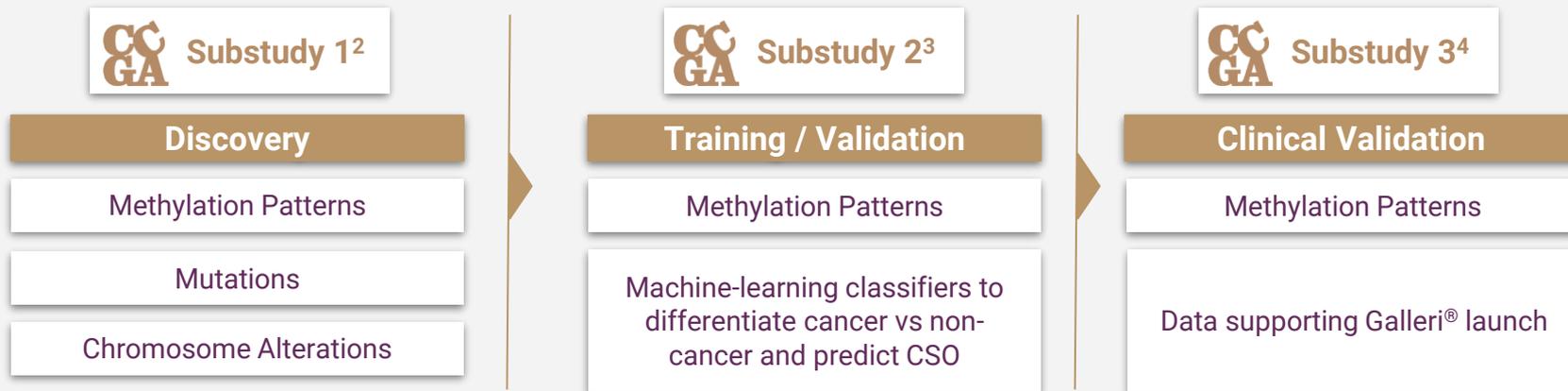
Supported by large-scale clinical validation studies
Performance translates to an intended-use population

≡≡≡ Agenda



☰☰☰ Circulating Cell-Free Genome Atlas (CCGA) Study

Prospective, observational, longitudinal, case-control study divided into 3 substudies with a total of 15,254 participants¹



☰☰☰ Circulating Cell-Free Genome Atlas (CCGA)

CCGA Substudy 1

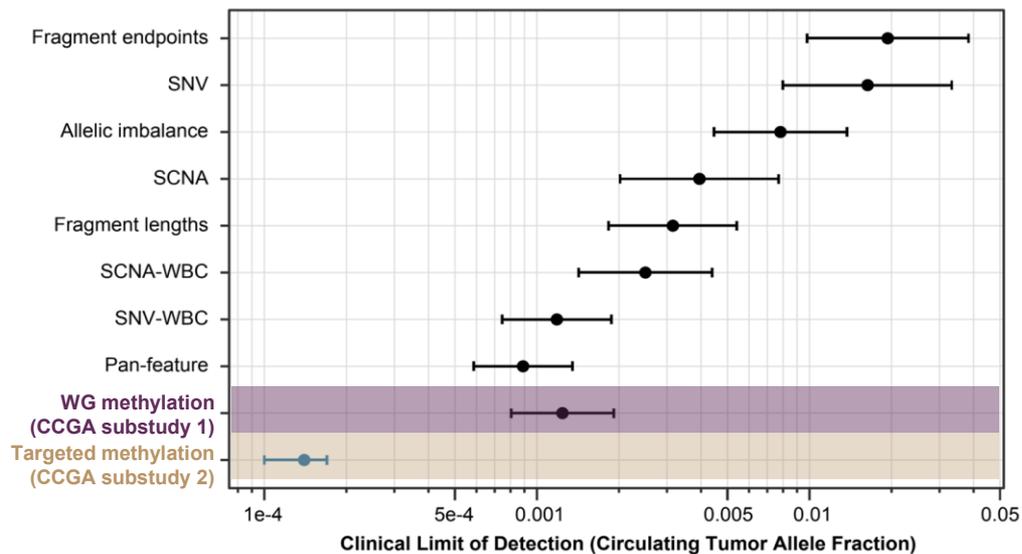
Discovery

Methylation Patterns

Mutations

Chromosome Alterations

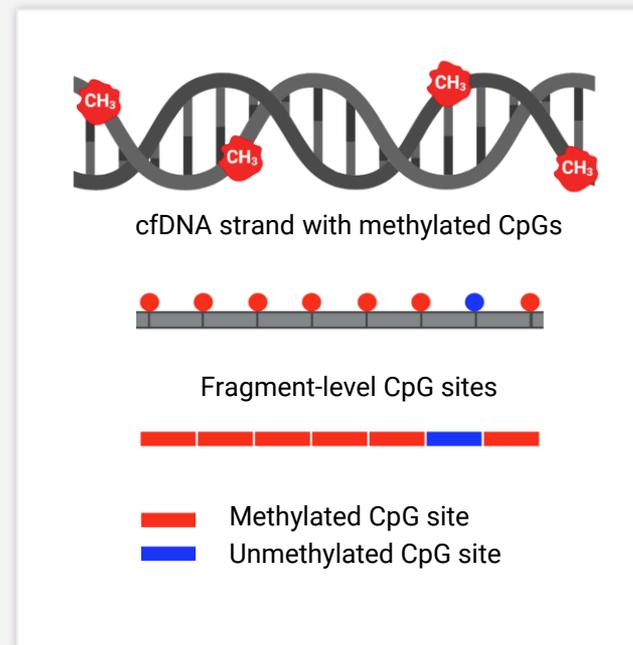
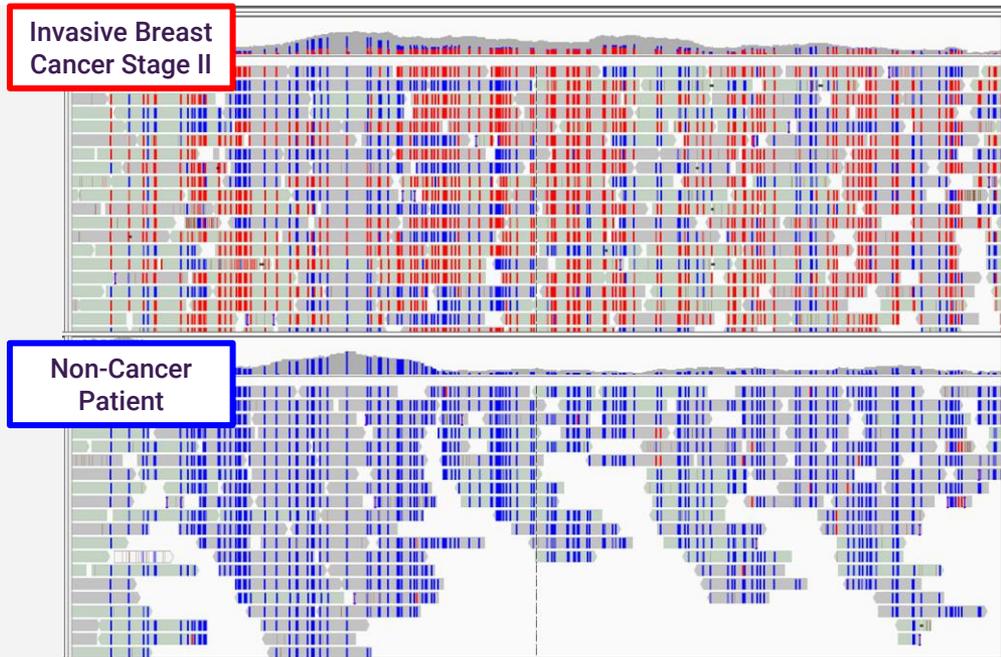
CCGA substudy 1 was designed to compare cfDNA approaches among the same set of samples



Combining other approaches did not increase methylation-only test performance

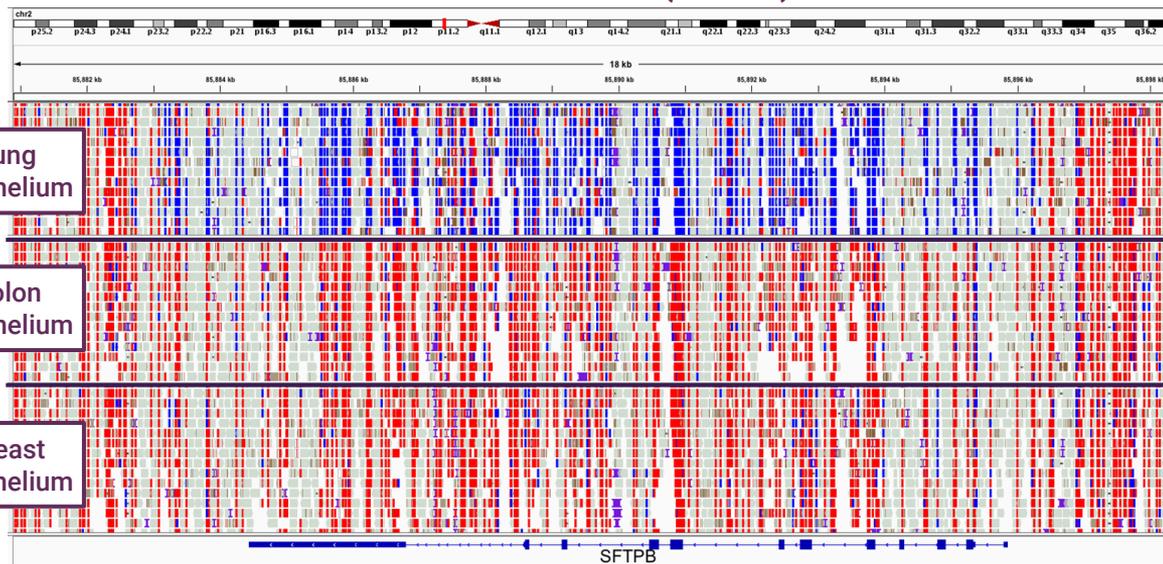
Discovery of a Shared Cancer Signal

DNA Methylation Patterns Distinguish Cancer from Non-Cancer



☰☰☰ Methylation Patterns Also Indicate Cancer Signal Origin

Surfactant Gene (SFTBP)



Methylation patterns are established during development in a cell type-specific manner

Each cell type in the body has a unique pattern of methylation and tissue-specific gene expression

unmethylated

methylated

Criteria for an Effective Multi-Cancer Early Detection (MCED) Test



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Predict **signal origin** to assist with diagnostic workup



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Supported by large-scale clinical validation studies
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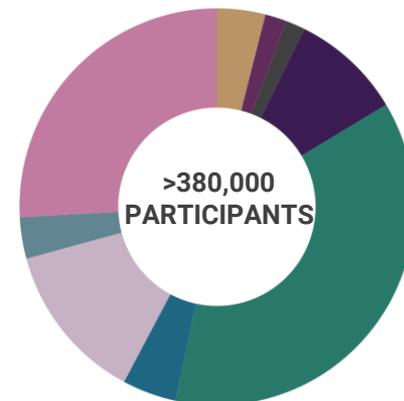
Implementing MCED into practice



GRAIL Clinical Development Program

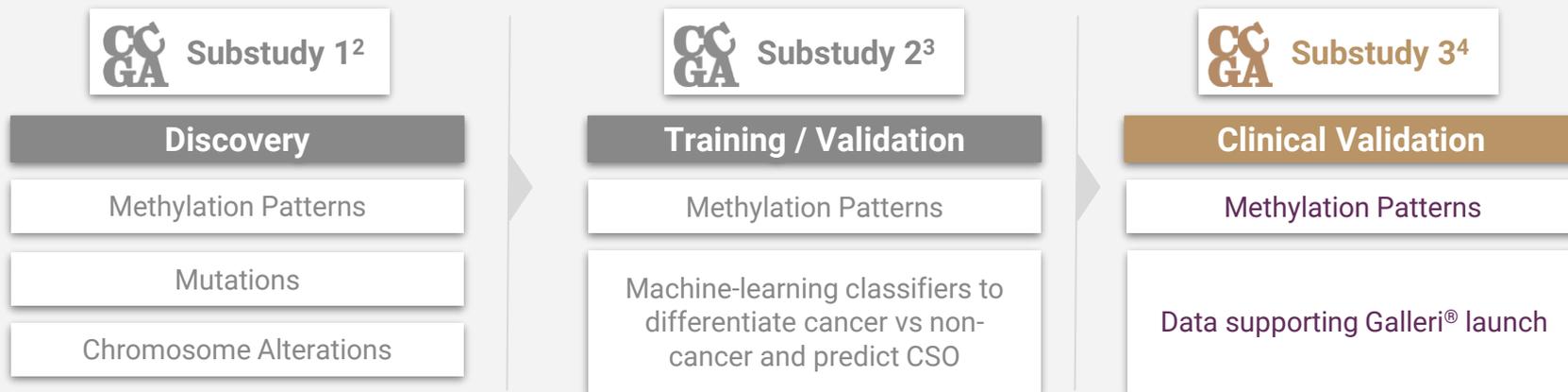
Test Development, Validation, and Implementation in Population-Scale Studies

1	CCGA (n=15,254)	Develop and validate a cell-free DNA-based MCED test <i>Enrollment: complete, published</i>	<i>Annals of Oncology and Cancer Cell 2020-2023</i>
2	PATHFINDER (n=6,662)	Evaluate clinical implementation and perceptions of MCED test <i>Enrollment: complete, published</i>	<i>The Lancet 2023</i>
3	SYMPLIFY (n=6,242)	Assess MCED test in individuals with signs/symptoms of cancer <i>Enrollment: complete, published</i>	<i>Lancet Oncology 2023</i>
4	PATHFINDER 2 (n≈35,000)	Evaluate MCED test performance in eligible screening population <i>Enrollment: completed</i>	
5	NHS-GALLERI (n≈142,321)	Assess clinical utility of MCED for population screening in the UK <i>Enrollment: complete</i>	
6	REFLECTION (n≈17,000)	Understand the real-world experience of Galleri® in clinical settings <i>Enrollment: ongoing</i>	
7	REACH (n≈50,000)	Understand health equity impact of Galleri in a Medicare population <i>Enrollment: ongoing</i>	
8	SUMMIT (n=13,035)	Clinical validation in individuals at high risk of lung cancer <i>Enrollment: complete</i>	
9	STRIVE (n=99,481)	Observational study in women undergoing mammography screening <i>Enrollment: complete</i>	

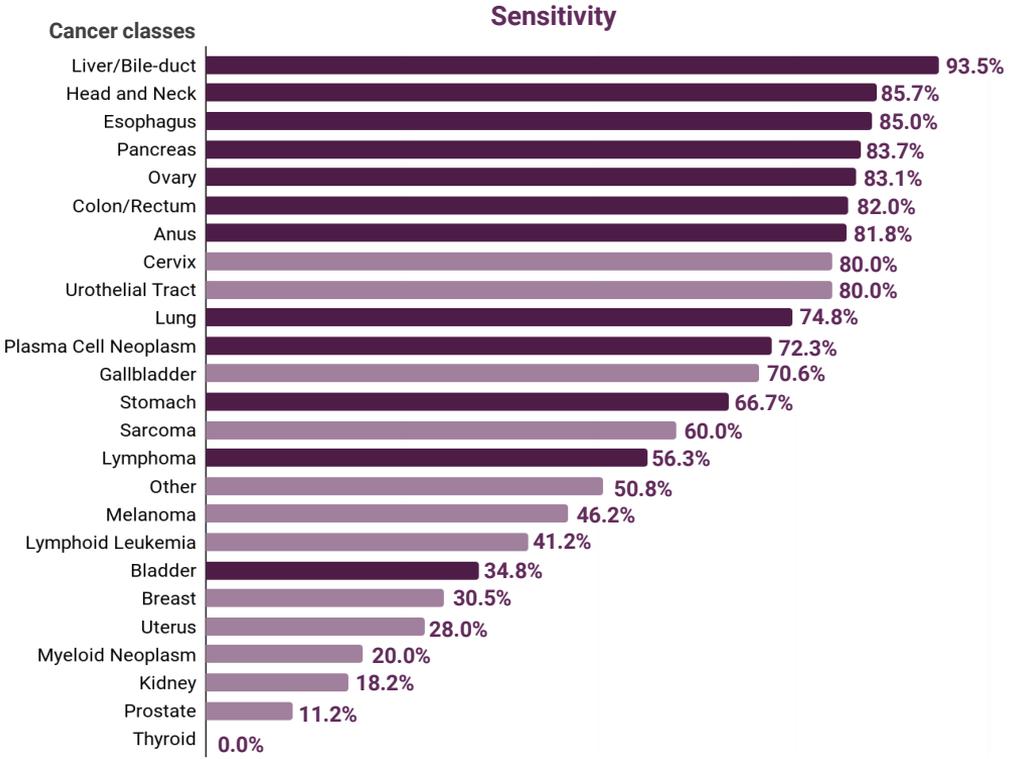


☰☰☰ Circulating Cell-Free Genome Atlas (CCGA) Study

Prospective, observational, longitudinal, case-control study divided into 3 Substudies with a total of 15,254 participants¹

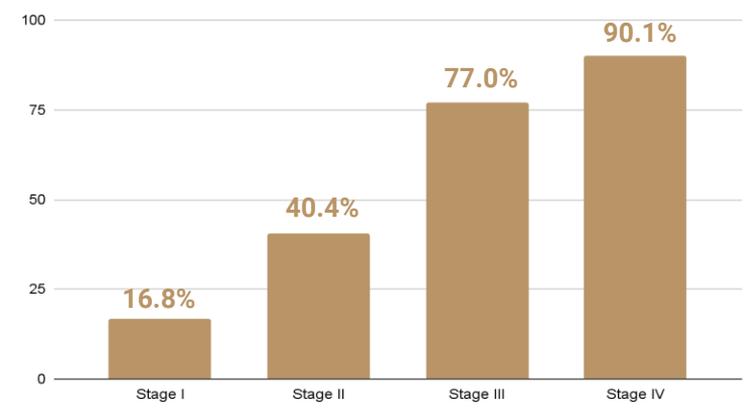


Sensitivity of Cancer Signal Detection



■ 12 prespecified cancer classes that cause 2/3 of cancer deaths in the US ■ Other cancer classes

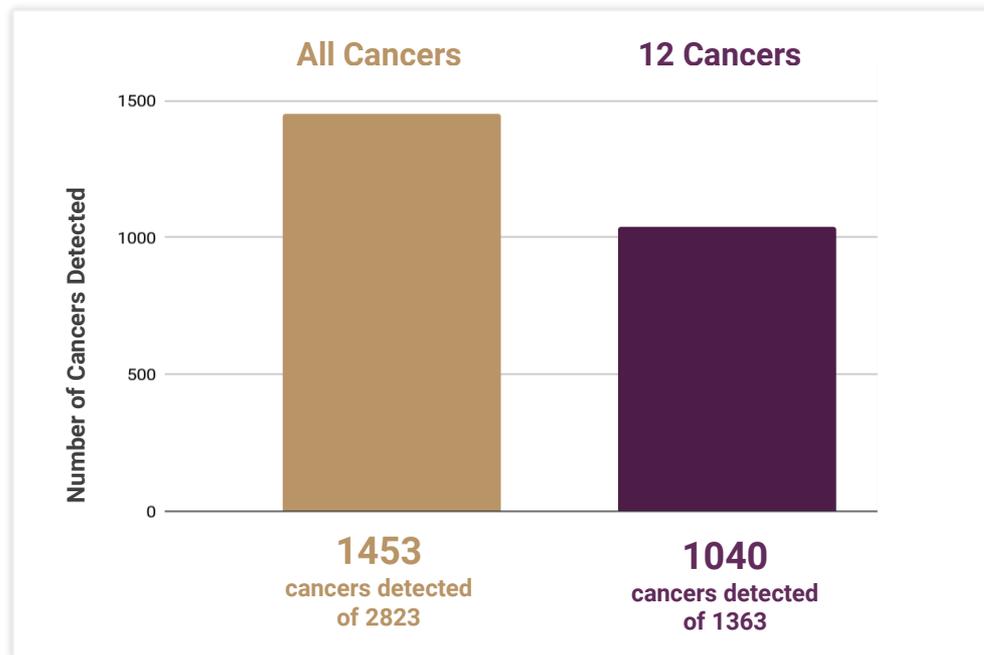
Sensitivity of Cancer Signal by Clinical Stage



More aggressive cancers tend to release more cell-free DNA into the bloodstream at early stages, making them more likely to be detected by Galleri®

Overall Yield is Greatest When all Cancers are Included

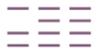
12 Pre-Specified Cancers Responsible for Two-Thirds of Cancer Deaths



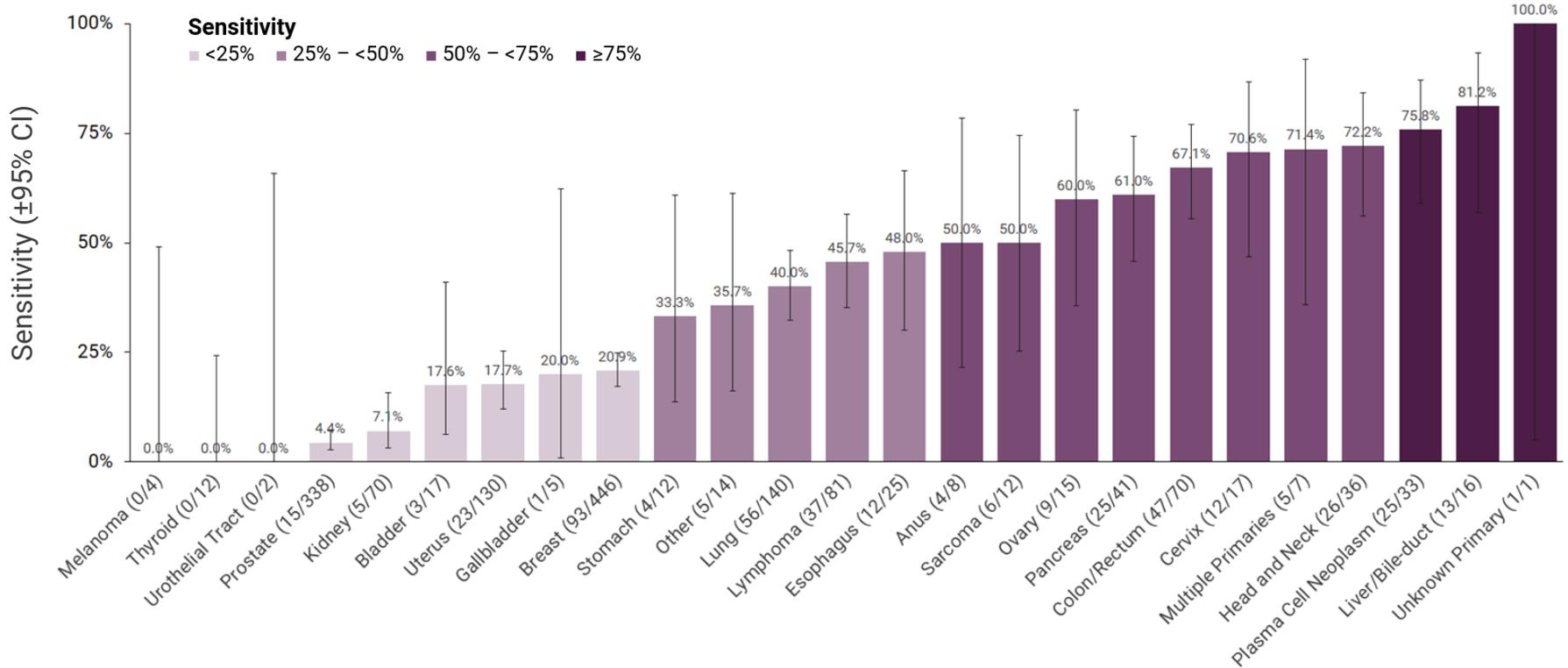
12 cancers that account for 2/3 of US cancer deaths¹

- Anus
- Bladder
- Colon/rectum
- Esophagus
- Head and neck
- Liver/bile duct
- Lung
- Lymphoma
- Ovary
- Pancreas
- Plasma cell neoplasm
- Stomach

"All" comprises all cancer stages, including missing stage and cancer classes that do not have staging per American Joint Committee on Cancer (AJCC) staging manual. CI, confidence interval. ¹American Cancer Society. Cancer Facts & Figures 2022. Atlanta: American Cancer Society; 2022. <https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2022/cancer-facts-and-figures-2022.pdf>. Klein E, et al. *Ann Oncol*. 2021;32(9):1167-1177. DOI: 10.1016/j.annonc.2021.05.806



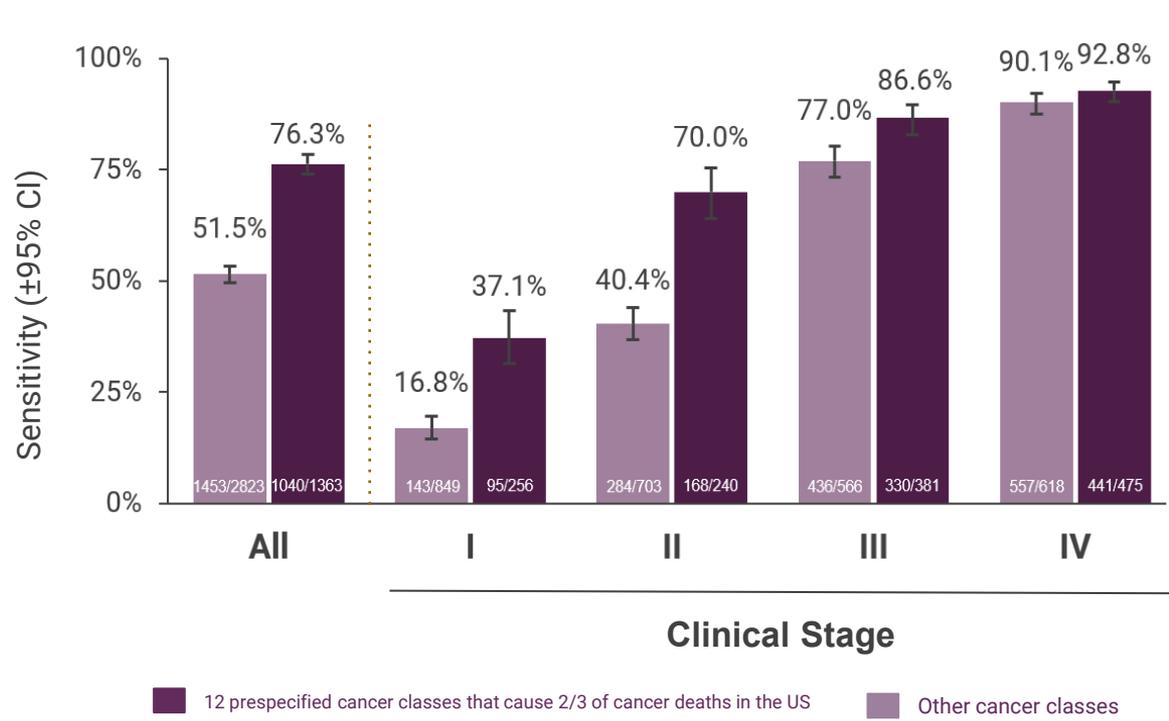
Sensitivity of Cancer Signal Detection by Cancer Class: **Stage I-II**





Sensitivity of Cancer Signal Detection by Clinical Stage

12 Pre-Specified Cancers Responsible for Two-Thirds of Cancer Deaths



- 12 cancers that account for 2/3 of US cancer deaths¹**
- Anus
 - Bladder
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¹American Cancer Society. Cancer Facts & Figures 2022. Atlanta: American Cancer Society; 2022. <https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2022/cancer-facts-and-figures-2022.pdf>. Klein E, et al. *Ann Oncol.* 2021;32(9):1167-1177. DOI: 10.1016/j.annonc.2021.05.806

GRAIL MCED Performance in Largest Clinical Validation Study

1

Shared Cancer Signal

89%

Cancer Signal Origin Accuracy^a

0.5%

False-Positive Rate

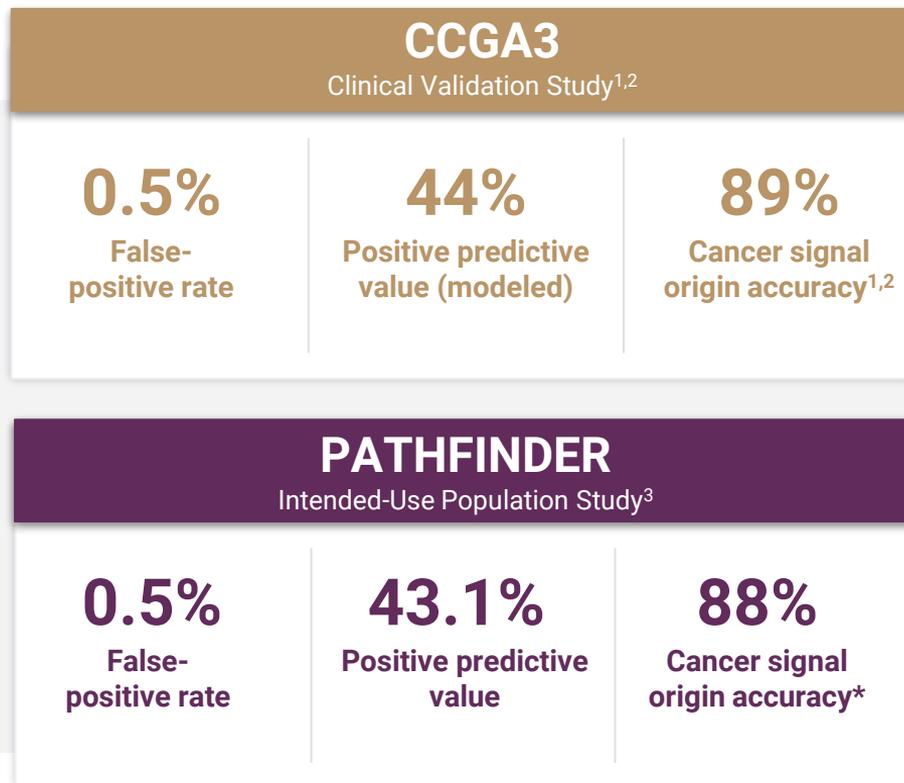
Cancers Identified by a Shared Signal

Anus	Larynx	Oro- and hypo-pharynx ^g
Breast	Leukemia	Ovary ^h
Cervix uteri	Liver	Plasma cell myeloma ⁱ
Corpus uteri (2 types ^b)	Lung	Prostate
Colon and rectum	Melanoma of the skin	Renal pelvis and ureter
Esophagus ^c	Malignant pleural mesothelioma	Soft tissue sarcoma (5 types ^j)
Exocrine pancreas	Merkel cell carcinoma	Small intestine
Gallbladder	Nasopharynx	Stomach
Hodgkin and non-Hodgkin lymphoma	Neuroendocrine (3 types ^e)	Testis
Bile duct (3 types ^d)	Oral cavity	Urinary bladder
Kidney	Oropharyngeal ^f	Vagina
		Vulva

Bold indicates cancer with USPSTF screening guideline^k

^aFor cancer participants with a positive cancer signal. ^bCorpus uteri carcinoma and carcinosarcoma; Corpus uteri sarcoma. ^cEsophagus and esophagogastric junction. ^dDistal bile duct; Perihilar ducts; Intrahepatic bile ducts. ^eNeuroendocrine tumors of the appendix; Neuroendocrine tumors of the colon and rectum; Neuroendocrine tumors of the pancreas. ^fHPV-mediated (p16+) oropharyngeal cancer. ^gOropharynx (p16-) and hypopharynx. ^hOvary, fallopian tube and primary peritoneal carcinoma. ⁱPlasma cell myeloma and plasma cell disorders. ^jSoft tissue sarcoma: of the abdomen and thoracic visceral organs; of the head and neck; of the retroperitoneum; of the trunk and extremities; unusual histologies and sites. ^kUSPSTF A, B, or C rating. AJCC, American Joint Committee on Cancer; CCGA, Circulating Cell-free Genome Atlas; USPSTF, United States Preventive Services Task Force. Klein E, et al. *Ann Oncol.* 2021;32(9):1167-1177. DOI: 10.1016/j.annonc.2021.05.806.

Consistent Test Performance in an Intended-Use Population



1. Based on tissue of origin class assigned in 96% of cases where cancer was detected accuracy of top Cancer Signal Origin for true positive cancer participants with a Cancer Signal Detected., 2. Klein EA et al. Clinical validation of a targeted methylation-based multi-cancer early detection test using an independent validation set. *Ann Oncol.* 2021;32(9):1167-1177. doi: 10.1016/j.annonc.2021.05.806., 3. Schrag D, et al. *The Lancet.* 2023;402(10409):1251-1260.

*Accuracy of top two cancer signal origin prediction for true positive patients, Based on prespecified reanalysis of blood samples with Galleri test.



Enhanced Cancer Signal Origin Prediction

Enabling a Focused and Efficient Diagnostic Evaluation



93.4%
UPDATED
**Rate of cancer signal origin
predicted correctly**

A Single Cancer Signal Origin is Reported

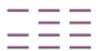
The revised classifier improved the accuracy of the CSO prediction to 93.4%

Streamlined Cancer Signal Origin Classes

The number of Cancer Signal Origin (CSO) classes has changed from 21 to 18 due to the refinement of the classifier

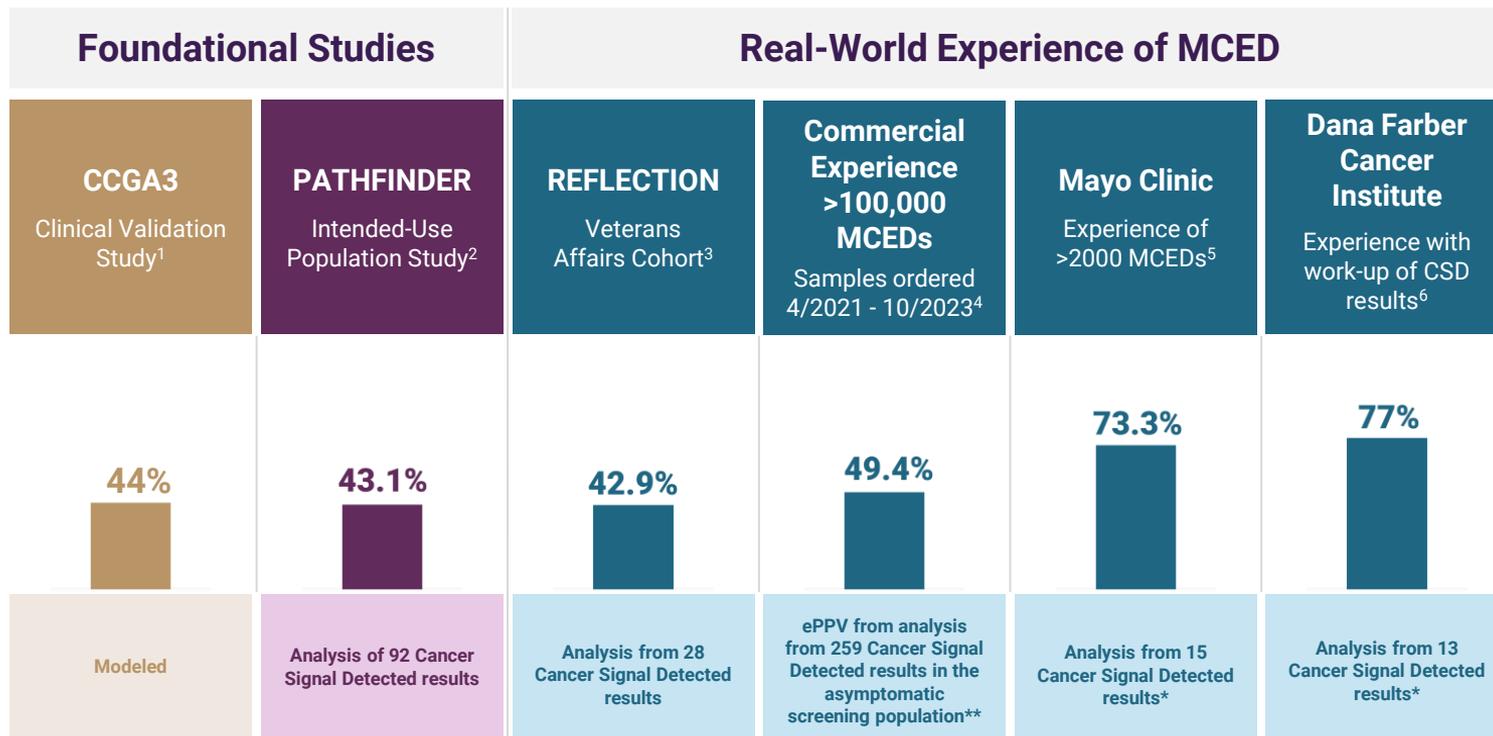
Additional Prediction Information Category

Identifies 7 types of cancer biology signals with a accuracy of 93% that enables a focused diagnostic evaluation



Consistent Performance in Real-World Clinical Experience

Positive Predictive Value (PPV)



*These studies were conducted independent of GRAIL.**ePPV is the cancer diagnosis rate in the population of patients who had a positive MCED test, completed workup, and follow-up information reported by a healthcare provider.

☰☰☰ Cancer Signal Origin May Aid in Prompt Diagnostic Resolution

Time to Cancer Diagnosis (days)

Standard of Care Practice
(No MCED Test)

Retrospective Claim Database¹ (n=458,818)

156.2^a

Clinical Study

PATHFINDER² (n=90) 57^b

MCED Test



Real-World Experience

MERCY Health³ (n=6) 8.7^c

Dana Farber Cancer Institute⁴ (n=10)

23^c

RWE⁵ (Asymptomatic Screening, n=115)

43^d

^aMean time to diagnosis. ^bMedian time to diagnosis in true positive cases. ^cMedian time to diagnosis. ^dMedian time to diagnostic resolution for those reported. CSO, cancer signal origin; MCED, multi-cancer early detection; RWE, real-world experience.

1. Gitlin M et al. *J Manag Care Spec Pharm*. 2023;29(6): 659-670. 2. Schrag D, et al. Presentation at European Society for Medical Oncology (ESMO) Congress; September 9-13, 2022. 3. Agarwal G et al. Poster presented at ASCO Annual Meeting. June 2-6, 2023. 4. O'Donnell, E. et al.. Poster presentation presented at ASCO Annual Meeting. May 30 - June 2, 2025. 5. Matrana M, et al. Poster presentation presented at AACR Annual Meeting. April 25-30, 2025.

Criteria for an Effective Multi-Cancer Early Detection (MCED) Test



Detect **many deadly cancers**, including unscreened cancers, using a single blood sample



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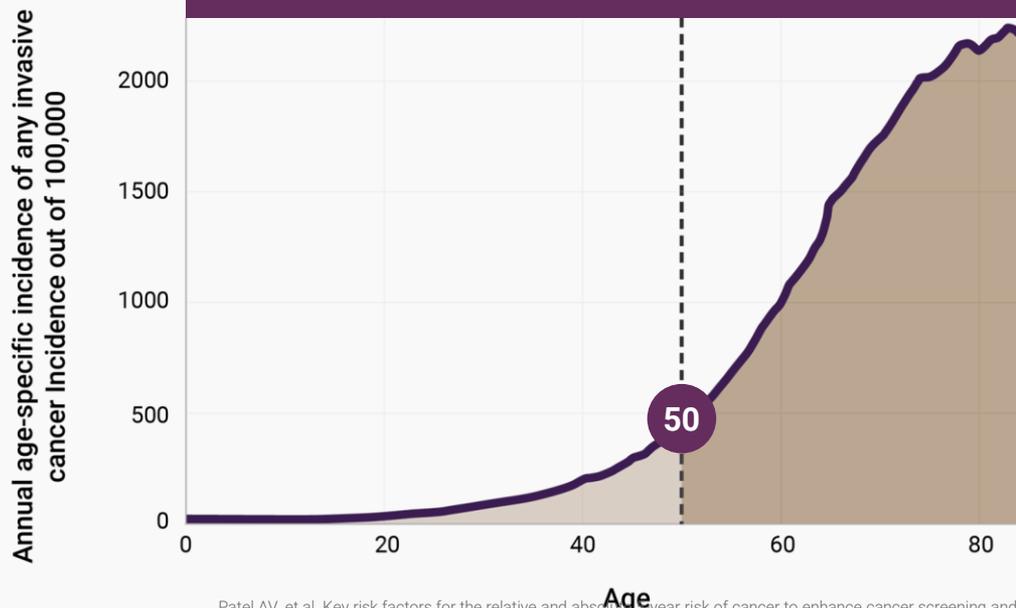


Implementing MCED into practice

Galleri® Intended Population and Risk of Cancer by Age

Age is the strongest risk factor for cancer

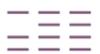
- Average rate over age 50 is **13x higher** than under age 50



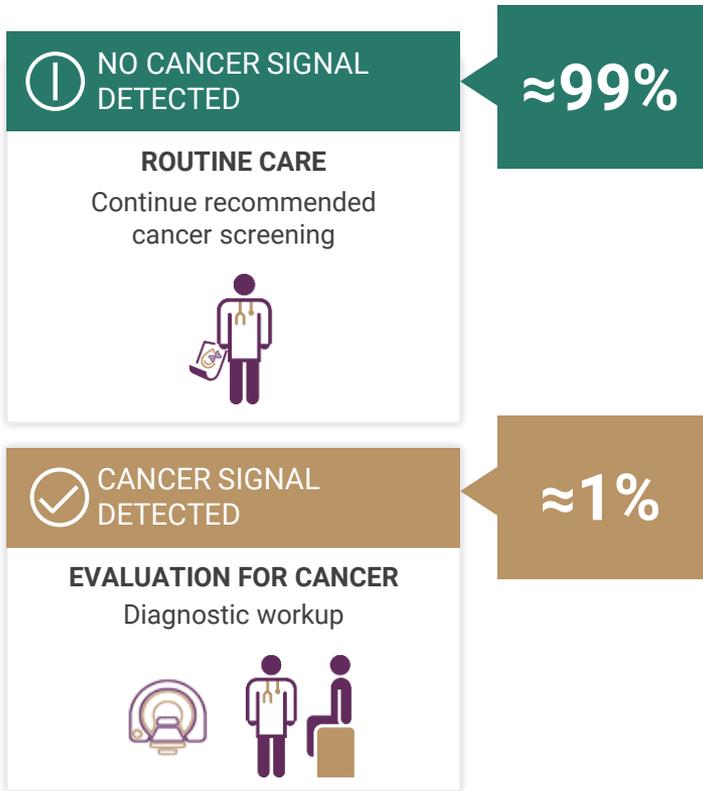
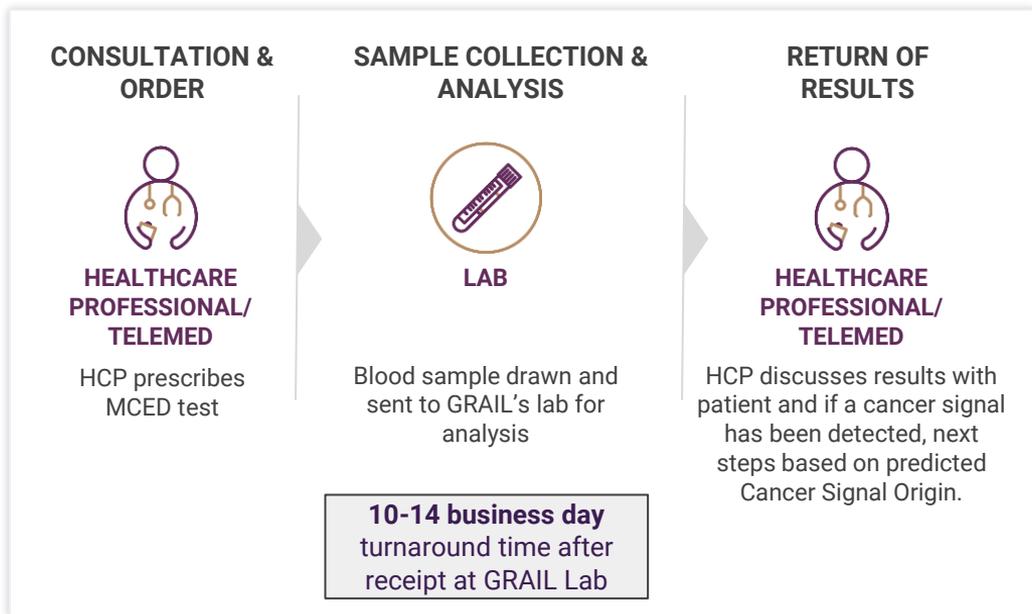
Other risk factors include:

- Current or previous smokers
- Personal history of cancer
- Family history of cancer
- Higher body mass index
- Infections
eg, HPV, HIV, chronic hepatitis B or C
- Environmental Exposures
eg, asbestos, Agent Orange, burn pits

Patel AV, et al. Key risk factors for the relative and absolute 5-year risk of cancer to enhance cancer screening and prevention. *Cancer*. 2022;128(19):3502-3515. doi: 10.1002/cncr.34396. Data: Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database Incidence - SEER Research Limited-Field Data, 21 Registries, Nov 2020 Sub (2000-2018) - Linked To County Attributes - Time Dependent (1990-2018) Income/Rurality, 1969-2019 Counties, National Cancer Institute, DCCPS, Surveillance Research Program, released April 2021, based on the November 2020 submission. Risk Factor Data on file: American Cancer Society Cancer Prevention Studies II/III. <https://www.cancer.gov/about-cancer/causes-prevention/risk/substances>. Cohen L, Jefferies A. Environmental exposures and cancer: using the precautionary principle. *Ecancermedicalscience*. 2019 Apr 16;13:ed91. doi: 10.3332/ecancer.2019.ed91.



Galleri[®] Can Easily Be Integrated Into Existing Clinical Workflows



Use of Galleri is not recommended in individuals who are pregnant, 21 years old or younger, or undergoing active cancer treatment.

Galleri® Sample Test Reports

NO CANCER SIGNAL DETECTED



Firstname Lastname
GRAIL ID: GRA-123456

Multi-Cancer Early Detection Test Report

Patient	Sample	Ordering Provider
Name: Firstname Lastname Patient ID: 1234567890 DOB: 01-JAN-1965 Bio Sex: Female	GRAIL ID: GRA-123456 Sample Type: Whole Blood Report Date: 20-DEC-2024 / 18:54 ET Collection Date: 09-DEC-2024	Name: Firstname Lastname, MD Location: Clinical Office Address: 123 Main Street, Suite 100 Anytown, CA 12345 Phone: (123) 456-7890 Fax: (123) 456-7899

Your Result

No Cancer Signal Detected

In a clinical study*, on average, fewer than 2 out of 100 people with a No Cancer Signal Detected result received a cancer diagnosis (Negative Predictive Value was 98.5%).

✔ What this result means

The Galleri test looked for a DNA methylation signal associated with cancer in your blood sample and did not find a signal. Continue with routine cancer screening tests your healthcare provider recommends.

⊗ What this result does not mean

Although the Galleri test did not find a cancer signal in your blood, this does not rule out the possibility of cancer. The Galleri test does not detect all cancers and not all cancers can be detected in the blood.

This result does not predict whether you will develop cancer in the future.

🗨️ Talk to your healthcare provider about the following topics

🏠 Continue routine cancer screenings

Discuss which screening tests are right for you. Screening is recommended for colon/rectum, breast, cervix, lung (for those at risk), and prostate cancers.

🔄 Repeat testing with Galleri

Adding Galleri to annual wellness visits can improve the chances of finding cancer early when it is more treatable. Talk to your healthcare provider about whether annual testing with Galleri is appropriate for you.

* NATHANIELSON (NCT02647765)^{††} was a prospective, observational return of results study (n = 6,862) to assess the implementation of an early version of the Galleri test in a clinical setting. Participants were a 50 years with and without additional cancer risk. A pre-specified reanalysis of blood samples (n = 6,576) was completed with the Galleri test.

GRAIL | Laboratory Director: Daniel Dunham, MD | CLIA #3402232314 | CAP #1915398
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CANCER SIGNAL DETECTED



Firstname Lastname
GRAIL ID: GRA-123456

Multi-Cancer Early Detection Test Report

Patient	Sample	Ordering Provider
Name: Firstname Lastname Patient ID: 1234567890 DOB: 01-JAN-1965 Bio Sex: Female	GRAIL ID: GRA-123456 Sample Type: Whole Blood Report Date: 20-DEC-2024 / 18:54 ET Collection Date: 09-DEC-2024	Name: Firstname Lastname, MD Location: Clinical Office Address: 123 Main Street, Suite 100 Anytown, CA 12345 Phone: (123) 456-7890 Fax: (123) 456-7899

Your Result

Cancer Signal Detected

In a clinical study*, on average, 4 out of 10 people with a Cancer Signal Detected result received a cancer diagnosis (Positive Predictive Value was 43%).

✔ What this result means

The Galleri test looked for a DNA methylation signal associated with cancer in your blood sample and found a signal. A healthcare provider should conduct a diagnostic evaluation for cancer.

⊗ What this result does not mean

A Cancer Signal Detected result is NOT a cancer diagnosis. Diagnostic evaluation by a healthcare provider is needed to confirm if you have cancer.

DETECTION

Your Predicted Cancer Signal Origin

To help guide diagnostic evaluation, the Galleri test provides a prediction about the most likely organ(s) associated with the Cancer Signal. The Signal Origin predictions are organized into 18 Cancer Signal Origins, which are listed in the methods section.

CANCER SIGNAL ORIGIN PREDICTION

Ovary

Additional prediction information:

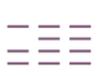
Female Reproductive Tract Signal

📍 What is included: Ovary, Fallopian tube, Primary Peritoneum.

📍 If the diagnostic evaluation based on the predicted Cancer Signal Origin does not lead to a cancer diagnosis, consider expanding the diagnostic evaluation to other organs possibly affected (Ovary, Uterus, Cervix).

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Medical Support for Cancer Signal Detected Results

Field-based and in-house Medical Science Liaisons (MSLs) for white glove support



Positive Result Resource Center for Diagnostic Referral Toolkit, Post-Positive Payer Coverage assistance for continuity of care and more



DocMatter Clinician Community online forum for on-the-go, **peer to peer insights** related to MCED



Medical Services team available for result review, inquiries, patient assistance, diagnostic center resources



To include your center in the diagnostic resource document, scan the QR code and complete the form



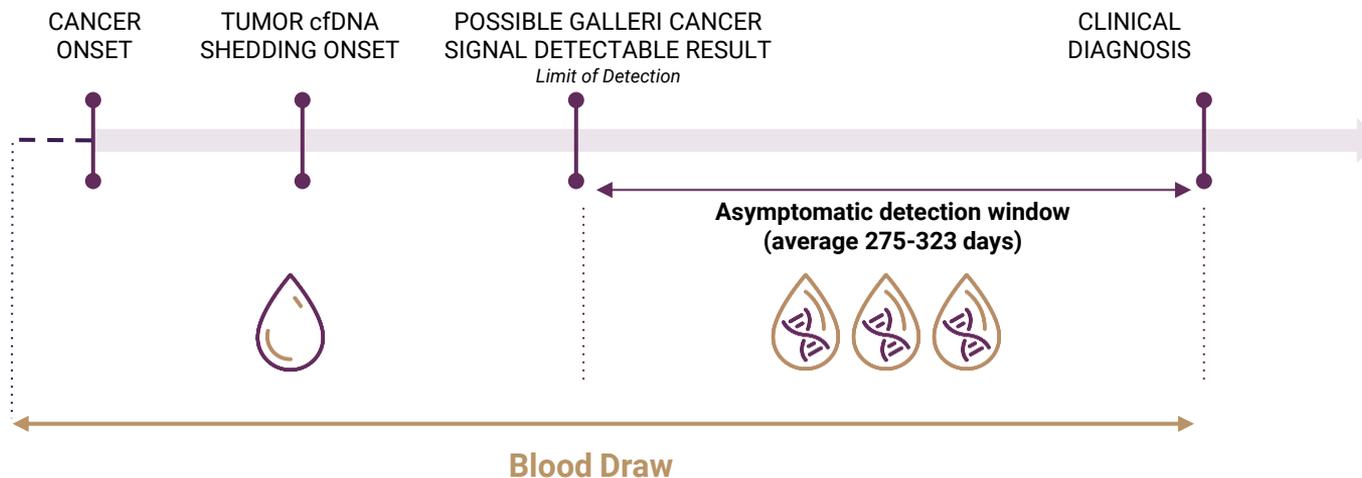
Galleri Retest Program if workup does not yield a cancer diagnosis



Peer to peer consultations and Early Cancer Detection Board with independent, **nationally recognized, physician specialists**

☰☰☰ Cancer Biology Driving Annual Screening

Cancer Signal Detection in Blood Is Determined by Cancer Biology¹⁻⁵

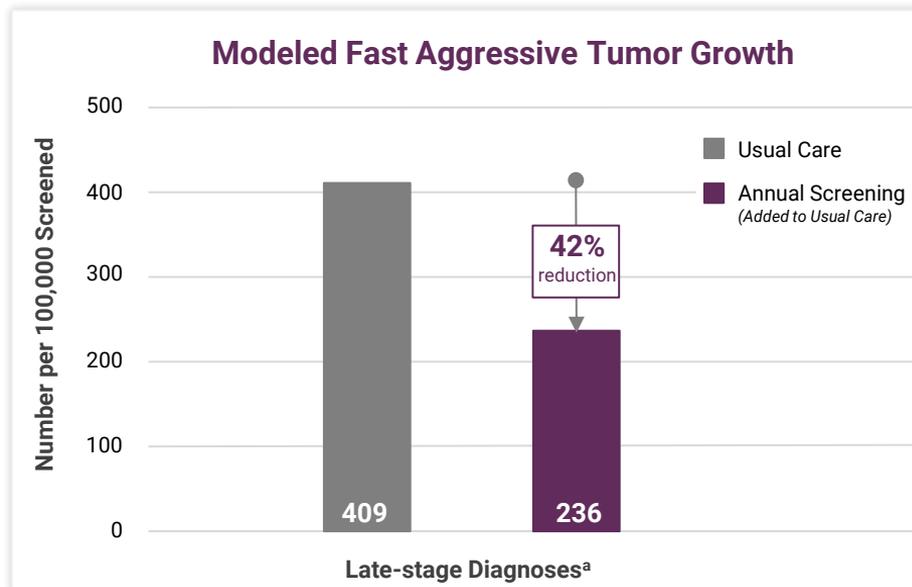


The American Cancer Society Cancer Prevention Study revealed an approximately 1-year (323 days) average detectable window, supporting the importance of an annual cancer screening interval

Annual Screening With Galleri Reduced Late-Stage Cancer Diagnosis

Fast aggressive modeled tumor growth rates with 1-2 year stage I dwell time

42%
reduction in late-stage diagnosis
with annual screening



Modeled data suggests that annual testing with Galleri improves the chance of finding cancer early, when it may be more treatable

**The future of cancer screening, validated
today.**

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