NORTHEAST
BUSINESS GROUP ON HEALTH

The New Frontier for Screening and Early Detection of Cancer

Wednesday, February 26, 2025 | 12:00 – 1:00pm

Webinar Procedures

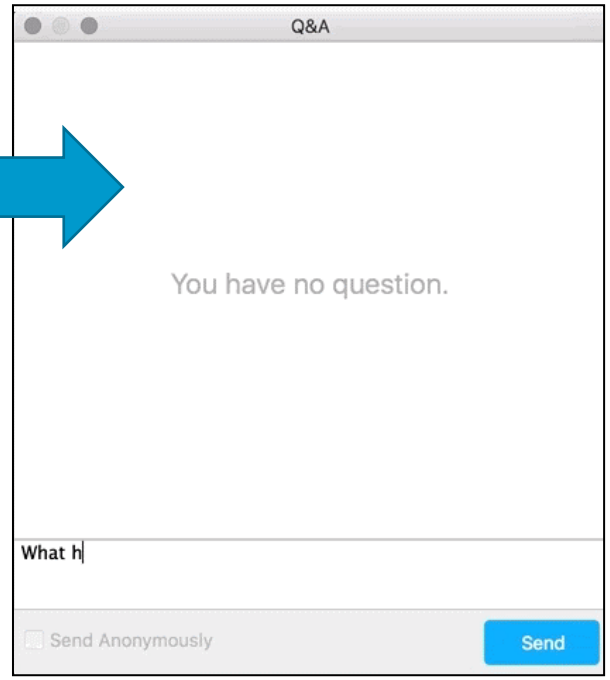
All lines will be muted

Please submit all questions using the “Q&A” dialog box

Email Diane Engel at dengel@nebgh.org with any issues during this webinar

The recording and a PDF of the presentation will be shared.

Recording will be stopped before Q&A



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Speakers

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NEBGH

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CEO
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The New Frontier for Screening and Early Detection of Cancer

Webinar

Trudy McKanna
Senior Field Medical Director
GRAIL

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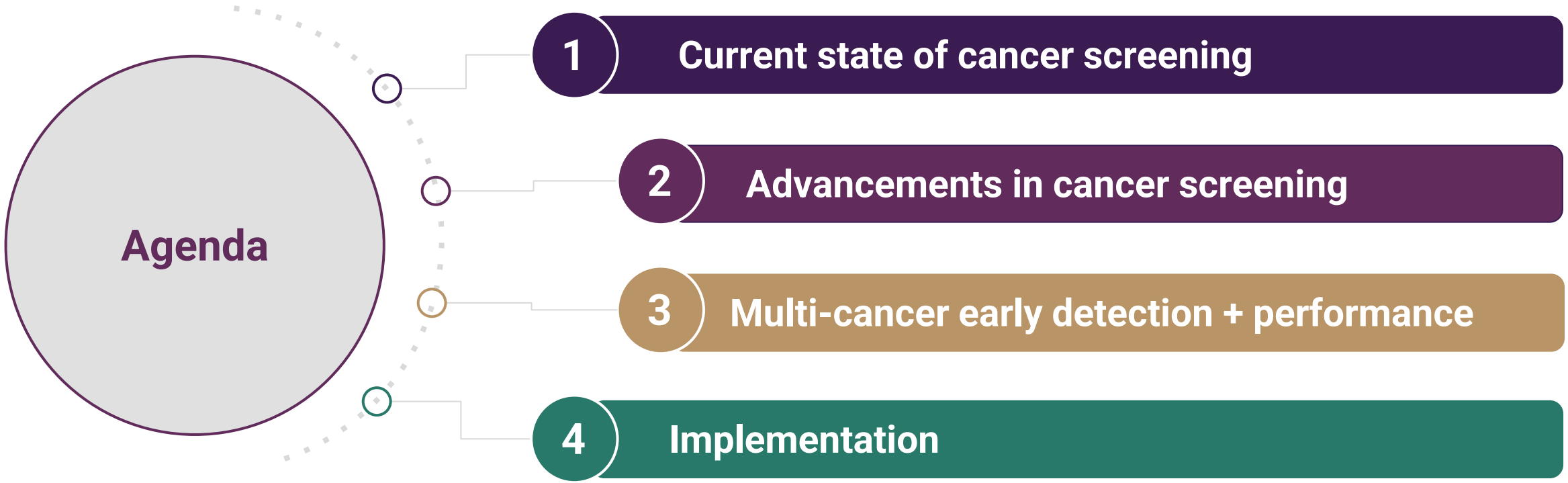

Agenda
1
Current state of cancer screening
2
Advancements in cancer screening
3
Multi-cancer early detection + performance
4
Implementation

Cancer Is a Leading Cause of Death in the United States[1]

~1 in 2 men
will be diagnosed with cancer in their lifetime*

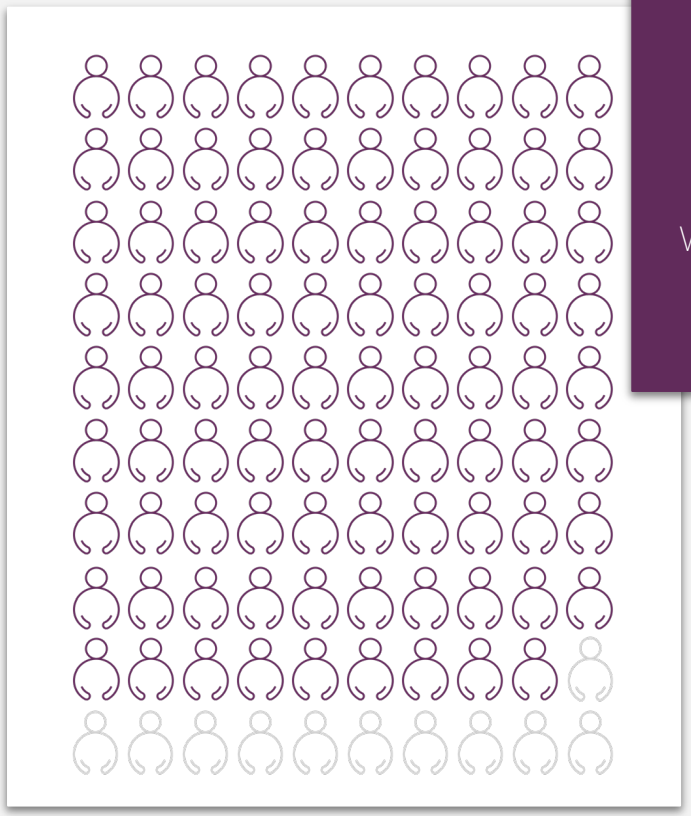
~1 in 3 women
will be diagnosed with cancer in their lifetime*

1 in 5 people
will die from cancer[2]

*41.6% of men will be diagnosed with cancer in their lifetime. 39.6% of women will be diagnosed in their lifetime.

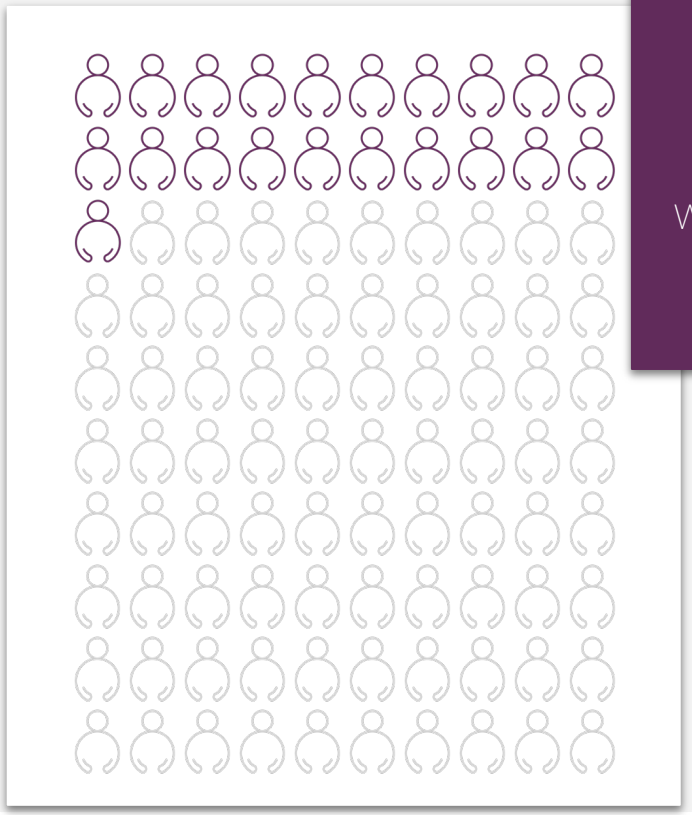
1. Leading Causes of Death https://www.cdc.gov/nchs/fastats/leading-causes-of-death.html.
2. American Cancer Society. Lifetime Risk of Developing or Dying from Cancer. https://www.cancer.org/cancer/risk-prevention/understanding-cancer-risk/lifetime-probability-of-developing-or-dying-from-cancer.html.

Diagnosing Cancer Early Can Make a Difference



89%

Survival rate when diagnosed **early**



21%

Survival rate when diagnosed **late**

"Early/Localized" includes invasive localized tumors that have not spread beyond organ of origin, "Late/Metastasized" includes invasive cancers that have metastasized beyond the organ of origin to other parts of the body.

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Based on 5-year cancer-specific survival rates. Source: Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence - SEER 18 Regs Research Data, Nov 2018 Sub. Includes persons aged 50-79 diagnosed 2006-2015. Data on file GA-2021-004.

Routine Screening Is Recommended for Only 5 Cancers Today

BREAST

Mammography

CERVICAL

Cytology / hrHPV Test

COLORECTAL

Colonoscopy, Sigmoidoscopy and Fecal tests

LUNG*

Low-dose computed tomography (LDCT)

PROSTATE**

Prostate-specific antigen (PSA) test

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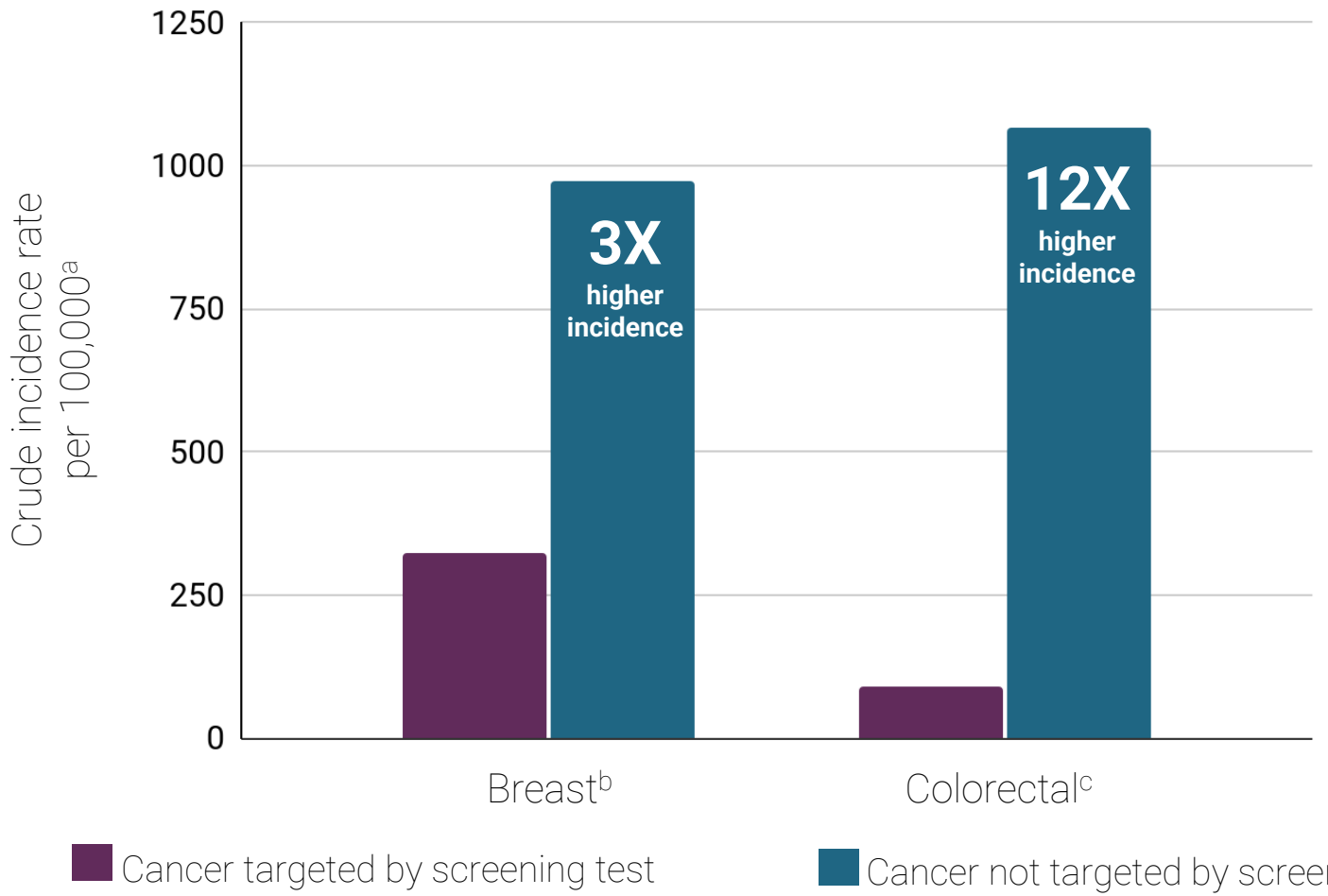
* Adults aged 50 to 80 years who have a 20 pack-year smoking history and currently smoke or have quit within the past 15 years. ** For men aged 55 to 69 years, the decision to undergo periodic screening for prostate cancer should be an individual one. U.S. Preventive Services Task Force (USPSTF) A, B, and C recommendations. https://www.uspreventiveservicestaskforce.org/uspstf/topic_search_results

Unscreened Cancers Represent ~70% of Cancer Deaths

*Assumes screening is available for all prostate, 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)

Among individuals 50-79 years old.
Source: Estimated deaths per year in 2022 from American Cancer Society Cancer Facts and Figures 2022. Available at: http://www.cancer.org/content/dam/cancer-org/research/cancer-factsand-statistics/annual-cancer-factsand-figures/2022/cancer-facts-andfigures-2022.pdf. Data on file GA-2021-0065.

Cancers Without Screening Tests Are Frequently Missed

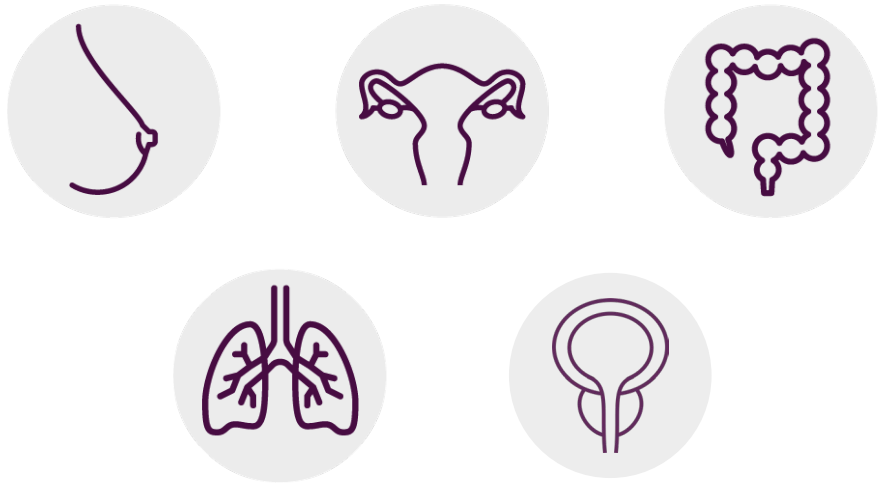


Individuals are **more likely** to have a **different cancer** than the one that is being screened

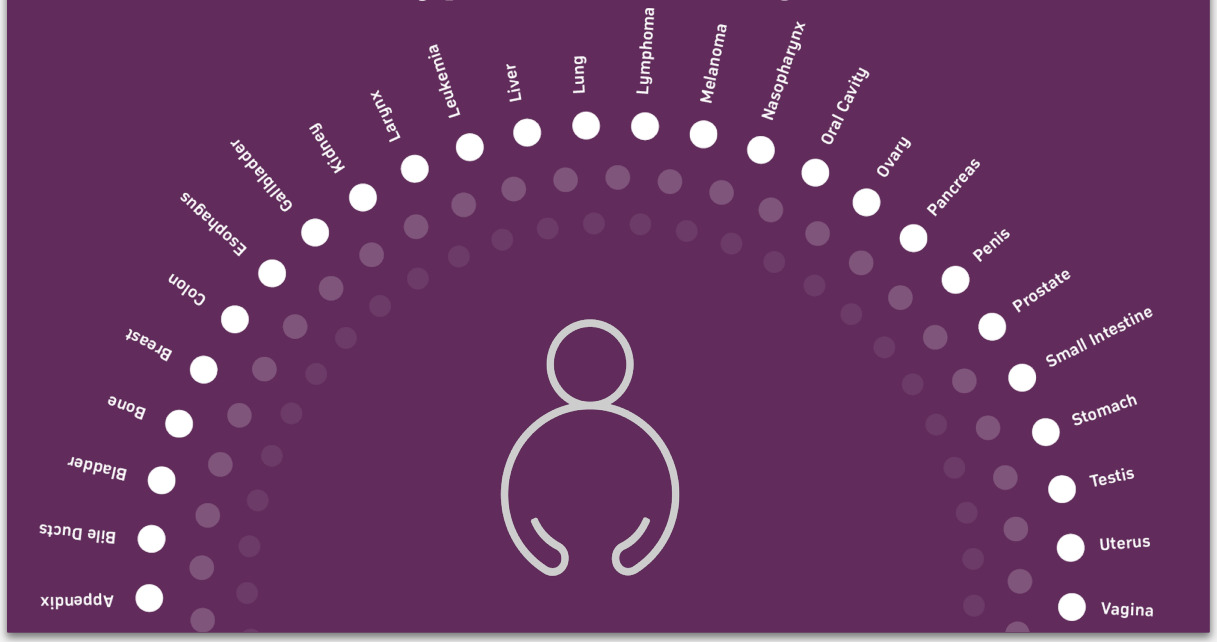
[a]All rates are crude per 100,000 from Surveillance, Epidemiology and End Results Program (SEER18; incidence of invasive cancers only) and National Center for Health Statistics (mortality). [b]Women aged 50-74 years (recommended biennial screening mammography). [c]Men and women aged 50-74 years (choice of approved modality for screening). Clarke CA et al. *Cancer Cell*. 2021;12;39(4):447-448. doi: 10.1016/j.ccell.2021.02.004. Data on file GA-2021-007.

Cancer Screening | Adding MCED Test to Recommended Screening

Recommended screening 1 cancer at a time[1]

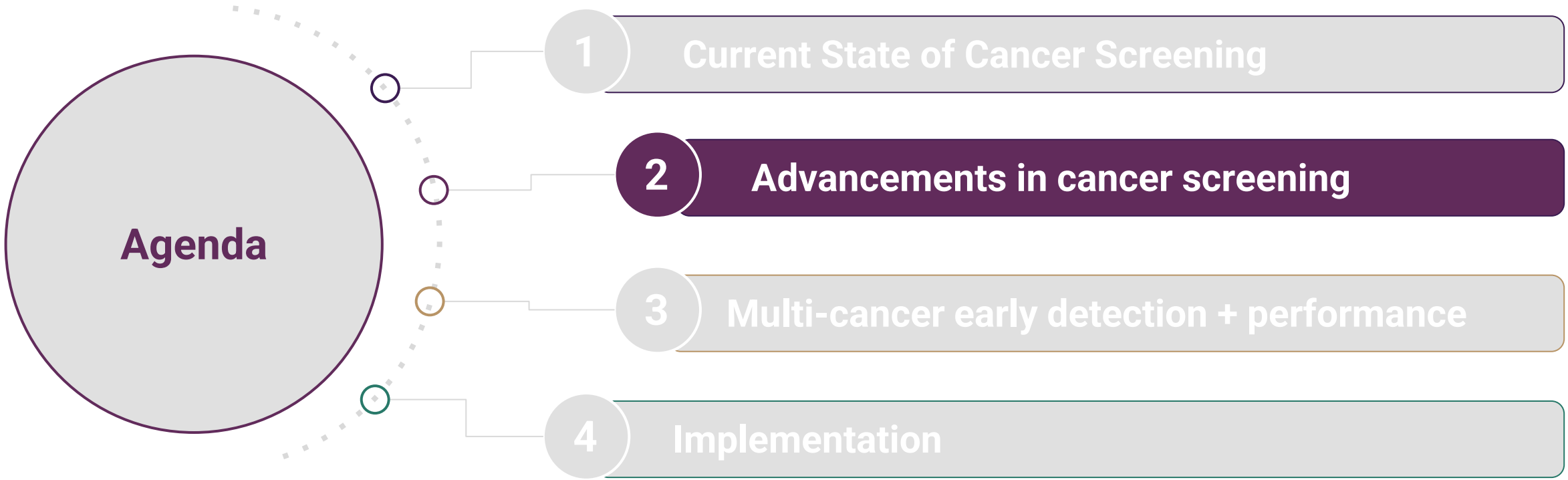


MCED screens for a signal shared by >50 cancer types with a single blood draw[2]



MCED does not detect a signal for all cancers and not all cancers can be detected in the blood. False positive and false negative results do occur. MCED should be used in addition to healthcare provider recommended screening tests.

1.U.S. Preventive Services Task Force (USPSTF) recommended cancer screening tests, Grade A,B,C. https://www.uspreventiveservicestaskforce.org/uspstf/topic_search_result
2.Klein EA, et al. *Ann Oncol*. 2021;32(9):1167-1177. doi: 10.1016/j.annonc.2021.05.806.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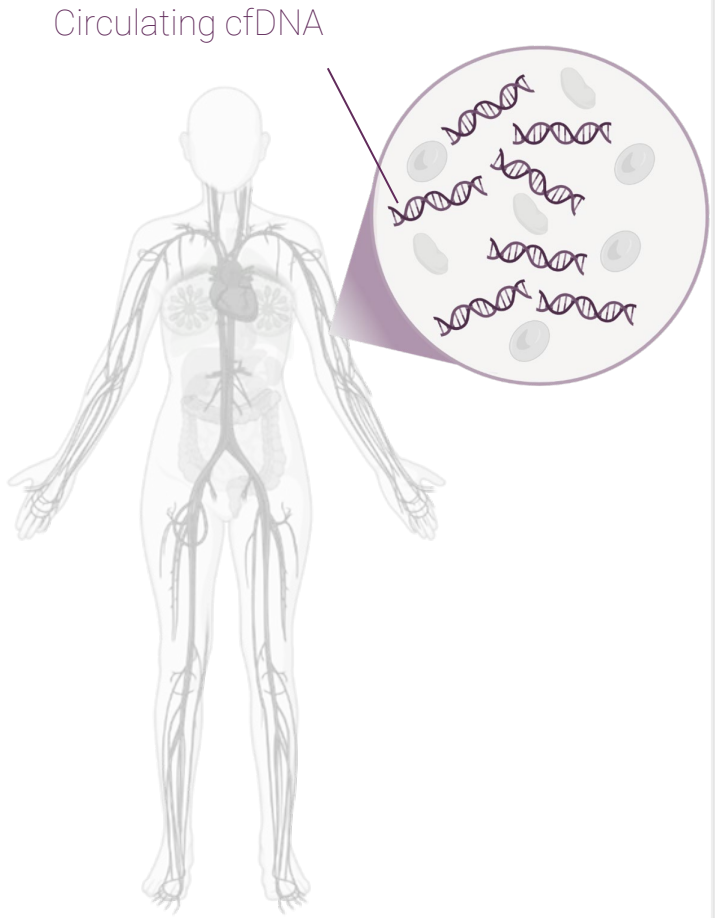
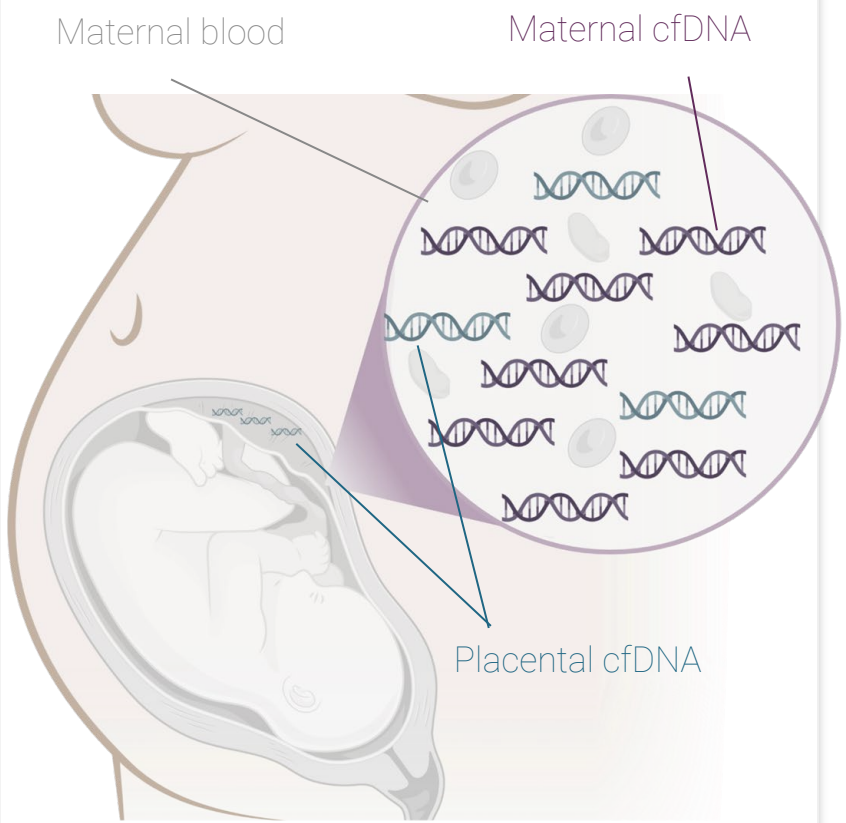
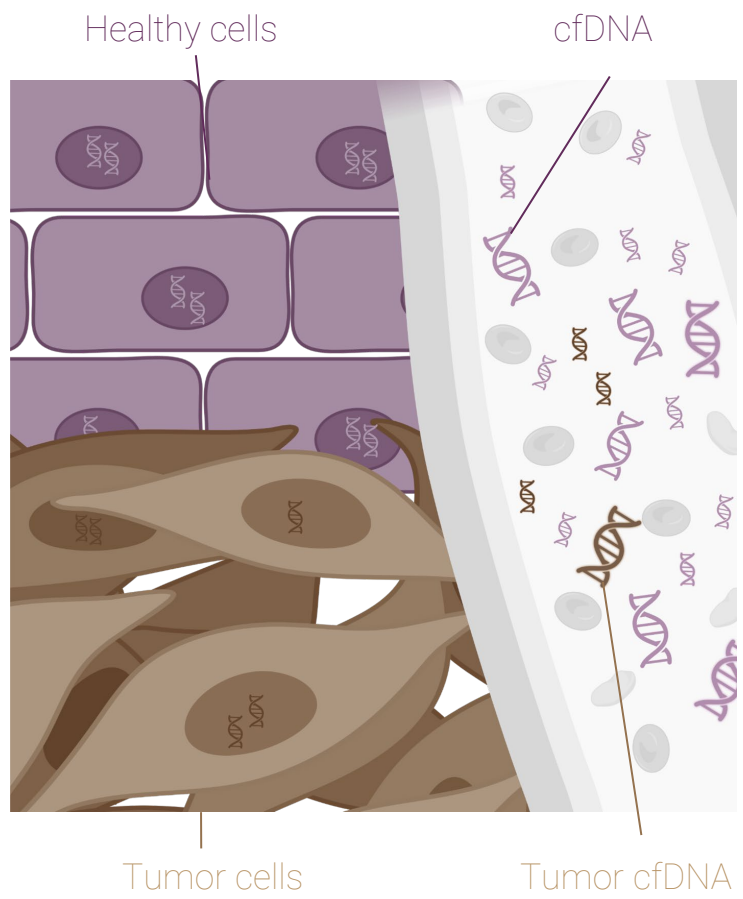
The Origin Story

Cancer Signal Detected in Circulating Cell-free DNA (cfDNA)





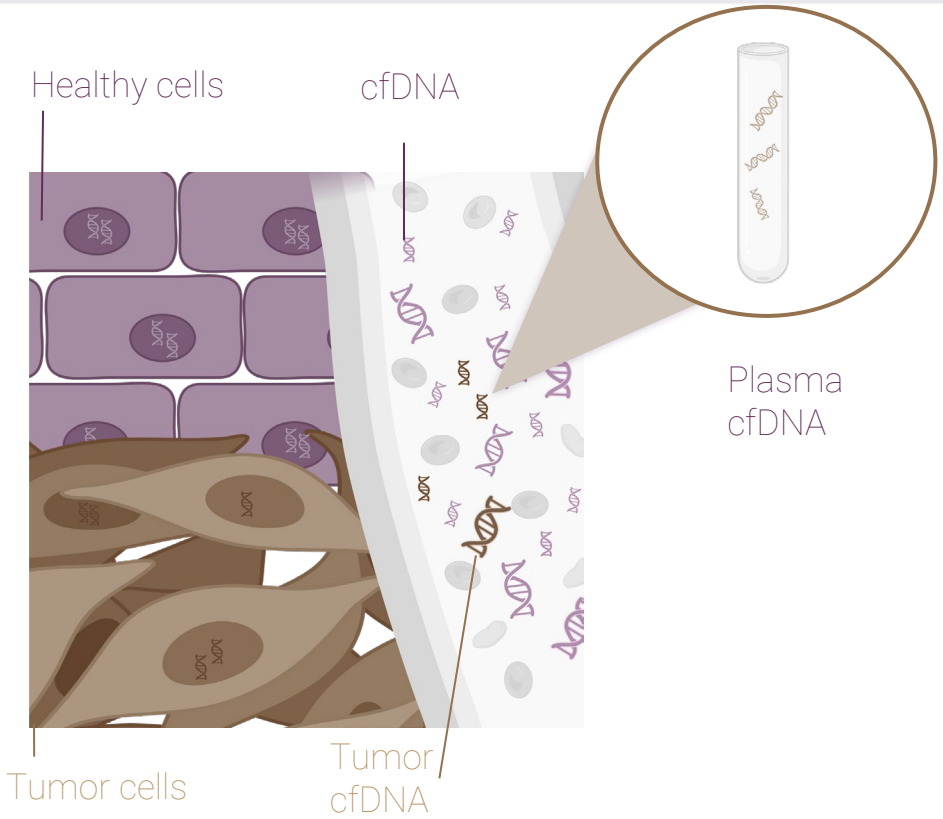
10 cancer cases found in over 125K tests[1]



[1]Bianchi DW, et al. *JAMA*. 2015;314(2):162-169.

Tracking Down Cancer in Blood

Tumors Shed DNA Into Blood and Other Body Fluids, Carrying Identifying Information



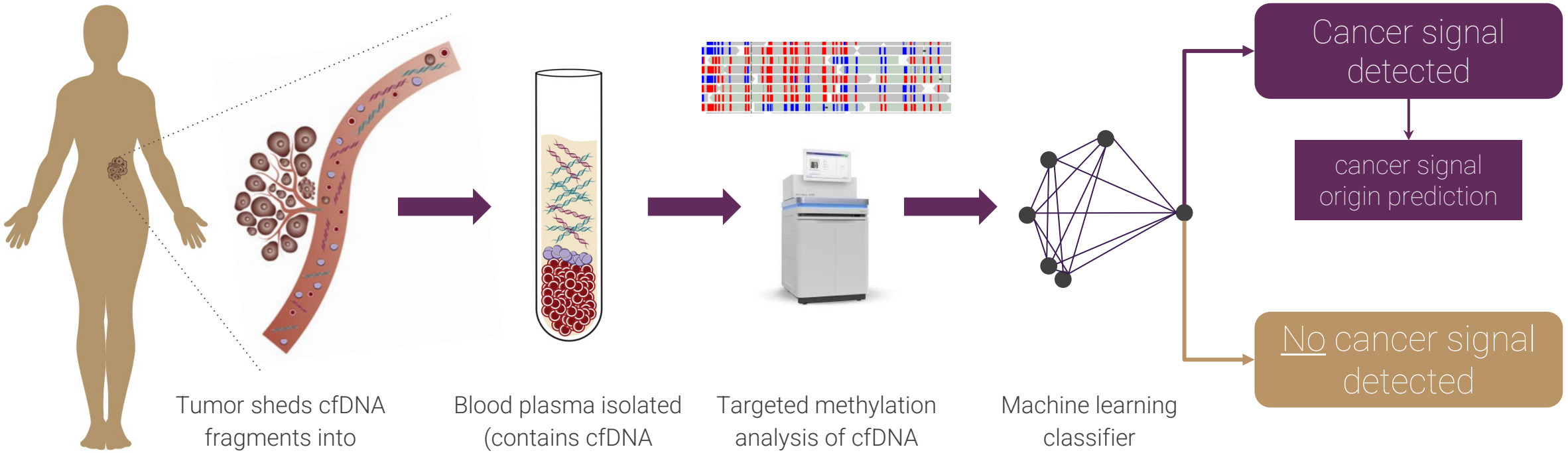
All cells, healthy and cancerous, release DNA into the bloodstream, but DNA from cancer cells is different from DNA from healthy cells

The MCED test is able to identify a pattern that may indicate the presence of a cancer signal

The Galleri test does not detect a signal for all cancers and not all cancers can be detected in the blood.
Galleri is a registered trademark of GRAIL, INC.
Liu MC, et al. Ann Oncol. 2020;31(6):745-759.

Process Overview of Multi-Cancer Early Detection Screening

Cancer can be anywhere: using a targeted methylation, next-generation sequencing (NGS)-based assay analyzing cfDNA and machine learning to detect a cancer signal and predict cancer signal origin



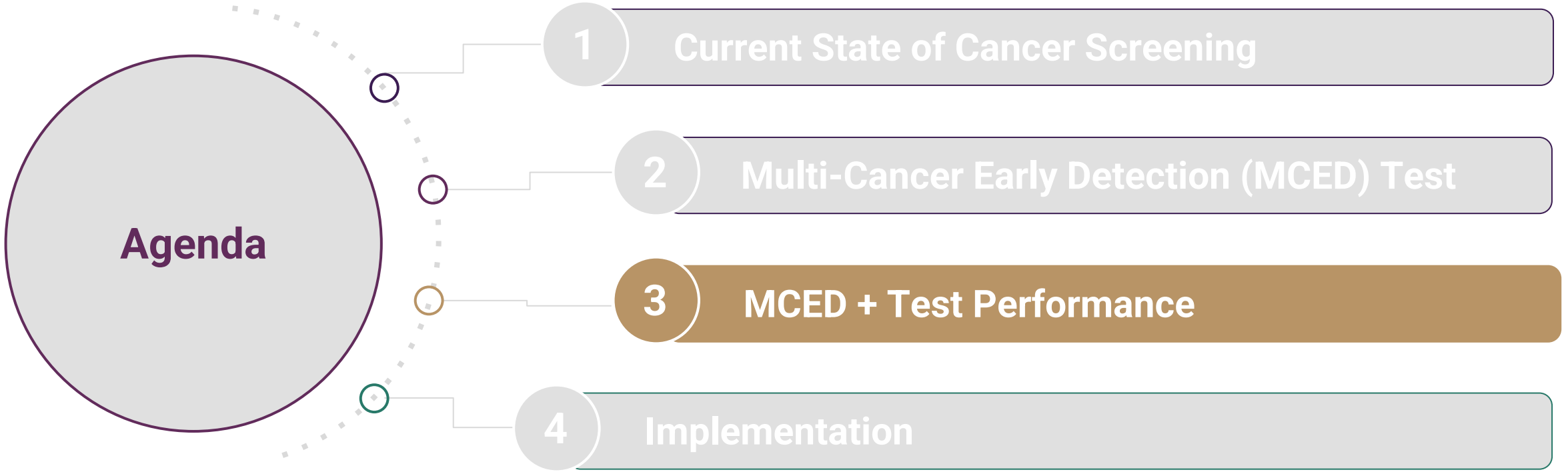
Tumor sheds cfDNA fragments into bloodstream

Blood plasma isolated (contains cfDNA fragments)

Targeted methylation analysis of cfDNA (sequencing, mapping, alignment)

Machine learning classifier

cfDNA, cell-free DNA. [a]Bisulfite treatment; targeted probes pull out fragments matching regions of interest.
The Galleri® test does not detect all cancers and should be used in addition to routine cancer screening tests recommended by a healthcare provider.
Adapted from Liu MC, et al. *Ann Oncol*. 2020;31(6):745-759. DOI:10.1016/j.annonc.2020.02.011.
Galleri is a registered trademark of GRAIL, Inc.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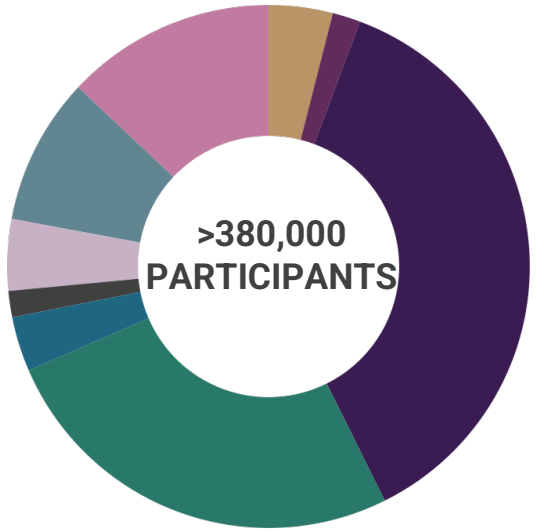
Clinical Development Program

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

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



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[a]In women undergoing mammography screening. [b]Study not yet available at clinicaltrials.gov.
n≈ indicates approximate enrollment.
CCGA, Circulating Cell-free Genome Atlas; DNA, deoxyribonucleic acid; MCED, multi-cancer early detection; UK, United Kingdom.

MCED Performance Summary

76.3%

Sensitivity in 12 deadly cancers
(51.5% overall sensitivity)[1]

In clinical study participants with cancer

0.5%

False positive rate*[1,2]
to minimize unnecessary medical procedures

In clinical study participants without cancer

43.1%

Positive predictive value[2]
Proportion of individuals diagnosed with cancer after a "Cancer Signal Detected" test result

In clinical study participants with cancer

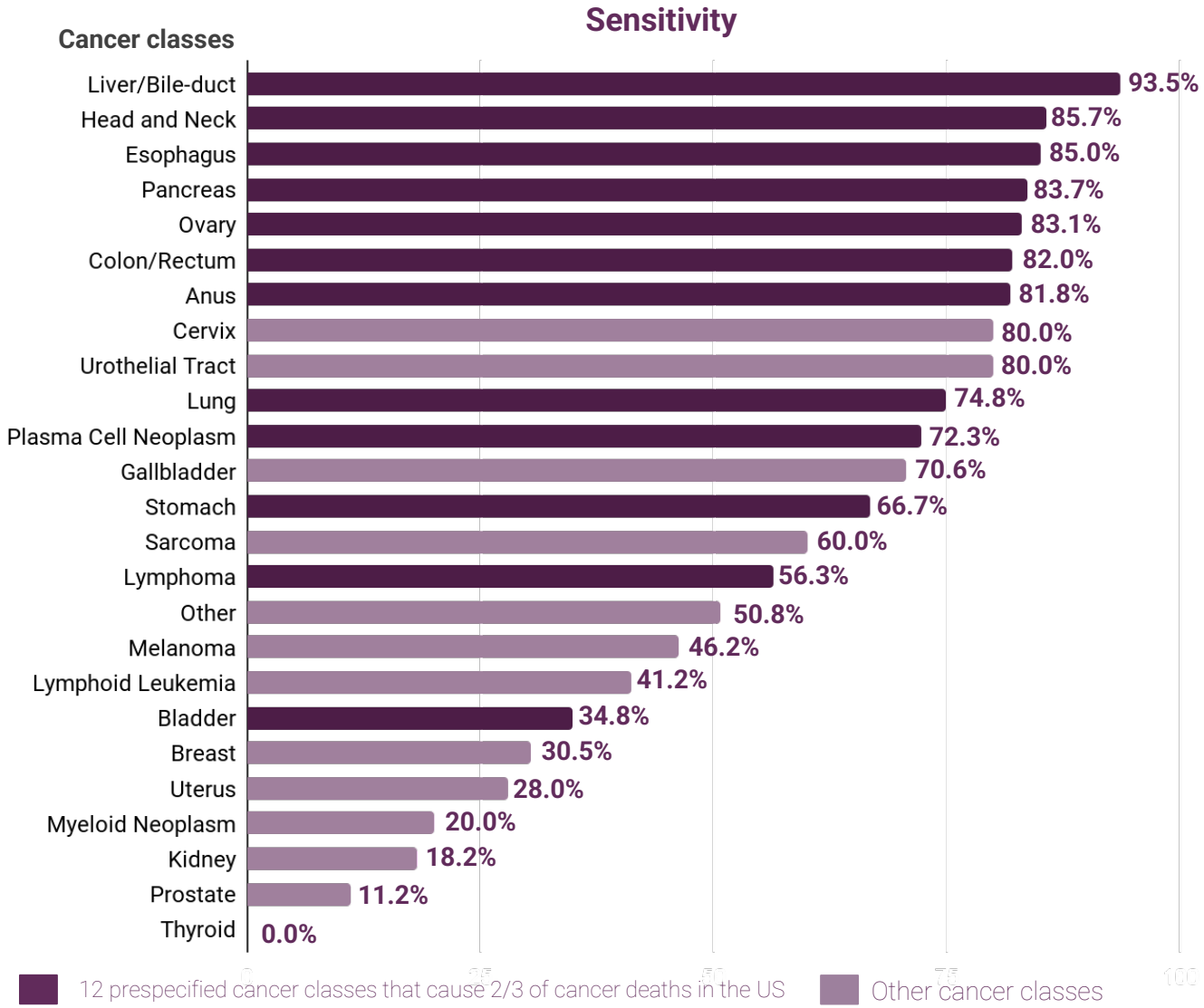
93.4%

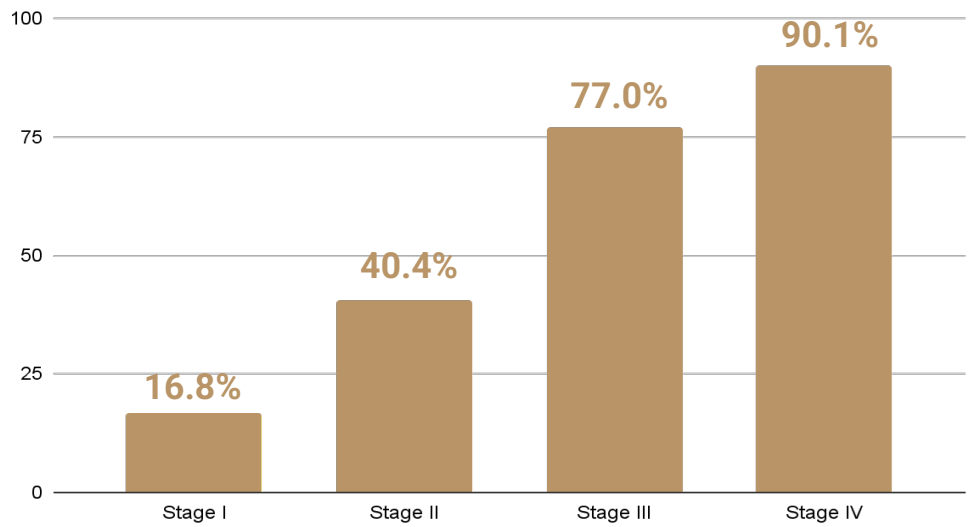
Accuracy in predicting origin of the cancer signal [3]

In participants with a cancer diagnosis after Cancer Signal Detected test result

1.Klein EA, et al. Ann Oncol. 2021;32(9):1167-1177. doi: 10.1016/j.annonc.2021.05.806.
2.Schrag D, Beer TM, McDonnell CH, et al. Blood-based tests for multi-cancer early detection (PATHFINDER): a prospective cohort study. Lancet. 2023;402:1251- 1260. doi: 10.1016/S0140-6736(23)01700-2.
3.GRAIL, Inc. Data on file: VV-TMF-59592 on clinical validation analysis in a subset of CCGA3 and PATHFINDER study participants.

Sensitivity of Cancer Signal Detection





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

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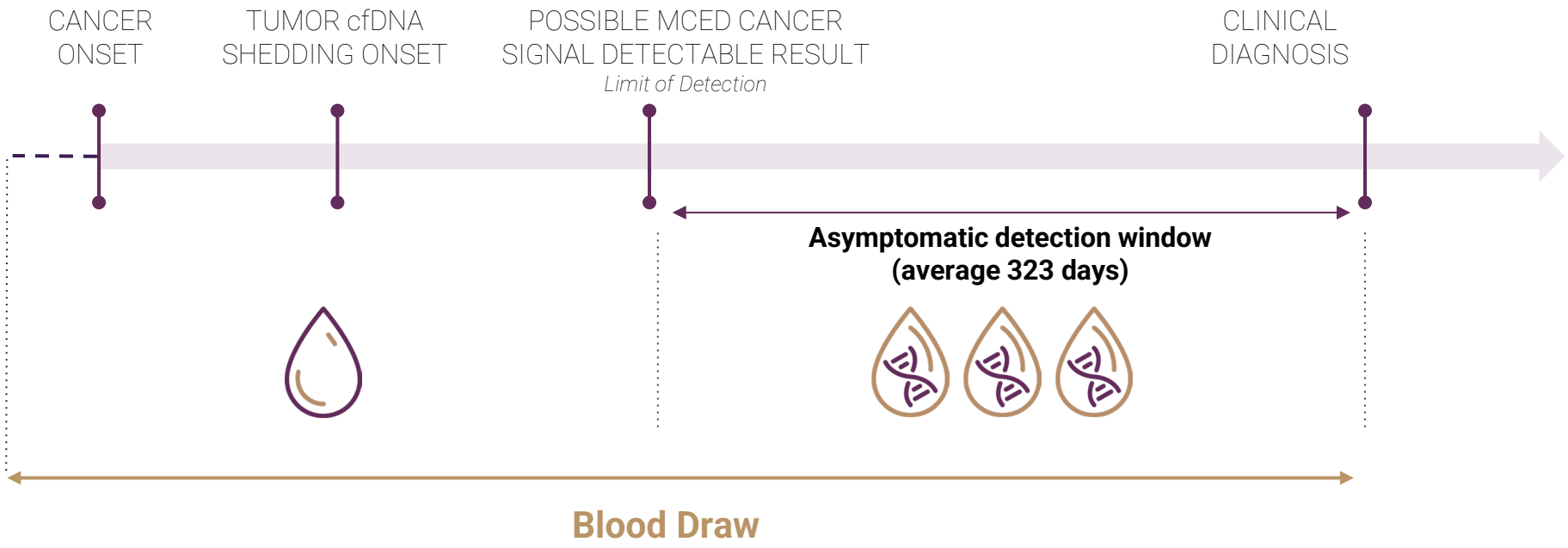
Klein E. et al. *Ann Oncol*. 2021;32(9):1167-77.

Cancer Biology Driving Annual Screening

Cancer Signal Detection in Blood Is Determined by Cancer Biology[1-5]



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

ctDNA, circulating tumor DNA.

1.Cheng et al. 2022. doi:10.21203/rs.3.rs-1203227/v1. 2. Chen et al. 2020. Nat Commun. 2020;11(1):3475. doi:10.1038/s41467-020-17316-z. 3. Harlid et al. Cancers. 2021;13(17):4406. doi:10.3390/cancers13174406. 4.Liu MC, et al. Ann Oncol. 2020;31(6):745-759. doi:10.1016/j.annonc.2020.02.011 5. Patel AV et al. Poster presented at ASCO Annual Meeting. June 2-6, 2023.

False Positive Rate and Positive Predictive Value

	Mammography	MCED test
Screening objective	Screen for **breast cancer**	Screen for **many of the deadliest cancers**
Sensitivity	**87%**[2] **Single cancer** screening tests usually have high sensitivity	**76%**[3] **for 12 deadliest cancers.*** Sensitivity for >50 cancer types is 51%. Sensitivity varies across cancer types
Specificity	**89%**[2] Higher sensitivity results in **lower specificity** and more false positives	**99.5%**[3] **Higher specificity** means fewer false positive results and unnecessary medical procedures
Positive predictive value	**4.4%**[2] Most women with an abnormal mammogram are not diagnosed with breast cancer	**43%**[4] Almost half of individuals with a MCED Cancer Signal Detected result will be diagnosed with cancer

Adding the MCED test to recommended single-cancer screens provides a greater opportunity to screen for more cancers. There have been no head-to-head clinical studies comparing the MCED test to mammography.

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*12 deadly cancers include anus, bladder, colon/rectum, esophagus, head and neck, liver/bile duct, lung, lymphoma, ovary, pancreas, plasma cell neoplasm, and stomach.

1 SEER*Stat Database: Incidence - SEER Research Limited-Field Data, 22 Registries (2018-2019), based on the 2023 Nov submission. 2 Lehman, et al. Radiology. 2017;283(1):49-58. 3 Klein E, et al. Ann Oncol. 2021;32(9):1167-77. 4 Schrag D, et al. Lancet. 2023;402:1251-60.

Cancer Signal Origin Prediction

Enabling a Focused and Efficient Diagnostic Evaluation

93.4%

Accuracy in predicting origin of the cancer signal

A Single Cancer Signal Origin is Reported

Additional Prediction Information Category reported when indicated

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GRAIL, Inc. Data on file: VV-TMF-59592 on clinical validation analysis in a subset of CCGA3 and PATHFINDER study participants.

Agenda

1. Current State of Cancer Screening
2. Multi-Cancer Early Detection (MCED) Test
3. MCED Test Performance
4. **Implementation**

Introducing Galleri®

Multi-cancer early detection test

Galleri Testing Process

ORDERING PROVIDER

Consultation and Order
Provider orders the Galleri test

LABORATORY

Sample Collection
Blood sample drawn and sent to GRAIL for analysis

~2 week turnaround time

*After receipt at the GRAIL Lab

ORDERING PROVIDER

Results Provided
Provider discusses results with patient

NO CANCER SIGNAL DETECTED

Routine Care
Continue routine care and recommended age- and risk-based cancer screening

~99%
of cases result in no cancer signal detected

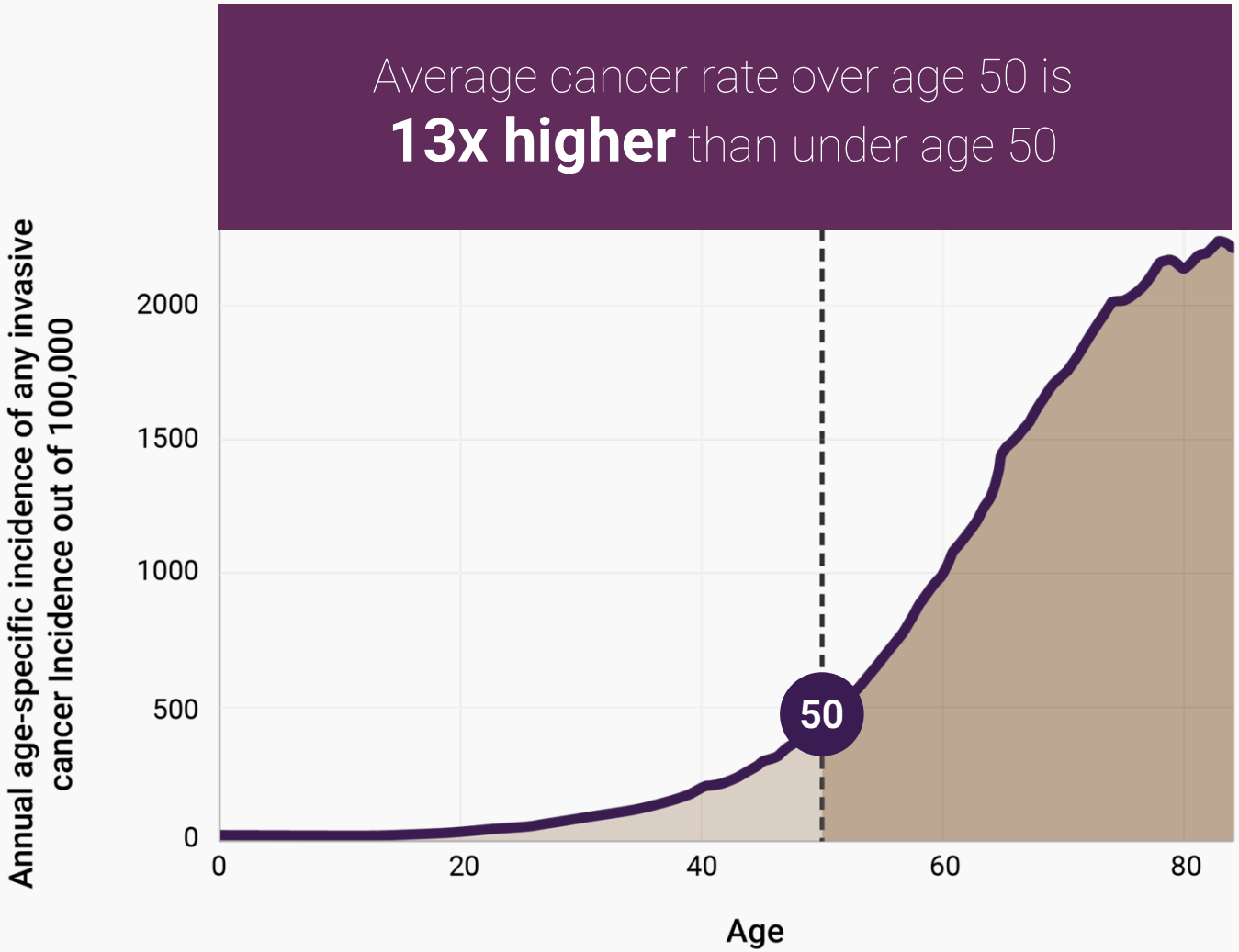
CANCER SIGNAL DETECTED

Evaluation for Cancer
Diagnostic work-up informed by predicted Cancer Signal of Origin

~1%
of cases result in a cancer signal detected

A Galleri result of No Cancer Signal Detected does not rule out cancer.

Age is the strongest risk factor for cancer



Other risk factors

Smoking

Personal history of cancer

Obesity

Diabetes

Exposures

Family history of cancer

Genetic predisposition

Health conditions

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

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

The GRAIL 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.

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Questions?

Upcoming NEBGH events:

- **March 10** – Mondays with Dr. Mark and Dr. Michael
- **March 19** – Colorectal Cancer Screening and Support: Addressing Challenges for Young Patients
- **March 27**– Powering Up Women's Health
- **April 2** – Future Impact of GLP-1s: Employer Educational Dinner
- **June 5** – 14th Annual Health & Wellness Benefits Conference
- **September 18** – 2025 Pharmacy Benefits Conference

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