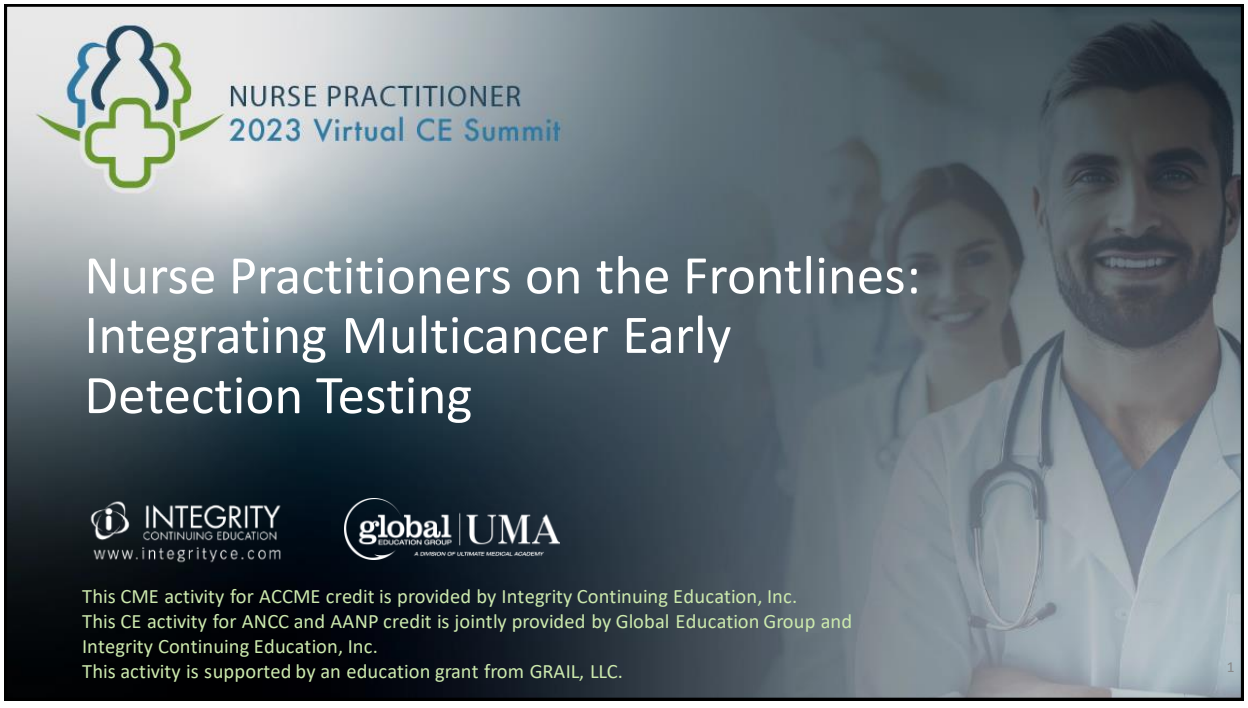

Learning Objectives

- Describe the science that underlies multicancer screening tests and the rationale for their application
- Differentiate among new and emerging blood-based multicancer screening tests
- Employ strategies to reduce barriers to effective population-scale cancer screening, including health and sociodemographic disparities, and challenges in patient engagement
- Utilize cancer screening integration tools that increase patient engagement, improve patient outcomes, and promote continuity of care

INTEGRITY CONTINUING EDUCATION 2

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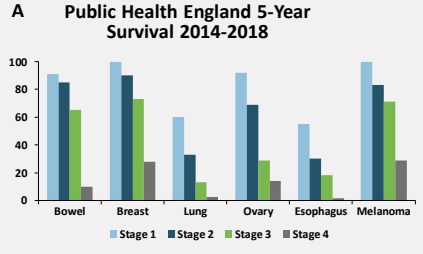
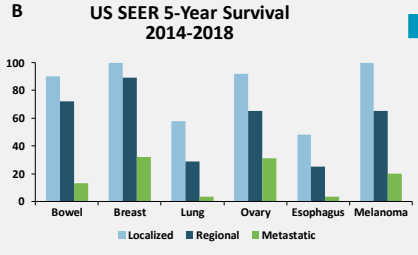
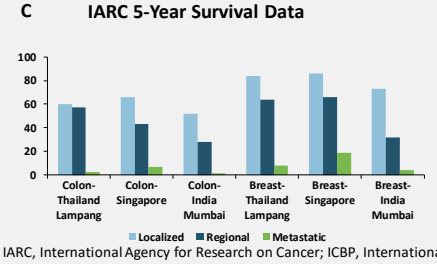
Overview of Cancer Screening

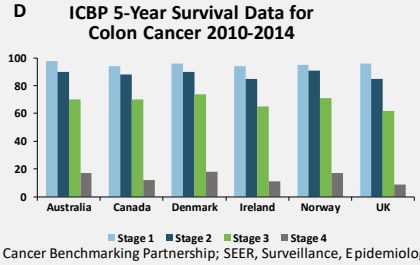
The Importance of Early Detection of Cancer





Across studies, survival rates are consistently higher among patients with cancer that is detected at earlier stages.





IARC, International Agency for Research on Cancer; ICBP, International Cancer Benchmarking Partnership; SEER, Surveillance, Epidemiology, and End Results Program.

Crosby D, et al. *Science.* 2022;375(6586):eaay9040.

INTEGRITY CONTINUING EDUCATION

Current USPSTF Recommendations for Cancer Screening

Cancer	Grade	Population	Modality/recommendation	Pathway and outcome
Cervical*	**A**	Women, 21 to 65 YO	• Regular screening (3–5 years) using cervical cytology and/or HPV tests	• HPV testing: USPSTF → CMS NCD
Colon	**A/B/C**	Adults, 45 to 75 YO (A: 50–75 YO, B: 45–49 YO, C: >75 YO)	• Regular annual screening • Multiple effective methods available	• Legislation → CMS NCD
Breast*	**B**	Women, 50 to 74 YO	• Biennial screening mammography • <50 years individual	• Mandate for coverage with no cost sharing (Balanced Budget Act of 1997, Section 4101)
Lung	**B**	Adults, 50 to 80 YO, with a history of smoking	• Annual LDCT screening • 20 pack-year history and currently smoke or quit in the past 15 years	• USPSTF → CMS NCD
Prostate	**C**	Men, 55 to 69 YO	• Periodic PSA screening on a **case-by-case basis**	• N/A

*Update currently in progress.
HPV, human papillomavirus; CMS, Centers for Medicare & Medicaid Services; NCD, National Coverage Determination; N/A, not applicable; LDCT, low-dose computed tomography; PSA, prostate-specific antigen; USPSTF, United States Preventive Services Task Force; YO, years old.
American Cancer Society. Guidelines for the early detection of cancer. Available at: https://www.cancer.org/cancer/screening/american-cancer-society-guidelines-for-the-early-detection-of-cancer.html; USPSTF. Screening for hypertensive disorders of pregnancy. Available at: https://www.uspreventiveservicestaskforce.org/uspstf/

Suboptimal Use of Cancer Screening Tests in the US

28.5% of women ages 50 to 74 are not up to date with breast cancer screening

17% of women ages 21 to 65 are not up to date with cervical cancer screening

38% of adults ages 50 to 75 are not up to date with colorectal cancer screening

96% of adults ages 55 to 80 who have smoked ≥1 pack of cigarettes per day for 30 years* and currently smoke or have quit in the past 15 years are not up to date with lung cancer screening

*Or the equivalent (eg, two packs per day for 15 years).
American Association for Cancer Research. AACR Cancer Disparities Progress Report 2020. Available at: https://cancerprogressreport.aacr.org/wp-content/uploads/sites/2/2020/09/AACR_CDPR_2020.pdf

Unmet Needs in Cancer Screening

- Lack of available screening tests for multiple cancer types
- Inadequate awareness of and access to screening in certain populations
- Lack of knowledge regarding specific recommendations for screening
- Misconceptions about the tests themselves
- Low patient engagement
- Disparities in screening practices across different communities/populations

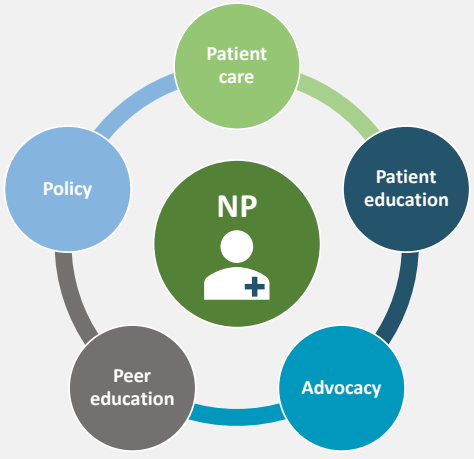
Disparities in Cancer Screening Across Populations

Breast Cancer
Example of Disparity: In 2018, only 63.0% of women with less than a high school education were up to date with breast cancer screening compared to 80.4% of those with a college degree
Cervical Cancer
Example of Disparity: In 2018, only 64.7% of gay or lesbian women were up to date with cervical cancer screening compared to 83.4% of straight women
Colorectal Cancer
Example of Disparity: Women living in rural areas between 2017 and 2020 were 19% less likely to be up to date with colorectal cancer screening than those living in urban areas
Lung Cancer
Example of Disparity: Compared to eligible non-Hispanic White individuals, eligible non-Hispanic Black individuals were 53% less likely to report that they have completed LDCT in the past year
Prostate Cancer
Example of Disparity: In 2018, only 8.9% of uninsured men age 65 and above were up to date with prostate cancer screening compared to 34.4% of those who had any private insurance

- Disparities are influenced by numerous factors that include geographic location, income, education, national origin, and race/ethnicity

Kaiser Family Foundation. Racial disparities in cancer outcomes, screening, and treatment. February 3, 2022. Available at: https://www.kff.org/racial-equity-and-health-policy/issue-brief/racial-disparities-in-cancer-outcomes-screening-and-treatment/; Liu D, et al. *J Racial Ethn Health Disparities*. 2021;8(1):107-126; American Association for Cancer Research. AACR Cancer Disparities Progress Report 2020. Available at: https://cancerprogressreport.aacr.org/wp-content/uploads/sites/2/2020/09/AACR_CDPR_2020.pdf

NPs Are Uniquely Well-Positioned to Promote Improvements in Cancer Screening



- Primary point of contact for health care in rural and underserved areas
- Expanding role in primary care
- Advanced skill in patient education and engagement, both of which are associated with greater adherence to cancer screening recommendations
- Positioned to advocate for and support effective screening policies

NP, nurse practitioner.

Krist AH, et al. *Stud Health Technol Inform*. 2017;240:284-302; Leslie NS. *Cancer Nurs*. 1995;18(4):251-257.

INTEGRITY CONTINUING EDUCATION

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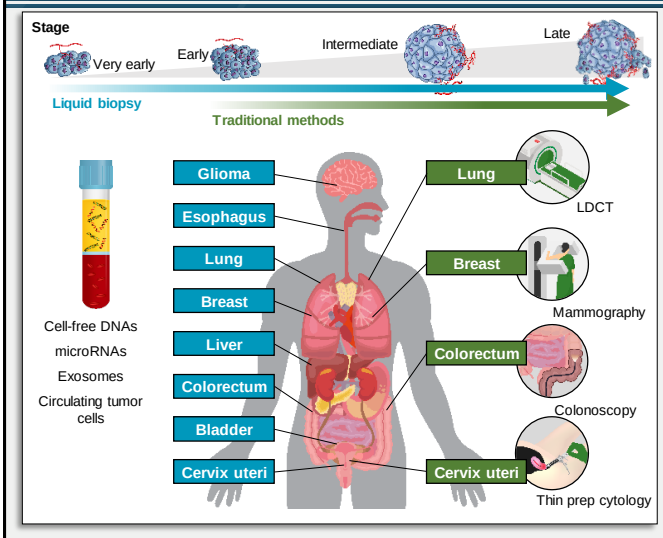
Blood-Based Multicancer Screening Tests for the Early Detection of Cancer

10

Overview of Blood-Based Multicancer Tests



- Minimally invasive with low procedural risk
- Detects cancer cells or genetic material in the blood from primary tumors
  - **Aberrations evident early** during tumorigenesis
  - **Abundant signals** for analysis
  - **Tissue-specific alterations** can help identify TOO
- Does not replace tissue-based diagnosis, but provides sampling for molecular characterization of tumors
- Detects cancers currently without recommended screening

TOO, tissue of origin

Cowling T, Loshak H. An overview of liquid biopsy for screening and early detection of cancer. In: *CADTH Issues in Emerging Health Technologies*; 2016.

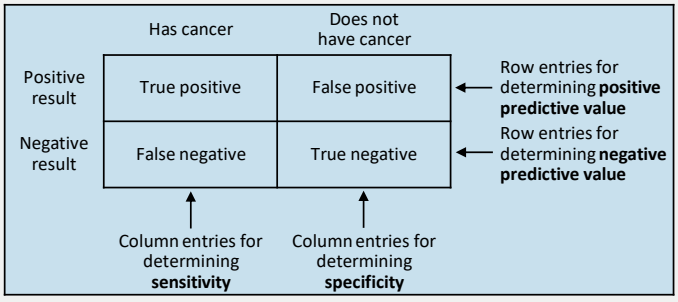
Comparison of Liquid Biopsy vs Traditional Tissue Biopsy

	Liquid Biopsy	Tissue Biopsy
Invasiveness	Minimal	Organ penetration required Repeated surgeries not feasible
Time	Shorter	Longer
Sensitivity	High	Low
Cost of sample isolation	Lower	Higher
Clinically validated	✓?	✓
Enables histological evaluation	×	✓

Lone SN, et al. *Mol Cancer*. 2022;21(1):79.

Evaluating the Utility of MCED Testing: Sensitivity, Specificity, and Positive and Negative Predictive Values

- **Sensitivity** = ability to correctly identify people *with* the disease
- **Specificity** = ability to correctly identify people *without* the disease
- **PPV** = probability of *having cancer* given a positive test
- **NPV** = probability of *not having cancer* given a negative test
- **NNS** = number of individuals needed to screen to detect one true positive



NNS, number needed to screen; NPV, negative predictive value; PPV, positive predictive value.
Trevethan R. *Front Public Health.* 2017;5:307; Barratt A, et al. *J Epidemiol Community Health*. 2002;56(12):899.

Multicancer Screening: The Power of Aggregate Prevalence

Prevalence

Defined as the proportion of the population with a specific trait in a given time period

PPV

Given a positive test, what is the probability of actually having cancer?

- Determined by **specificity** and **prevalence**
- Aggregate prevalence rates of all cancers vs single-organ screening means **a much higher PPV is achievable**

Ahlquist DA. *NPJ Precis Oncol*. 2018;2:23. doi:10.1038/s41698-018-0066-x

Multicancer Screening: The Power of Aggregate Prevalence

NNS

Among GI cancers, only CRC is considered prevalent enough for population screening

- NNS = **167** for **colorectal** cancer
- NNS = **500** for **pancreatic** cancer
- NNS = **1000** for **esophageal** cancer
- NNS for **all GI cancers = 83**
- NNS for **all cancers = 33**

CRC, colorectal cancer; GI, gastrointestinal.

Ahlquist DA. *NPJ Precis Oncol.* 2018;2:23. doi:10.1038/s41698-018-0066-x

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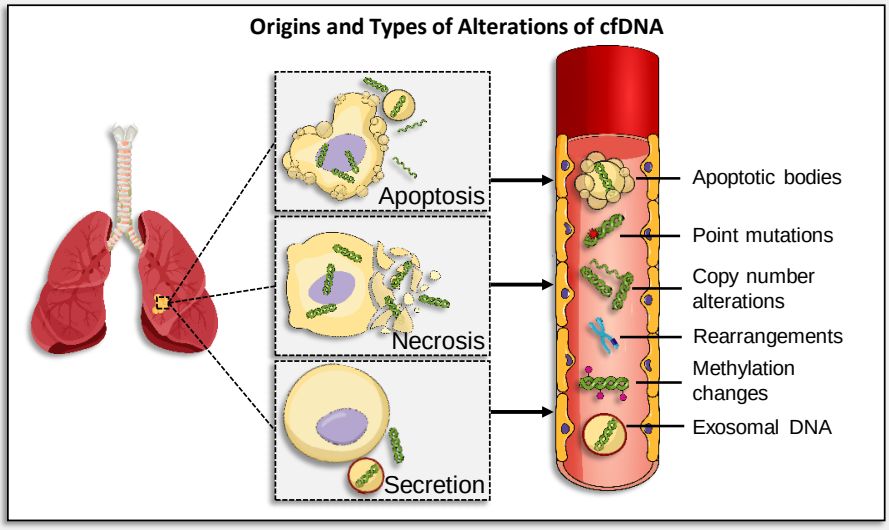
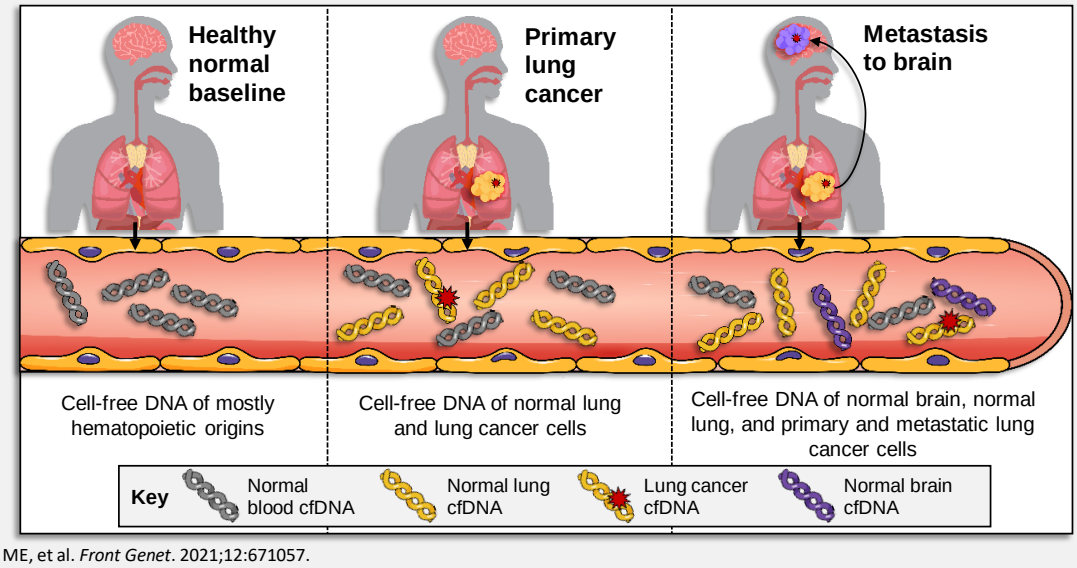
The Science Underlying Cell-Free DNA-Based Multicancer Early Detection Tests

What is Cell-Free DNA?



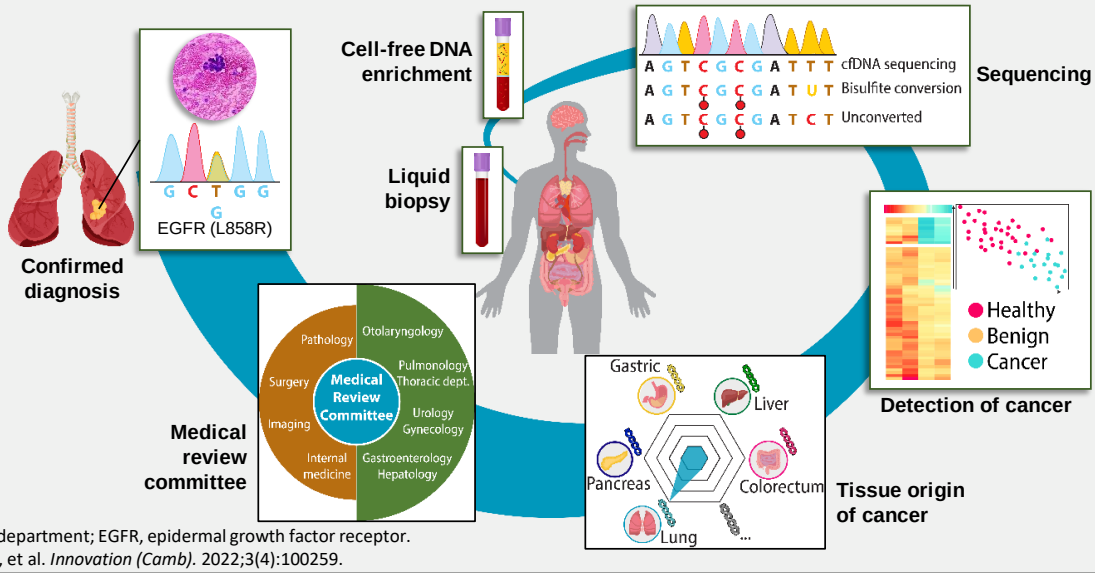
cfDNA, cell-free DNA.
Wan JCM, et al. *Nat Rev Cancer*. 2017;17(4):223-238.

Composition of cfDNA in Patients With Cancer



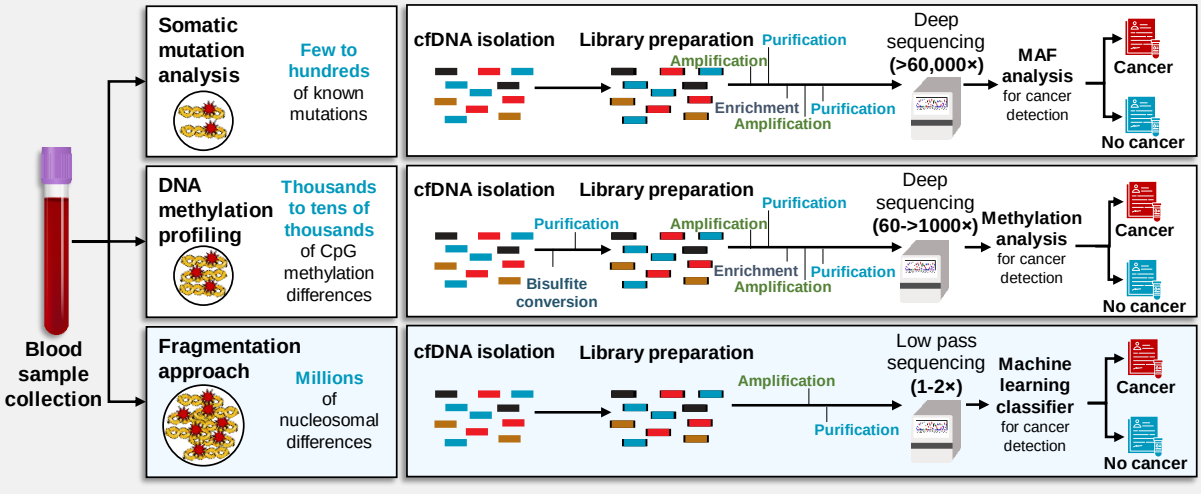
Barefoot ME, et al. *Front Genet*. 2021;12:671057.

Overview of cfDNA-based Testing



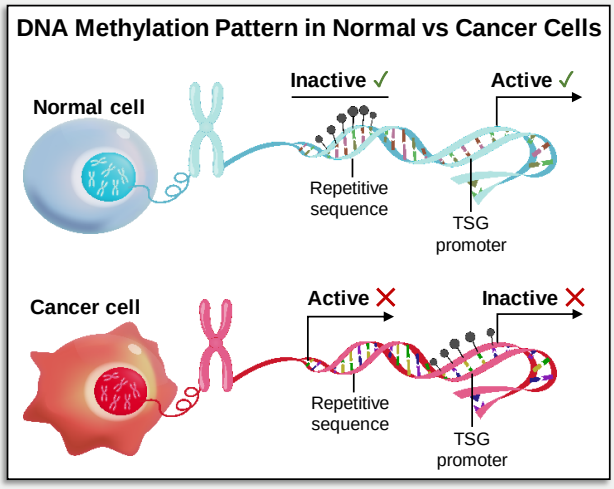
Dept, department; EGFR, epidermal growth factor receptor.
Gao Q, et al. *Innovation (Camb).* 2022;3(4):100259.

Types of cfDNA-based Tests



MAF, mutant allele frequency.
Medina JE, et al. *J Immunother Cancer.* 2023;11(9).

DNA Methylation Profiling in Early Cancer Detection: Rationale for Use



TSG, tumor suppressor genes
Nunes SP, et al. *Cells*. 2020;9(8).

DNA methylation

- In normal cells: most repetitive sequences are methylated whereas TSG promoters are unmethylated and active, leading to active tumor suppression (*green check mark*)
- In cancer cells: repetitive sequences become unmethylated and active (contributing to genomic instability) whereas TSG promoters are methylated and inactive, promoting cell aggressiveness and escape (*red cross mark*)
- Occurs **early** in tumorigenesis and **can be tissue- and cancer-type specific**

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Blood-Based Multicancer Early Detection Testing

Available Options and Clinical Trial Evidence

22

Selected MCED Tests in Development (DNA-methylation Based)

Tumor Types	Sample*	Methods	Main Findings	Test/ Company
>50 cancer types	• 2482 cancer patients • 4207 healthy individuals	Bisulfite sequencing	• Developed a target methylation assay combined with a machine learning classifier for detecting and discrimination TOO in >50 cancer types using cfDNA • 54% sensitivity and 99.3% specificity obtained in the validation set • 93% accuracy for TOO prediction	Galleri® (GRAIL)
	• 2823 cancer patients • 1254 healthy individuals		• Developed a refined assay and classifiers optimized for screening purposes and performed clinical validation • 51% sensitivity and 99.5% specificity were obtained • 88.7% accuracy for TOO prediction • PPV of 44.4% and NPV of 99.4% for cancer detection	
Lung, colorectal, gastric, liver, and esophageal	• 191 prediagnosis cancer samples • 223 postdiagnosis cancer samples • 414 healthy samples	Bisulfite sequencing (using semi-targeted PCR libraries)	• Developed PanSeer, a blood test combining the analysis of 477 cancer-specific differentially methylated regions with machine learning for cancer detection • 87.6% and 94.9% sensitivity for postdiagnosis and prediagnosis samples, respectively; 96.1% specificity obtained in the testing set • Cancer detected by PanSeer up to 4 years before conventional diagnosis with 95.7% sensitivity	PanSeer (Singlera Genomics)

- Numerous MCED tests are currently in development
- Galleri® is currently the only commercially available MCED test. Though not FDA approved, it is available under a CLIA waiver and can be obtained with a prescription**

*Sample from plasma; **CLIA allows use of the test because the testing itself is done in a central laboratory.
CLIA, Clinical Laboratory Improvement Amendments; PCR, polymerase chain reaction.
Brito-Rocha T, et al. *Cells*. 2023;12(6).

INTEGRITY CONTINUING EDUCATION

Selected MCED Tests in Development (Circulating Protein- and cfDNA Mutation-Based)

Tumor Types	Sample*	Methods	Main Findings	Test/ Company
Lung, breast, colorectal, pancreas, gastric, liver, esophageal, and ovarian	• 1005 cancer patients • 812 healthy individuals	Targeted sequencing and bead-based immunoassay	• Developed CancerSEEK, a blood test based on cfDNA mutations on 16 genes and 8 circulating proteins combined with machine learning for cancer detection and TOO discrimination • 62% sensitivity, 99% specificity, and AUC of 0.91 were obtained for discriminating cancer from healthy samples • 63% accuracy for TOO prediction	CancerSEEK (Exact Sciences)
	• 9911 women not previously known to have cancer		• Evaluated feasibility of CancerSEEK testing combined with PET-CT to detect cancer in a prospective cohort • Blood test was positive for 134 participants. • 127 were further evaluated by PET • 64 showed imaging concerning for cancer • 26 were proven to have caner by biopsy or other method • 27.1% sensitivity, 98% specificity, and 19.4% PPV were obtained for blood testing alone • 15.6% sensitivity, 99.6% specificity, and 28.3% PPV were obtained for blood texting combined with PET	

*Sample from plasma.
AUC, area under the curve; PET-CT, positron emission computed tomography.
Brito-Rocha T, et al. *Cells*. 2023;12(6).

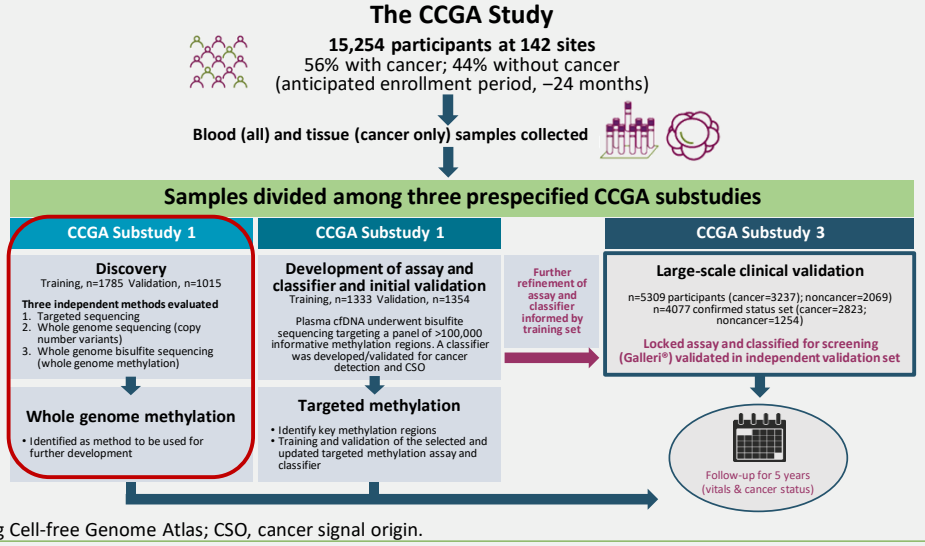
INTEGRITY CONTINUING EDUCATION

Selected MCED Test Clinical Trials

MCED Test	Study	Participants	Study Objective
Galleri®	**CCGA**	15,254 ♂♀	• Demonstrate feasibility of detecting cancer and predicting tissue of origin with minimal false positives
	PATHFINDER	6621 ♂♀	• Evaluate implementation in clinical practice
	STRIVE	99,481 ♀	• Confirm performance in individuals with no known active cancer diagnosis
	SUMMIT	~25,000 ♂♀	• Evaluate performance in individuals with no known active cancer diagnosis and clinical utility in a high-risk population
	PATHFINDER 2	20,000 ♂♀	• Evaluate safety and performance in individuals eligible for guideline-recommended cancer screening
	SYMPLIFY	6238 ♂♀	• Evaluate performance in symptomatic patients referred from primary care
CancerSEEK	**DETECT-A**	10,006 ♀	• Demonstrate feasibility when combined with PET-CT to screen for cancer and guide intervention
PanSeer	**Taizhou Study**	1,379 ♂♀	• Confirm performance in asymptomatic individuals years before conventional diagnosis in a longitudinal study

Blue shading indicates study finding have recently been presented and/or published.

Development and Validation of a cfDNA-Based Assay for Multicancer Detection (The CCGA Study)

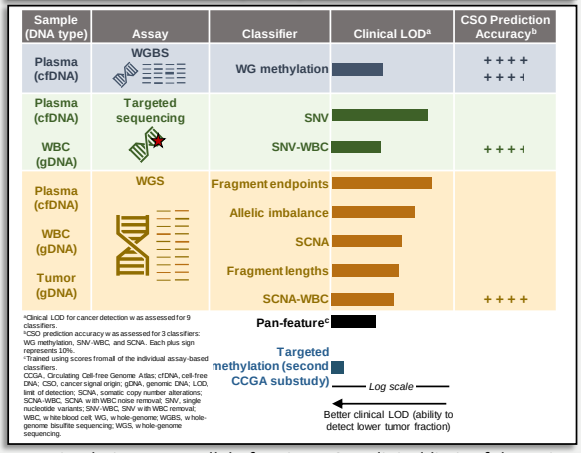


CCGA, Circulating Cell-free Genome Atlas; CSO, cancer signal origin.

Klein EA, et al. *Ann Oncol.* 2021;32(9):1167-1177.

Findings from CCGA Substudy 1

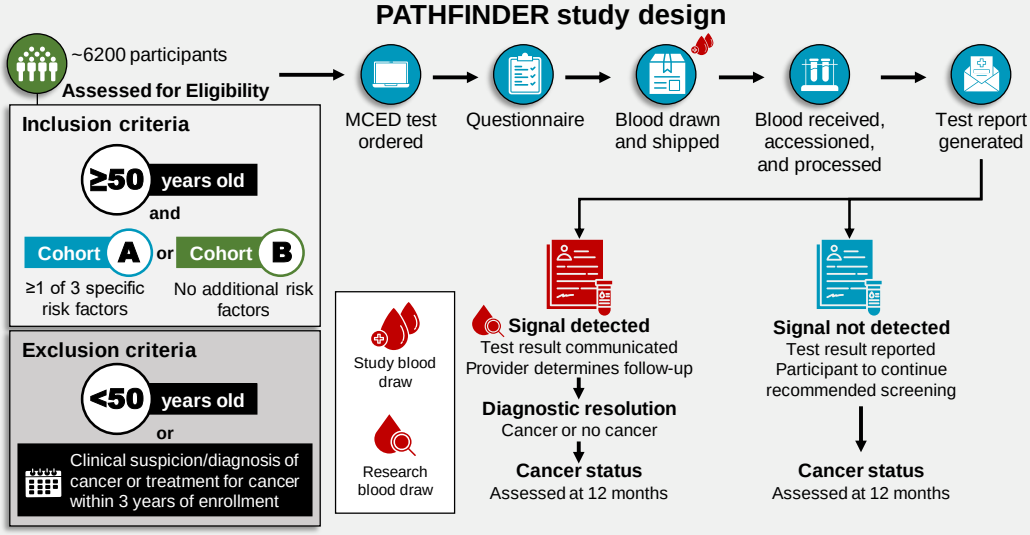
The first CCGA substudy aimed to compare genomic features using cfDNA for the development of a Multicancer Early Detection (MCED) test



- Clinical LOD is a useful benchmark to assess cfDNA-based test performance
- cTAF accounts for cfDNA cancer signal variation across cancer types and stages
- **cfDNA methylation was the most promising genomic feature for cancer signal detection**
- The results informed the development of a cfDNA-based MCED test

cTAF, circulating tumor allele fraction; LOD, clinical limit of detection; MCED, multicancer early detection.
Jamshidi A, et al. *Cancer Cell*. 2022;40(12):1537-1549.e1512.

Evaluation of MCED Testing in a Clinical Setting (PATHFINDER)



Nadauld LD, et al. *Cancers (Basel)*. 2021;13(14).

PATHFINDER Findings: Time to Achieve Diagnostic Resolution

	True Positive n=35	False Positive n=57	Total N=92
Extent of diagnostic testing (Primary)	n=33	n=57	n=90
>1 Imaging test, %	90.9	93.0	92.2
>1 Invasive procedure, %	81.8	29.8	48.9
Time to resolution, median days (IQR)	57 (33, 143)	162 (44, 248)	**79 (37, 219)**

- **Time to achieve diagnostic resolution (confirm presence or absence of cancer): 79 days**
- **Diagnostic resolution achieved within 3 months for 73%**

IQR, interquartile range.

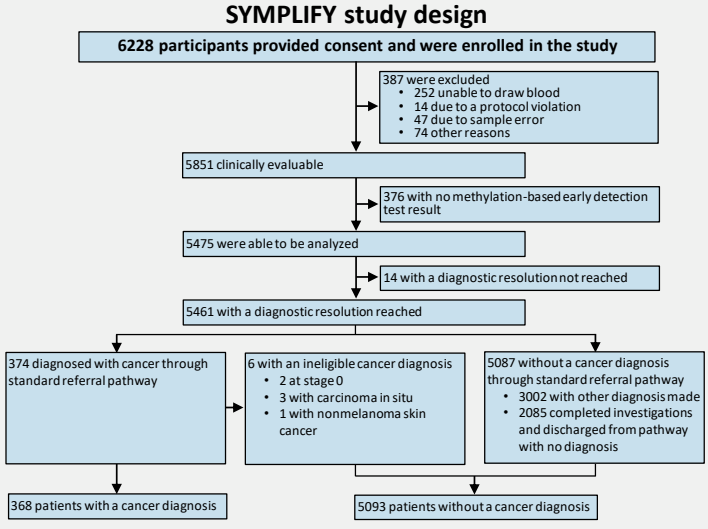
Beer TM, et al. *J Clin Oncol*. 2021;39(15_suppl):3010-3010; GRAIL. GRAIL announces final results from the PATHFINDER study. Available at: https://grail.com/press-releases/grail-announces-final-results-from-the-pathfinder-multi-cancer-early-detection-screening-study-at-esmo-congress-2022/; Schrag D. ESMO 2022; Abstract 903O. *Ann Oncol*. 2022;33(7):S417-S426.

PATHFINDER Findings: MCED Test Findings

Cancer Signal Detection	Specificity and Sensitivity	Identification of TOO	Safety	Psychological Impact of Test
• Signal detected in 92/6621 (1.4%) participants • **71% for cancer types with no routine screening available** • 40% of non-recurrent cancers were Stage I or II	• 44.6% PPV • 98.6% NPV • 99.1% specificity • 189 NNS to detect 1 cancer	• 96.3% accuracy • 13 types of cancer diagnosed	• No study-related serious AEs • No diagnostic workup-related AEs	• 97.1% highly satisfied (92% true positive; 82.3%) false positive) • 83% *Very* or *Extremely Confident* the test is beneficial • 95% *Likely* or *Very Likely* to follow recommended screening

Beer TM, et al. *J Clin Oncol*. 2021;39(15_suppl):3010-3010; GRAIL. GRAIL announces final results from the PATHFINDER study. Available at: https://grail.com/press-releases/grail-announces-final-results-from-the-pathfinder-multi-cancer-early-detection-screening-study-at-esmo-congress-2022/; Schrag D. ESMO 2022; Abstract 903O. *Ann Oncol*. 2022;33(7):S417-S426.

MCED Testing of Symptomatic Patients Referred From Primary Care (SYMPLIFY)



Nicholson BD, et al. *Lancet Oncology*. 2023;24(7):733-743.

SYMPLIFY Findings

Cancer Signal Detection	Specificity and Sensitivity	Identification of TOO
• Signal detected in 323 participants	• 75.5% PPV • 97.6% NPV • 66.3% sensitivity • 98.4% specificity	• 85.2% accuracy

Nicholson BD, et al. *Lancet Oncol*. 2023;24(7):733-743.

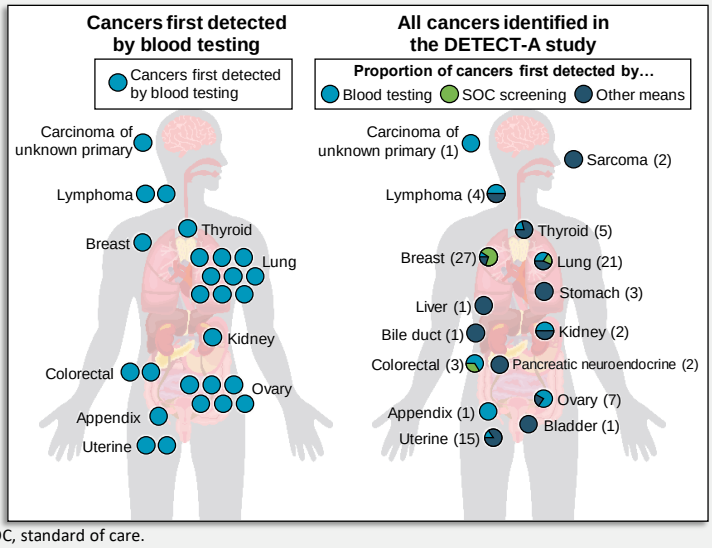
Sensitivity of MCED-Detected Cancer Signal, by Stage and Site

	Total Cancers (n=368)	Cancer Signal Detected (n=244)	Sensitivity (95% CI)
Overall	—	—	66.3% (61.2–71.1)
Cancer stage			
I	95	23	24.2% (16.0–34.1)
II	63	36	57.1% (44.0–69.5)
III	108	92	85.2% (77.1–91.3)
IV	86	82	95.3% (88.5–98.7)
Uncertain	16	11	68.6% (41.3–89.0)
Cancer stage group			
I–II	158	59	37.3% (29.8–45.4)
I–III	266	151	56.8% (50.6–62.8)
I–IV	352	233	66.2% (61.0–71.1)
II–IV	257	210	81.7% (76.4–86.2)
III–IV	194	174	89.7% (84.5–93.6)
Cancer site			
Colorectal	137	97	70.8% (62.4–78.3)
Lung	81	55	67.9% (56.6–77.8)
Lymphoma	14	8	57.1% (28.9–82.3)
Oesophagogastric	22	21	95.5% (77.2–99.9)
Other*	47	30	63.8% (48.5–77.3)
Ovarian	14	9	64.3% (35.1–87.2)
Pancreas	12	11	91.7% (61.5–99.8)
Prostate	11	1	9.1% (0.2–41.3)
Uterus	30	12	40.0% (22.7–59.4)

*Other includes the following cancer site categories: breast (7 cases), mesothelioma (6 cases), anus (5 cases), kidney (5 cases), liver and bile duct (4 cases), cervix (4 cases), cancer of unknown primary (3 cases), urothelial (3 cases), vaginal (2 cases), bladder (2 cases), and one instance each of bone and soft tissue, central nervous system, gallbladder, head and neck, malignant immunoproliferative disease, and thyroid.

Nicholson BD, et al. *Lancet Oncol*. 2023;24(7):733-743.

DETECT-A: MCED Testing Combined With PET-CT to Screen for Cancer and Guide Intervention



- CancerSEEK MCED test used to screen 9,911 women without history of cancer
- MCED coupled with diagnostic PET-CT identified cancers including those not detected by SOC screening, the majority of which were localized or regional
- Additional biomarkers, new analytic methods, and algorithms currently being incorporated in the development of the next generation of the test

SOC, standard of care.

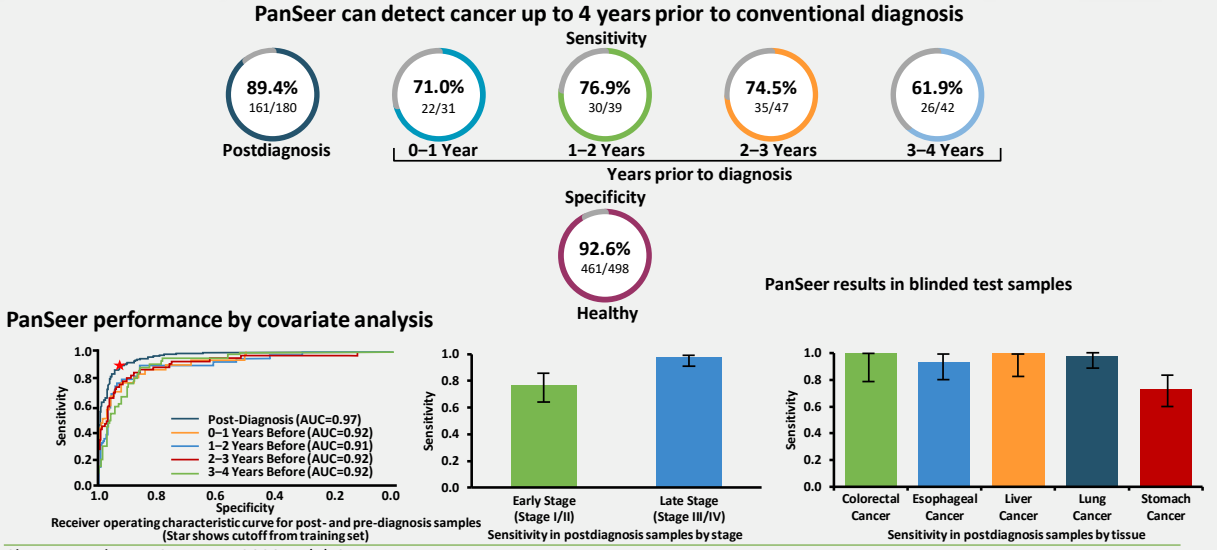
Lennon AM, et al. *Science*. 2020;369(6499):eabb9601.

DETECT-A (Observational Follow-Up Study)

- **Study objective:**
  - Evaluation of clinical outcomes in patients diagnosed with cancers as a result of abnormal MCED results
- **Median follow-up:**
  - 4.4 (IQR: 4.1-4.6) years from initial MCED test
- **Outcomes:**
  - MCED testing detected cancers earlier in patients who, when treated subsequently with conventional methods, achieved long-term survival
  - Half of all patients with an MCED-detected cancer remained cancer-free after treatment >4 years (median) after initial MCED test

Buchanan AH, et al. *J Clin Onc*. 2023;41(16_suppl):3037-3037.

Detection of Cancer Four Years Before Conventional Diagnosis Using an MCED Test



Chen X, et al. *Nat Commun*. 2020;11(1):3475.

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Overcoming Barriers to Cancer Screening

CDC-Recommended Evidence-Based Interventions to Improve Cancer Screening

Patient-Oriented Interventions

Patient reminders

- Schedule screenings by contacting patients or during visits
- Send appointment & test reminders
- Provide support to help overcome barriers & prepare for tests (eg, colonoscopies)

Structural barrier reduction

- Reduce paperwork
- Help with scheduling
- Offer screening at more locations
- Expand clinic & screening hours
- Provide transportation
- Provide translation services
- Provide child care

Other interventions

- Use small media (eg, videos, brochures, or newsletters) & 1-on-1 or group education to motivate screening
- Use vouchers, reimbursement, or reduced copays to remove economic barriers

Provider-Oriented Interventions

Provider reminders

- Use stickers/ notations on medical charts or program EHRs to send alerts to providers
- List patients who are due for cancer screening daily

Provider assessment and feedback

- Track screening for clinics & individual providers
- Review clinic policies & practices
- Tell providers how many of their patients get screened & receive follow-up care

CDC. Evidence-based interventions. Available at: https://www.cdc.gov/cancer/community-resources/interventions/index.htm

Case Patient Description

- Jonathan is a 52-year-old Black man with a family history of prostate cancer who presents for routine primary care visit. He has recently come across information about MCED tests and requests further information. Specifically, he would like to know if it might be a good option for him.

? Audience Question

What type of education is needed to help guide his evaluation of this testing option?

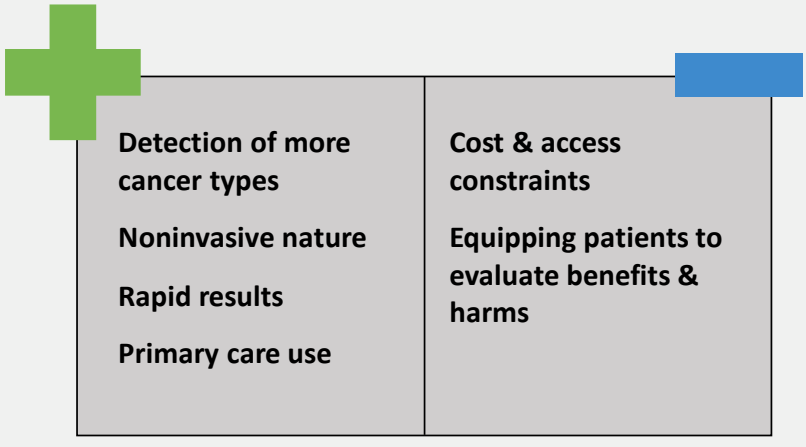
A. Implications of test results (positive or negative)
B. Information on the likelihood of getting a false positive or a false negative (test sensitivity and specificity)
C. Rationale for how the test works

? Audience Question

Which of the following most strongly influences whether or not you would offer testing to a patient like Jonathan?

A. A family history of cancer
B. Patient has a history of cancer
C. Whether the patient is up to date on screening
D. Patient ability to pay for the test

Potential Challenges and Benefits of MCED Testing



Best Practices for MCED Implementation: Effective Discussions With Patients

Eligible populations for existing tests

- Patients age 50 years and older at elevated cancer risk
- Not recommended for individuals who are pregnant, aged 21 years or younger, or undergoing active cancer treatment
- Importance of interpretation of results as 1 tool in a set of therapeutic screening options
- Important and continuing role of other tests (eg, mammography, colonoscopy, PSA screening, cervical cancer screening)

Gelhorn H, et al. *Patient*. 2023;16(1):43-56; Hackshaw A, et al. *Cancer Cell*. 2022;40(2):109-113.

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Promoting Effective Shared Decision-Making: What Patients Need to Know About MCED

Summary of questions from cancer patient advisory board when asked: "What would patients need to know before considering MCED?"	
Acceptance	• How accurate is the test • What kinds of cancer can and cannot be detected? Can it detect rare cancers? • What kinds of regulations and approvals has the screening test gone through? • Is this test effective for those in remission? • Can it detect precancerous cells? • Can it detect the difference between precancerous and cancerous cells? • Could it detect multiple diagnoses with 1 test? • What kinds of information and support are available with a positive screening result? • What are the side effects of the screening test, if any? • Could this kind of screening be sensitive enough for aggressive forms of cancer in which the results may change within weeks?
Access	• Where would I get this test? My primary care physician's office? • Who can get it (everyone in the community or only certain subsets of based on cancer risk, history, age, etc)? • Would this be available to those older than 70 years? • Do people need to have symptoms or a family history of cancer? • How often can someone use the screening?
Affordability	• Will insurance cover the cost of screening? • What would it cost me?
Accountability	• Who has access to the screening results? What does the pharma company do with our data? • How might the results relate to results of genetic testing for hereditary cancer?

Schear RM, et al. *Cancer*. 2022;128(S4):909-917.

Current Commercially Available MCED Test (Not Yet FDA Approved)

To order the test:

- List Price: $949 (may vary depending on practice/provider)
- Visit www.galleri.com/hcp.order
- Complete a blood draw per test instructions
- Receive results through provider portal, typically within 10 days of reception of blood specimen
- Results:
  - Result 1: Cancer signal NOT detected
  - Result 2: Cancer signal detected, with signal origin. Confirm with diagnostic testing

Case Patient Description

- Marlena is a 58-year-old White woman with a family history of ovarian cancer. She has recently undergone MCED testing. The results indicate a positive signal for cancer and cfDNA fragmentation patterns suggest a pancreatic TOO

? Audience Question

What is your next step once Marlena's test results have been received?

A. Explain the meaning of cancer signal detection
B. Order a blood work-up
C. Order a biopsy
D. Repeat the MCED test to ensure results

? Audience Question

What additional testing is needed to diagnose Marlena?

A. Blood tests
B. Imaging studies
C. Tissue biopsy
D. All of the above

? Audience Question

How would you sequence Marlena's follow-up evaluation referrals?

A. Blood work, imaging, biopsy
B. Imaging, blood work, biopsy
C. Biopsy, imaging, blood work

Discussing MCED Testing Results With Patients

- Explain the meaning of signal detection and the potential for false-positive or false-negative results
  - Psychosocial impact of screening is relatively low overall and short-lived, even with false-positive results
  - Those at high cancer risk tend to experience more symptoms of anxiety
- Discuss more intensive screening (eg, PET-CT) for patients with a positive signal

Kim A, et al. *BMC Cancer*. 2022;22(1):223.

? Audience Question

What is the most challenging aspect of supporting a patient after a positive screening test result?

A. Ensuring they follow up with diagnostic referrals
B. Helping them navigate cost barriers to obtaining appropriate diagnosis
C. Helping them manage the long-term negative psychological impact

Barriers to Seeking Further Detection and Testing After a Positive Screening Test Result

Table 1. Common Barriers to Seeking Further Detection and Testing After a Positive Cancer Screening Test Result[a,b]

Psychological Barriers	Access Barriers
• In shock/don't believe results/no symptoms • Don't know or understand next steps or where to go • Fear • Don't believe traditional treatment like chemotherapy are safe • Don't understand how serious this may be	• Medical centers are far away • Need practical support like transportation or child care • Can't take off time from work • Don't have a loved one to serve as a caregiver • Cost

[a]From a discussion with Livestrong cancer Institutes' Community Cancer Advisory Board on Multicenter Early Detection. Monthly Online Meeting; August 13, 2020 (facilitated and recorded on Zoom).
[b]See Fiscella K, Humiston S, Hendren S, et al. Eliminating disparities in cancer screening and follow-up of abnormal results: what will it take? *J Health Care Poor Underserved.* 2011;22:83-100. doi: 10.1353/hpu.2011.0023[37] Schear RM, et al. *Cancer*. 2022;128(S4):909-917.

Key Points

- Early diagnosis is crucial for achieving improved treatment outcomes and survival in patients with cancer
- Blood-based biopsies can promote earlier diagnosis by enabling simultaneous detection of biomarkers of multiple cancers early on, as well as information on cancer type and tissue of origin
- Multiple MCED tests have been/are being developed and have shown promise in clinical trial investigations
- Although no MCED tests are currently FDA approved, one test has recently been made available via CLIA approval
- MCED tests have the potential for routine application in primary care and may help reduce barriers to effective population-scale cancer screening

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Thank You!