



MCED: The Future of Cancer Screening

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Disclosures

Consulting and Speakers Bureaus	AstraZeneca, Merck, BMS, Astellas, Eisai, Janssen, SeaGen, Exelixis, EMD Serano, Daiichi Sankyo, Pfizer, Novartis
Scientific Advisory Board	Tempus



Clinical Case

- 70 yo asymptomatic, healthy male underwent MCED testing as part of a clinical trial
- Two weeks later, a positive result was reported with a CSO suggesting a primary kidney cancer
- A CT CAP done the next day revealed a 5.1 x 3.8 by 3.8 cm heterogeneous mass arising from inferior right renal cortex
- Pt was referred to urologic oncology and two weeks underwent a partial nephrectomy
- Path revealed a 5 cm chromophobe renal cell carcinoma with tumor extension into the perinephric adipose tissue, lymphovascular invasion was present, although margins were negative.
- Pt has been on post-op surveillance for over a year with NED

Why MCED? Why Now?

1. Unmet need

Current guideline screening leaves many lethal cancers outside the ropes.

2. Test performance

High specificity and high PPV matter when screening asymptomatic adults.

3. Workup efficiency

CSO prediction gives clinicians a map instead of a mystery.

4. Outcomes signal

Prospective and randomized data show more screen detection and less stage IV disease.

5. Real-world feasibility

>100,000 commercial tests support clinical implementation in diverse settings.

6. Evidence still maturing

Despite uncertainty, a technology can be worth fighting for.

The Screening Gap is Real

14%

Cancer detected by
guideline-
recommended
screening

~83%

U.S. cancer deaths from
cancers detected outside
recommended screening
strategies

50+

Cancer types
screened by Galleri

1 blood draw

A pragmatic doorway
into multi-cancer
signal detection

The opportunity is not “replace colonoscopy or mammography.”
The opportunity is “find lethal cancers that currently enter the ring only after symptoms”

Round 2: The biology is elegant enough to be clinically useful

Targeted methylation of cfDNA plus cancer signal origin

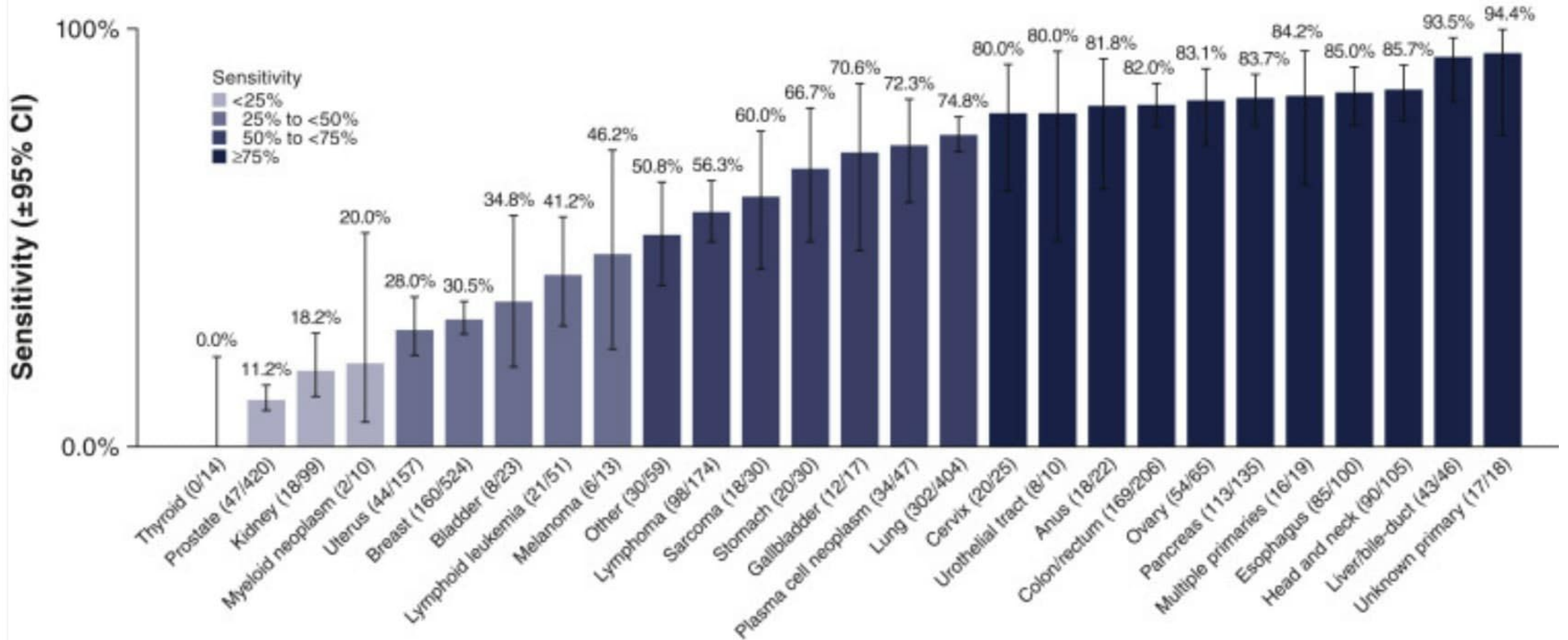
Galleri looks for cancer-associated methylation patterns in cfDNA, then predicts where the signal likely comes from



CSO turns “positive blood test” into a focused diagnostic pathway

Sensitivity by Tumor Type

B



Evidence ladder: Grail Galleri, Not Just One Punch

Analytical validity, clinical validation, interventional performance, randomized utility, real-world experience

CCGA clinical validation

Specificity 99.5%; sensitivity rises with stage; CSO accuracy 88.7%

Ann Oncol 2021

Analytical validation

Targeted methylation assay robust across input, reproducibility and interferents

PLOS ONE 2023

PATHFINDER study

First prospective implementation returning results to participants and clinicians

Lancet 2023

PATHFINDER 2

35,878 pt registrational study; 6.5x increased detection with SOC screening

Nature Medicine 2026

NHS-Galleri RCT

142,250 participants; stage IV reductions in rounds 2 and 3

ASCO 2026

Real-world data

111,080 tests; outcomes across 32 cancer types; 87% CSO match

Nat Commun 2025

REACH / Vanguard

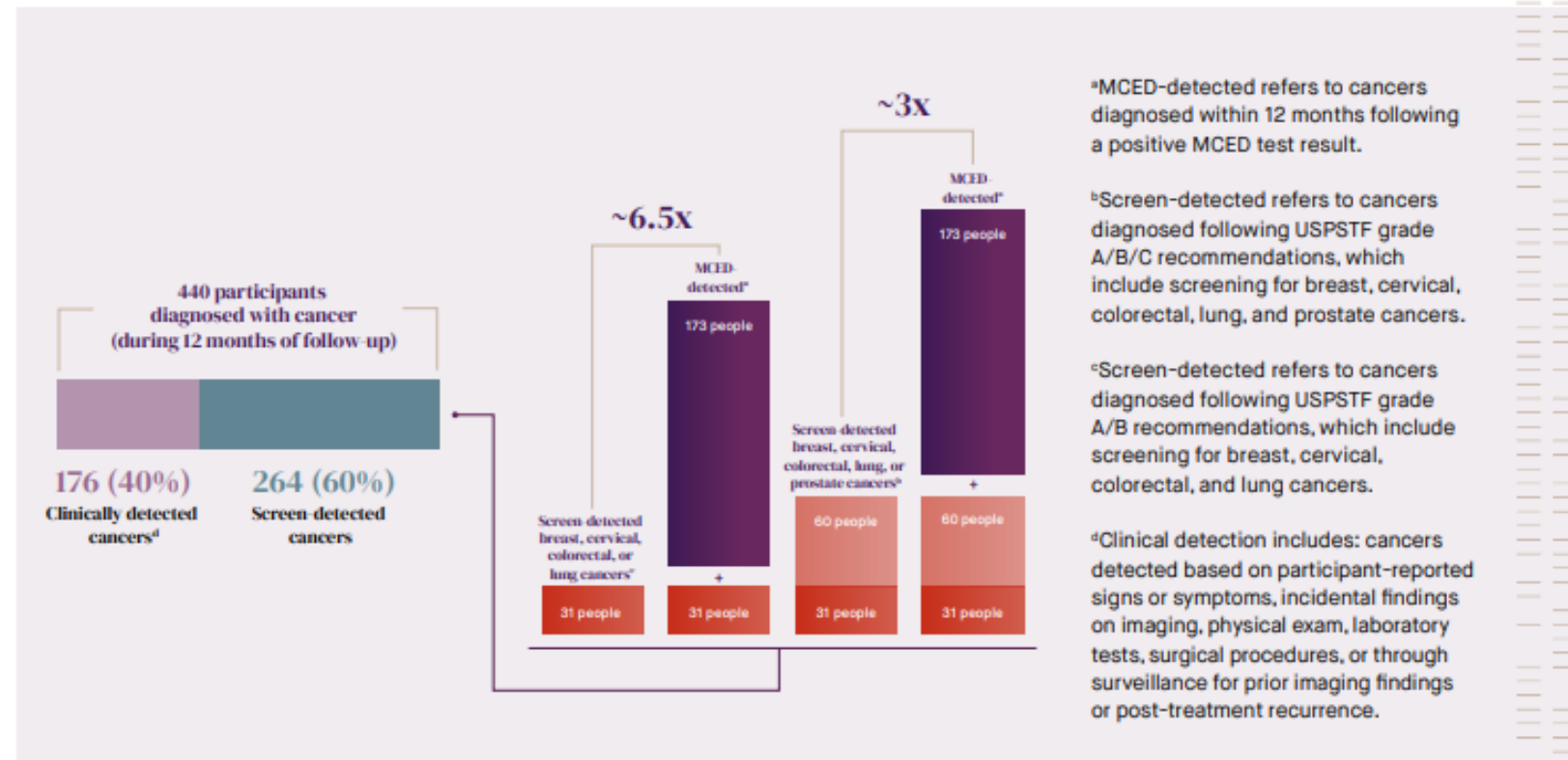
Medicare impact and NCI randomized feasibility infrastructure

ClinicalTrials.gov

Primary Results from PATHFINDER 2 Study¹

The Galleri test **increased the number of cancers detected more than six and a half-fold** when added to USPSTF A and B guideline-recommended screening tests for breast, cervical, colorectal, and lung cancer.

Galleri **nearly tripled the number of cancers detected** when added to USPSTF A, B, and C guideline-recommended screening tests, which include prostate cancer, in addition to breast, cervical, colorectal, and lung screening.



Pathfinder2

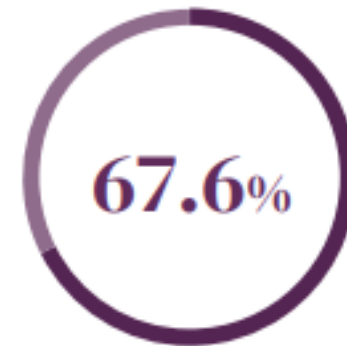
Galleri detected most cancers at an early stage, when they can be easier to treat and are potentially curable.¹



of the new primary cancers diagnosed were Stage I and II.



of the new primary cancers diagnosed were Stage I-III.



of cancers detected were types without USPSTF grade A/B/C screening recommendations.^{1,†}

Pathfinder2

- PPV was 60.3% compared to 3-10% for routine mammograms
- Cancer detection rate was 0.54% compared to 0.5 – 2% for screening colonoscopy
- Specificity was 99.6%, reflecting a false positive rate of less than 0.4%

Performance and safety of a multi-cancer early detection test: the PATHFINDER 2 study

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 Check for updates

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Early cancer detection improves survival; however, most cancer types do not have guideline-recommended screening. We previously reported the first PATHFINDER study that established feasibility of cancer screening with a blood-based multi-cancer early detection (MCED) test that predicts cancer signal origin (CSO) to guide diagnostic workup. The prospective, interventional PATHFINDER 2 study expands clinical evidence for the MCED test by evaluating co-primary endpoints of MCED performance metrics and safety in participants aged 50 years or older without clinical suspicion of cancer. Performance measures included cancer detection rate, positive and negative predictive values, episode sensitivity, specificity and CSO prediction accuracy. Safety was evaluated in terms of number and type of invasive procedures performed and adverse events due to diagnostic testing, after 12 months of follow-up. Endpoints were analyzed descriptively; no hypothesis testing was performed. Between December 2021 and July 2024, 35,878 participants were enrolled. Among 32,007 performance-analyzable participants, cancer detection rate was 0.54% (95% confidence interval (CI): 0.47–0.63%), positive predictive value was 60.3% (95% CI: 54.5–65.8%), negative predictive value was 99.2% (95% CI: 99.1–99.3%) and specificity was 99.64% (95% CI: 99.57–99.70%). Episode sensitivity was 39.3% (95% CI: 34.9–44.0%; all cancers) and 69.8% (95% CI: 62.8–76.0%; prespecified 12-cancer subgroup). Positive and negative likelihood ratios were 108.9 (95% CI: 87.6–135.2) and 0.61 (95% CI: 0.56–0.66), respectively, and the number needed to screen to detect one cancer was 185 (95% CI: 159–215). CSO prediction accuracy was 91.3%. Among 35,335 safety-analyzable participants, 213 (0.6%) had invasive procedure(s) after a positive MCED test; 90.5% were nonsurgical. No serious study-related adverse events were reported by the time of this analysis. These results provide insights into performance and safety of the MCED test in an intended-use population. Randomized trials and longer follow-up are needed to assess the clinical utility of MCED tests. ClinicalTrials.gov identifier: [NCT05155605](https://clinicaltrials.gov/ct2/show/study/NCT05155605).

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UK NHS Galleri Trial

- World's first population-scale randomized controlled trial of an MCED test
- Enrolled over 140,000 asymptomatic participants aged 50 - 77 in England.
- The primary endpoint of statistically significant reduction in combined Stage III/IV diagnoses was not officially met within the initial follow-up window.



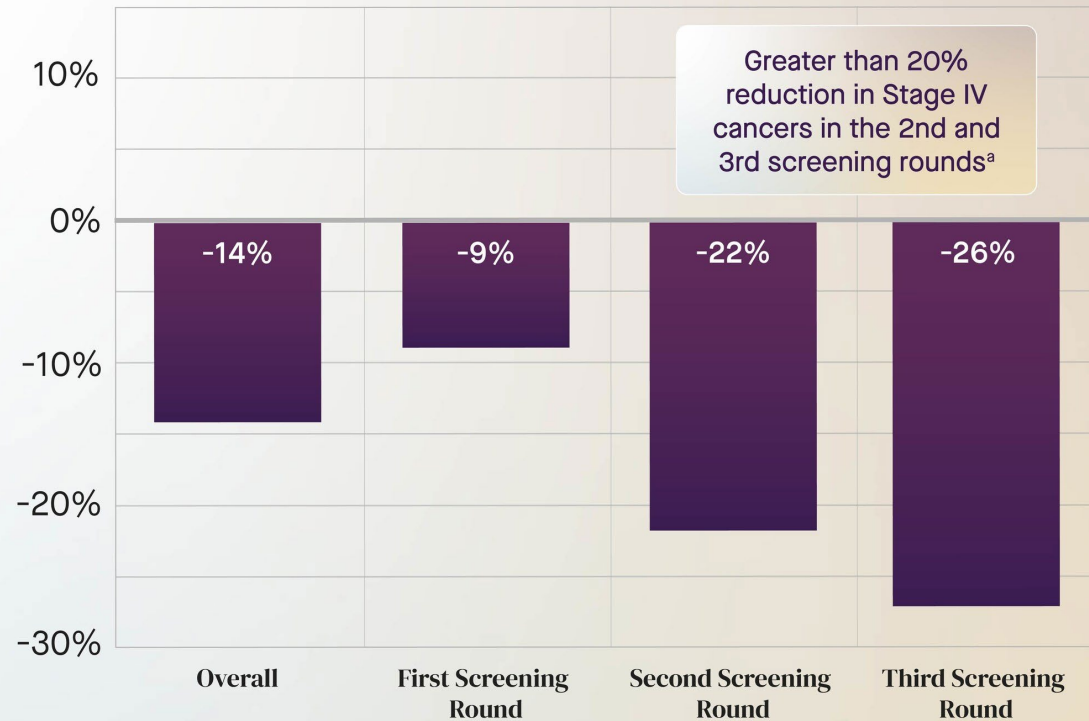
UK NHS Galleri Trial

Quadrupled the number of overall screen-detected cancers

Stage IV cancer diagnoses dropped noticeably over time, and emergency room presentations for cancer fell by 21%

Showed high specificity (99.55%) with a favorable safety profile and no serious related adverse events.

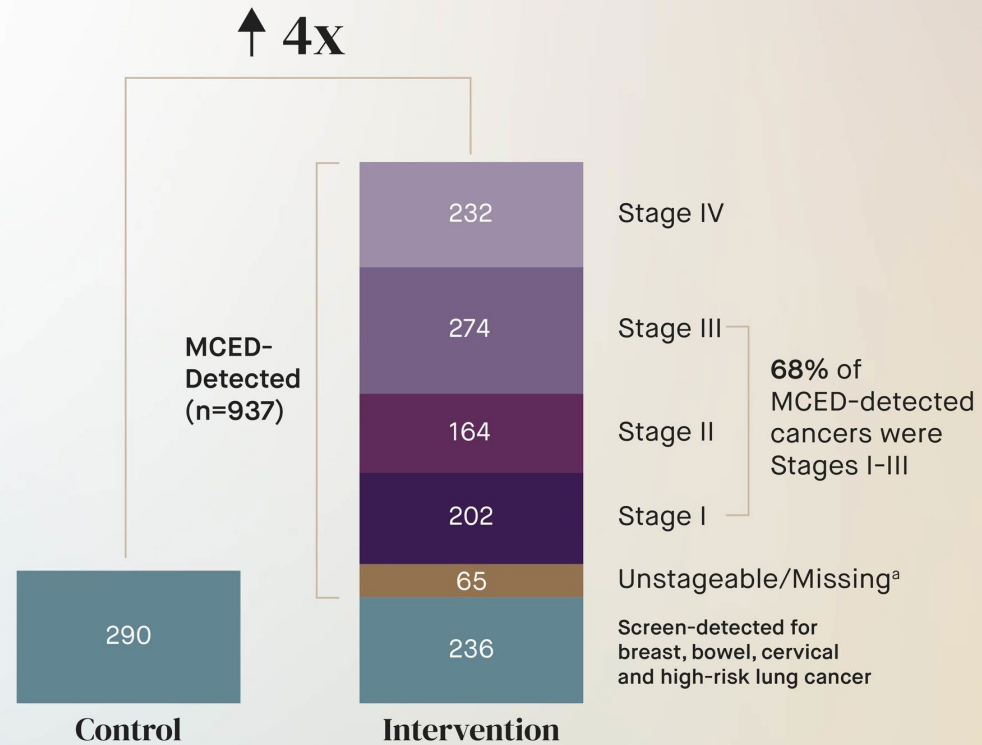
Percent Difference in Stage IV Cancers*



* Assessed in 12 prespecified cancer types: anus, bladder, colorectal, esophagus, head and neck, liver/bile duct, lung, lymphoma, myeloma/plasma cell neoplasm, ovary, pancreas, stomach.

^a A statistically significant reduction was not observed in combined stage III/IV diagnoses across three screening rounds for the 12 prespecified cancers.

Screen Detected Cancers



^aIncludes 10 unstageable cancers (no staging system exists) and 55 cancers with missing staging information



Real-world data and clinical experience from over 100,000 multi-cancer early detection tests

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Blood-based multi-cancer early detection (MCED) has the potential to simultaneously screen for multiple deadly cancers with high positive predictive value. To assess real-world performance, we evaluated the Galleri® MCED test (GRAIL, Inc.) across 111,080 individuals (median age 58 years, 55.5% males). This MCED test analyzes methylation patterns of cell-free DNA to detect presence of a cancer signal and predict the anatomical cancer signal origin (CSO) to facilitate diagnostic evaluation. Cancer signal detection rate was 0.91% (1011/111,080), consistent with clinical studies and independent modeled values. Providers reported clinical outcome for 459 of 1011 individuals with cancer signal detected MCED tests. Of these, 258 had an invasive cancer diagnosis, spanning 32 cancer types. The MCED test correctly predicted the CSO in 87% of cases with a reported cancer type, consistent with previous clinical studies. CSO enabled efficient workup in most patients, with a median 39.5 days from result receipt to cancer diagnosis.

Matrana, et al. Nature Comm



Broad Scale: We analyzed data from **111,080 tests** from by over 8,100 providers across the United States.



Cancer Detection Rate: The test achieved a **0.91% cancer detection rate** in the real-world clinical setting.



High Accuracy: It showed an **87% accuracy rate** in predicting the specific origin of the cancer signal

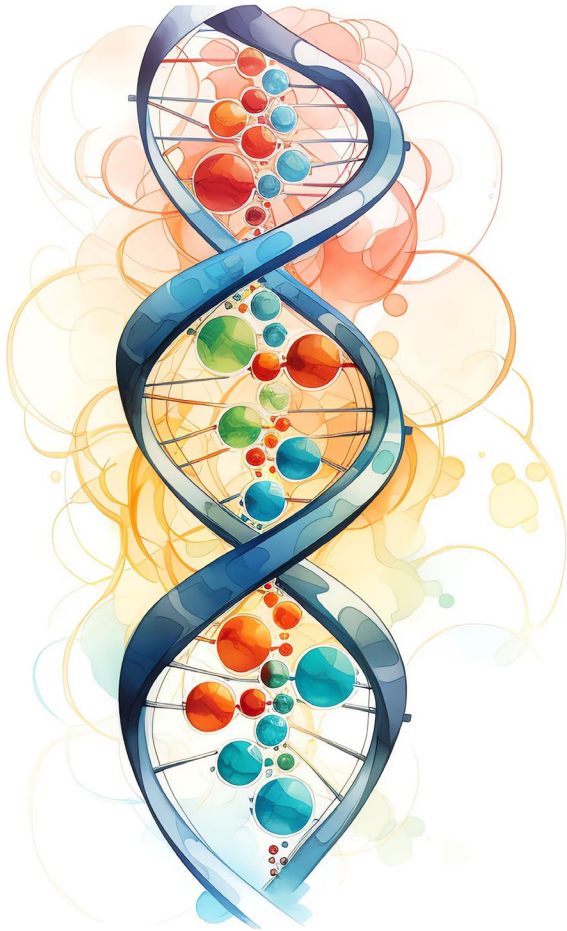


Screening Gaps: Out of the patients diagnosed with invasive cancer following a positive signal, **74% had cancers that lacked standard, recommended screening guidelines** (such as pancreatic or kidney cancers).



Diagnostic Efficiency: Median time from a positive test result to final confirmed cancer diagnosis was **39.5 days**

Summary – Data is Still Maturing



- **Galleri - one blood draw screens for 50+ cancers**
- **Detects cancers that have no recommended screening tests**
- **Very high specificity (~99.5%), limiting false positives.**
- **Accurate cancer signal origin (CSO) prediction to direct workup**
- **Feasible, efficient diagnostic resolution demonstrated prospectively in Pathfinder studies**
 - Real-world data across >111,000 tests showed a cancer signal detection rate of ~0.91% (similar to colonoscopy)
- **Modeled potential for stage shift and mortality reduction.**
 - Natural-history/interception modeling using UK incidence data estimated that MCED screening of adults aged 50–79 could meaningfully reduce late-stage diagnoses and cancer deaths (e.g., **~17% fewer cancer deaths per year** in one conservative scenario)
- **Modeled time analyses support annual screening.**

What's Next?

- Nancy Gardner Sewell MCED Screening Coverage Act signed into law
- Pathfinder2 and NHS data still maturing
- REACH study still enrolling
- Galleri is currently undergoing FDA review – AdCom vote was FAVORABLE
- Grail dropped price of Galleri to \$599
- New MCED tests are emerging very quickly
 - Caris Detect MCED launched July 2026 (\$3,000)
 - Freenome SimpleScreen for CRC launched July 2026
 - Guardant Shield (CRC only) – FDA approved, doesn't meet HEDIS metrics
 - Exact Cancer Guard >50 cancers multi-marker MCED
- Need to define who to test and when (High risk syndromes? Familial? Environmental exposures/high risk occupations? Everybody?) -- AI tools are in development

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