Multi-Cancer Early Detection (MCED) Blood Tests

How MCED Tests Work

- MCED tests analyze cell-free DNA (cfDNA) that tumors shed into the bloodstream. Cancerguard and Galleri look primarily for cancer-associated methylation patterns (Cancerguard also measures tumor-associated protein levels). Caris Detect uses whole-genome and whole-transcriptome sequencing (DNA and RNA) with artificial intelligence.
- They screen for signals from many cancer types at once (> 50 for Cancerguard and Galleri), including cancers with no recommended screening test (e.g., pancreatic, ovarian, liver).
- Three tests are available in the U.S.: Cancerguard (Exact Sciences), Galleri (GRAIL), and Caris Detect (Caris Life Sciences). All are laboratory-developed tests (LDTs) that are not FDA cleared or approved. Cancerguard and Galleri are prescription-only; Caris Detect can also be ordered online through Everlywell. GRAIL has submitted a PMA for Galleri; an FDA advisory panel voted in its favor in September 2026, and a final decision is pending.
- MCED tests supplement, not replace, guideline-recommended screening. Sensitivity is low for early-stage cancers and for cancers with established screening (e.g., breast and prostate).
- Intended use: Cancerguard - adults 50 - 84 years. Galleri - adults with elevated cancer risk (e.g., ≥ 50 years); not for people who are pregnant, ≤ 21 years, or in active cancer treatment. Caris Detect - adults ≥ 21 years; not for people who are pregnant, in active cancer treatment or < 3 years after treatment, or transplant recipients.

How results are reported

- **Cancerguard:** qualitative positive or negative cancer signal; individual biomarker levels are not disclosed.
- **Galleri:** "Cancer Signal Detected" or "No Cancer Signal Detected." A positive result includes a predicted cancer signal origin (CSO), chosen from 18 tissue/organ types, to direct the workup.
- **Caris Detect:** "Cancer Signal Detected" (with likely tissue of origin ranked across 15 organ systems), "Atypical Signal Detected" (free repeat test in about 3 months), or "No Cancer Signal Detected."
- A negative result does not rule out cancer; continue guideline-recommended screening.

Follow-up of a Positive Test

Cancerguard (standardized pathway)

- CT of the neck, chest, abdomen, and pelvis with iodinated IV contrast.
- If CT is negative or indeterminate, proceed to whole-body FDG PET-CT.
- Exact Sciences offers an imaging reimbursement program for eligible patients.

Galleri (CSO-guided)

- Confirmatory workup (imaging, labs, endoscopy, or biopsy) directed by the predicted CSO; GRAIL does not specify a standard imaging pathway.
- PATHFINDER 2 approach: evaluate the 1st CSO, then the 2nd CSO, then PET/CT if the targeted evaluation is negative (11.1% of these PET/CT-only workups found cancer).

Caris Detect (ranked tissue of origin)

- Single anatomically focused scan of the top-ranked site.
- If inconclusive, targeted scan of the next-ranked site or CT covering multiple candidate sites.
- Imaging reimbursement program (application required).

NHS-Galleri Trial (NEJM 2026)

- Design: Randomized trial of 142,250 adults aged 50 - 77 years in England comparing Galleri plus usual care vs usual care alone over 3 annual screening rounds (funded by GRAIL).
- Primary outcome: Galleri screening did not reduce stage III or IV cancer across 12 prespecified cancers (IRR 1.03; 95% CI 0.92 - 1.14; p=0.63).
- Stage IV (key secondary): IRR 0.86 (95% CI 0.74 - 1.00). In supplementary analyses, the reduction emerged by round 3 (IRR 0.74), and more total cancers were diagnosed in the screening group (3,431 vs 3,177), so overdiagnosis cannot be excluded.
- Only about one-third of cancers (32.3%) in the screening group were found through screening; the rest were diagnosed clinically. Cancer mortality results are expected 3 and 6 years after the last study visit.

Bottom line: No trial has shown that MCED screening reduces cancer mortality.

MCED Blood Tests: Accuracy and Cost Comparison

Feature	Cancerguard (Exact Sciences)	Galleri (GRAIL)	Caris Detect (Caris Life Sciences)
Test basics			
Technology	cfDNA methylation + tumor-associated protein levels	cfDNA methylation (hundreds of thousands of sites)	Whole-genome and whole-transcriptome sequencing (DNA and RNA) with artificial intelligence
Cancers targeted	> 50 cancer types and subtypes (not intended for breast or prostate cancer screening)	> 50 cancer types	Not reported
Intended population	Adults 50 - 84 years	Adults with elevated cancer risk (e.g., ≥ 50 years)	Adults ≥ 21 years
Result reported	Positive or negative	Cancer Signal Detected (with predicted CSO) or No Cancer Signal Detected	Cancer Signal Detected (ranked tissue of origin), Atypical Signal Detected, or No Cancer Signal Detected
Accuracy			
Evidence source	Case-control validation study (N=1,124; 324 with known cancer, 800 cancer-free)	PATHFINDER 2, prospective study of adults ≥ 50 years without suspected cancer (N=32,007)	ACHIEVE 1, manufacturer validation study (N=3,014) enriched for cancer (high-risk, symptomatic, or mass on imaging); not peer-reviewed
Sensitivity, all cancers	41.4%	39.3%	Not reported
Sensitivity, excluding breast and prostate	55.6%	54.9% (post hoc)	Not reported
Sensitivity, other subgroups	Stage I - 26.8%, Stage II - 42.9%, Stage III - 63.6%, Stage IV - 89.3% (excluding breast and prostate)	69.8% for 12 cancers that cause two-thirds of U.S. cancer deaths; 53.0% of detected cancers were stage I - II	Stage I - 56.8%, Stage II - 67.7%, Stage III - 79.0%, Stage IV - 98.6%
Breast / prostate sensitivity	Breast 16.0%; prostate 3.9%	Low; 38.6% of false negatives were stage I - II breast or prostate cancer	Stage I - II: breast 53.7%; prostate 74.1%
Specificity	97.4% (false-positive rate 2.6%)	99.64% (false-positive rate 0.36%)	99.2% in asymptomatic participants (n=141); 96.0% in benign/high-risk participants
Positive predictive value	9.7% - 30.4% (estimated for an undiagnosed cancer prevalence of 0.5% - 2%)	60.3% (observed)	Not reported
Negative predictive value	Not reported	99.2%	Not reported
Tissue-of-origin accuracy	Not applicable	91.3% (top two CSO predictions)	Not reported
Number needed to screen to detect one cancer	Not reported	185	Not reported
Cost and status			
Price	**$689** self-pay	**$949** list; **$799** self-pay ("Bill to Patient")	**$3,500** self-pay (through Everlywell)
Insurance	Not covered; may be HSA/FSA eligible; imaging reimbursement program for follow-up	Limited plans; TRICARE with prior authorization; may be HSA/FSA eligible	Not covered; HSA/FSA may be used; imaging reimbursement program (application required)
FDA status	LDT; not FDA cleared or approved	LDT; PMA submitted January 2026; FDA panel voted in favor September 2026 (decision pending)	LDT; not FDA cleared or approved

- The numbers are not directly comparable. Cancerguard accuracy comes from a case-control study of people already known to have or not have cancer. Galleri accuracy comes from a prospective study in the intended-use population, where only cancers diagnosed within 12 months were counted. Caris Detect accuracy comes from manufacturer-reported data (not peer-reviewed) in a population with a higher cancer prevalence than the general screening population, and was generated with whole-genome sequencing alone.
- PPV depends on the prevalence of undiagnosed cancer in the population tested; it falls in younger and lower-risk patients.
- In PATHFINDER 2, of 440 cancers diagnosed within 12 months, 39.3% were detected by Galleri, 20.7% by USPSTF-recommended screening, and 40.0% clinically.
- Sources: Exact Sciences Cancerguard provider information; Galleri provider FAQs; PATHFINDER 2 (PMID 42773207); NHS-Galleri (PMID 42776074); FDA Executive Summary for Galleri; Caris Detect website; Caris ACHIEVE 1 press release (March 2026); Everlywell Caris Detect pricing.