THE ARISING

Finding Cancer Earlier

CANCER SCREENING



NOVEMBER 2026

Finding Cancer Earlier

The promise needs an outcome

A blood draw that looks for several cancers at once is an appealing idea. It could reach diseases for which routine screening offers few options. It might also make the first step easier. But the first step is only the beginning of a much longer clinical journey.

Screening means looking before symptoms appear. An abnormal result opens a question; it does not settle a diagnosis. The useful question is whether offering the whole pathway helps people live longer or better, after the costs of investigation and treatment are counted. [4]

Multi-cancer early-detection tests, often shortened to MCED, look for biological signals associated with cancer. The test studied in PATHFINDER and NHS-Galleri analyzes patterns of chemical tags on DNA fragments circulating in blood. It can also suggest where a cancer signal originated, helping direct further investigation. [1,2]

That is a technical achievement. Its clinical value still has to be measured. A test can find cancers without showing that the people offered testing have fewer cancer deaths. A larger number of early diagnoses is encouraging only if the rest of the pathway delivers a meaningful benefit.

Three questions should stay separate: Can the test detect a signal? What happens after a result? Does offering the test improve health? Each needs its own evidence. Collapsing them into a single claim that a test "works" makes it harder to understand both the promise and the uncertainty.

Established screening also deserves careful discussion. Evidence and eligibility differ by cancer, test and population. The uncertainty around one newer technology is not a reason to abandon screening with an established role. Nor does the success of an established program automatically validate a new blood test. [4]

What PATHFINDER actually found

PATHFINDER / 92 positive signals



35 cancer diagnoses | 57 without a cancer diagnosis

Positive results only. Not all participants, and not all cancers. [1]

PATHFINDER followed adults aged 50 or older without cancer symptoms at seven US health networks. It was a prospective cohort, not a randomized comparison of screening against no screening. Its central question concerned the time and testing needed to resolve a cancer signal. [1]

Among 6,621 participants with analyzable results, 92 had a positive signal. Cancer was diagnosed in 35; the other 57 had no cancer diagnosis. Thus, about 38% of positive results led to a cancer diagnosis in this study. That is the positive predictive value, not the proportion of all cancers the test could find. [1]

For false-positive participants, the median time to diagnostic resolution was 162 days. Most underwent imaging, and 17 of 57 underwent a procedure. A blood draw can therefore lead to a substantial investigation even when cancer is not found. [1]

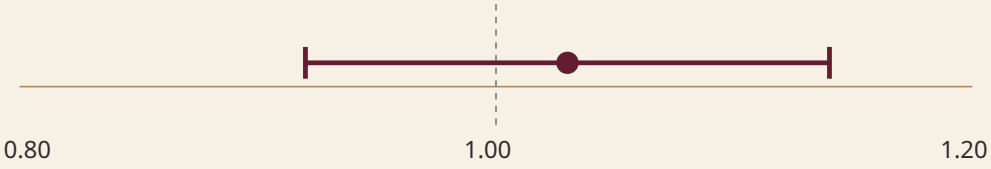
The study was funded by GRAIL. Participants were a convenience sample, and 91.7% were White. These features matter when considering how well the experience might transfer to other populations and care settings. [1]

The practical lesson is to evaluate a screening program as a pathway. The initial result is connected to appointments, imaging, interpretation, possible tissue sampling and a plan for unresolved findings. Access to those steps belongs in any discussion of access to the test itself.

A positive result is not a cancer diagnosis. A negative result is not a guarantee that cancer is absent. Those two statements are easy to repeat and surprisingly easy to lose when a test is marketed as a simple answer. [4]

The randomized test of the idea

PRIMARY OUTCOME / stage III or IV incidence rate ratio [2]



1.03 (95% confidence interval 0.92 to 1.14)

NHS-Galleri brought the question into a much larger randomized trial in England. It assigned 142,250 people aged 50 to 77 to testing plus usual care or a control group whose blood was stored. Participants attended up to three annual blood draws, with at least 12 months of follow-up after the last participant's third visit. Participants were not under investigation for suspected cancer and had no cancer diagnosis or treatment within the previous three years. The primary outcome was the incidence of stage III or IV disease across 12 prespecified cancer types. GRAIL sponsored and funded the trial. [2]

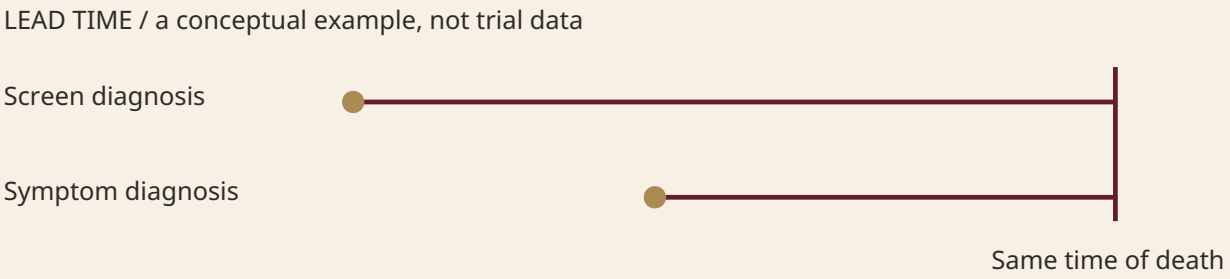
The 2026 report did not find a significant reduction in that primary outcome: the incidence rate ratio was 1.03, with a 95% confidence interval of 0.92 to 1.14. The interval includes both a modest reduction and an increase. This was not evidence that the trial's main aim had been achieved. [2]

For stage IV disease alone, a secondary outcome, the rate ratio was 0.86, with a 95% confidence interval of 0.74 to 1.00. The authors treated secondary results descriptively after the primary test failed; those intervals were not adjusted for multiple testing. This potentially useful signal warrants follow-up, rather than a declaration that the test has proved it saves lives. [2]

Late-stage incidence is not mortality. The trial report calls for longer follow-up, and the trial was not powered to establish a mortality reduction. Its findings leave room for future benefit without establishing that benefit now. [2]

A companion performance report illustrates a different part of the picture. Across three rounds, specificity was 99.50% to 99.60%, while episode sensitivity for all cancers was 26.7% to 37.2%. Positive predictive value ranged from 45.8% to 58.0%. These measures describe different denominators. High specificity should not be mistaken for finding nearly every cancer. [3]

Earlier does not always mean longer



Imagine two clocks that stop at the same moment. One begins counting at a screening diagnosis; the other begins later, when symptoms would have led to diagnosis. The first records more time, even though neither clock stops later. This is the logic of lead-time bias: longer survival measured from diagnosis can occur without a longer life. [4]

Overdiagnosis is a separate problem. It means finding a cancer that would never have caused symptoms or death during that person's lifetime. Unlike a false-positive result, the cancer is real. The harm can come from a diagnosis and treatment that the person would not otherwise have needed. [4]

A shift toward earlier stages must also be read carefully. If screening adds early diagnoses, the fraction of all diagnoses that are late-stage can fall even if the actual rate of late-stage disease has not changed. Rates in randomized groups answer a different question from the proportions displayed in a stage chart. The NHS-Galleri report explicitly makes this distinction. [2]

For that reason, a persuasive evaluation needs more than a detection count. It needs comparable groups, enough follow-up, clear outcomes and a careful accounting of downstream harm. Cancer-specific mortality asks about deaths attributed to cancer. All-cause mortality asks about deaths overall. Neither should be replaced by the number of cancers found.

Harms can also be missed when data collection ends too soon. In NHS-Galleri, adverse events after referral into the health system depended on direct reporting by a participant or clinician. The authors state that the trial did not fully characterize safety during diagnostic evaluation. A low reported event count is therefore not a complete estimate of the burden after a positive test. [2]

A better conversation before testing

The most useful conversation begins with purpose. Is the question routine screening in someone without symptoms, investigation of a symptom, or surveillance after a previous cancer? Those situations should not be treated as interchangeable.

A general discussion can ask:

- What evidence supports this test for people with this age and risk profile?
- Is the claimed benefit better detection, fewer late-stage diagnoses, or fewer deaths?
- What happens after a positive result, and who coordinates the investigation?
- What happens if the result is positive but no cancer is found?
- What does a negative result leave uncertain?
- How will this fit alongside established screening, rather than displace it?
- What are the likely burdens, costs and access barriers across the whole pathway?

These are questions for shared decision-making, not a personal recommendation to buy or decline a test. A clinician can connect them to medical history, family history, local guidelines and the person's preferences.

The scientific promise is worth taking seriously. So is the obligation to distinguish finding something from helping someone. The strongest case for a new screening program will connect its signal to better outcomes while making false alarms, missed cancers, overdiagnosis and treatment burden visible.

Health information, not individual medical advice. Symptoms or concerning changes need clinical assessment even after a negative screening result. Do not delay that assessment or replace recommended screening on the basis of this article.

Sources & further reading

1. Schrag D, et al. Blood-based tests for multicancer early detection (PATHFINDER): a prospective cohort study. *The Lancet*. 2023;402:1251-1260. PubMed record and abstract · Article.

2. Sasieni P, et al. Effect of Screening with Multicancer Early-Detection Test on Late-Stage Cancer Diagnosis. *New England Journal of Medicine*. 2026;395:1374-1386. PubMed record · Article.

3. Neal RD, et al. Performance of a multi-cancer early detection test in the randomized controlled NHS-Galleri trial. *Nature Medicine*. 2026;32:3770-3780. PubMed record and abstract.

4. National Cancer Institute. Cancer Screening Overview (PDQ), Patient Version. Benefits, harms and interpretation.

PATHFINDER describes feasibility and diagnostic follow-up. NHS-Galleri tests stage-based outcomes in randomized groups. The performance report describes detection characteristics. These sources answer related but different questions; none should be substituted for another.