Multicancer detection tests: holy grail or cautionary tale?

A single blood test that can identify most cancers remains the aspirational goal of cancer screening. The US biotechnology company Grail has been closest to developing a viable multicancer detection test. In June, 2026, the high hopes of many were dashed at the annual American Society of Clinical Oncology (ASCO) scientific meeting: Grail's landmark Galleri trial, which randomly assigned 140 000 UK residents to usual care plus multicancer detection testing versus usual care alone, failed to meet its primary endpoint—a reduction in late-stage cancers.[1] The cancer prevention community's reaction was negative, as was Wall Street's. The company's value dropped by 50%, a loss from which it has yet to meaningfully recover. The full trial report has yet to appear in a biomedical journal, precluding a comprehensive assessment of clinical outcomes and patient safety, and an economic assessment necessary for clinical adoption.

Disappointing results have not halted the marketing of multicancer detection tests. Although not approved by the US Food and Drug Administration (FDA), several companies in the USA are authorised to offer multicancer detection as laboratory-developed tests that can be obtained through online health platforms without a doctor's office visit. Laboratory-developed tests are only required to show analytic validity, not clinical validity.[2] A wave of advocacy in the USA propelled the Nancy Gardner Sewell Medicare Multi-Cancer Early Detection Screening Coverage Act (H.R.842) into law,[3] mandating Medicare coverage for multicancer detection blood tests beginning in 2028—contingent upon FDA approval. Grail's final pre-market approval application to the FDA is due to be reviewed on Sept 23, 2026, with potential approval anticipated in early 2027.

Based on the ASCO 2026 abstract, we calculated the absolute risks for cancer by stage in the two groups of the UK study.[1] We believe they are important for patients, caregivers, and policy makers. The primary endpoint of the trial, comparing the combined risk of stage III and IV cancers across groups after 3 years, was similar at 1%. The overall risk of cancer was 0·3% higher in the multicancer detection test group (5·1%) compared with the control group (4·8%). These data provide no convincing evidence of clinical benefit. The slight increase in early-stage disease could be beneficial or could signal potential harm from overdiagnosis, which is the identification of a cancer that would otherwise not cause symptoms or death. After South Korea introduced widespread, low-cost thyroid ultrasound screening in the late 1990s and 2000s, diagnoses rose 15-fold, but mortality rates remained flat.[4] The rise in incidence came from detecting harmless, slow-growing tumours, not aggressive disease.[4] A very useful manoeuvre Grail could pursue is to continue the UK trial to better understand the balance of benefit and harm over time before marketing the test. Unfortunately, the trial protocol does not allow for continuation of the Galleri trial.[5]

Despite the impressive preclinical science behind multicancer detection tests, the underwhelming clinical trial data should not be entirely surprising. Another recent Grail trial, PATHFINDER 2, reported a cancer detection sensitivity of approximately 40%, but a specificity of nearly 99%.[6] Because the pre-test probability of cancer is not more than 1–2% for an average-risk screening population around age 60 years, even a highly specific test will generate as many false-positive results as true positives. In other words, a positive result performs about as well as a coin flip.

Beyond test characteristics, stage shift as the primary endpoint in the UK trial has generated substantial controversy, as has a perceived lack of transparency about the relationship between the company and the UK National Health Service.[7,8] A study designed to explicitly show improvement in a traditional endpoint, such as cancer mortality, would require long follow-up and demand large resources, often beyond the interest of industry sponsors. For-profit companies are eager to bring their products to market ahead of the competition, while investors wish positive returns sooner rather than later. Although the economic reasoning is understandable, longer follow-up is indispensable to prove the clinical use of any new diagnostic test.

To date, there is no evidence that any multicancer detection testing prevents cancer, consistently detects it at an earlier stage, or reduces cancer-associated mortality. Meanwhile, false-positive rates have been predictably high. The costs associated with evaluating false-positive results are very real, as are the psychological burdens borne by patients who are incorrectly told they have cancer—or incorrectly reassured that they do not. At their present state of development, multicancer detection tests more often incorrectly inform patients that they have cancer (false positive) than identify when they do. The widespread, sanctioned introduction of multicancer detection tests for the average-risk population continues to be driven predominantly by hope, not by evidence.

We believe that meticulous, high-quality clinical trial testing with patient-important endpoints must be prioritised. To serve as trustworthy stewards of public health, governments and health-care leaders must resist pressure—public or corporate—to pursue easy solutions that might expose patients to harm. Other topical examples, such as whole-body MRI scanning for disease

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detection or peptide infusions to promote health, do not have strong human safety data or regulatory oversight.

Novel cancer detection tests should be evaluated in adequately powered trials using endpoints of cancer incidence and cancer mortality. Developing a new drug takes 10 to 20 years from laboratory testing to patient use. We contend that multicancer detection tests should be evaluated in a similar manner. This approach takes time, is expensive, and delays potential patient benefit. However, such rigorous evaluation guards against physical and psychological harm. For good reason, *primum non nocere* (first, do no harm) has been a guiding principle for medical professionals for centuries. Ironically, the risks of multicancer detection testing are better understood than the benefits. Until this balance is established, the medical profession, starting at the level of the individual provider, must serve as the educated gatekeeper for an individual patient's best interests.

For the future, better testing of new cancer screening tests can most readily be achieved by embedding clinical trial testing within the framework of learning health systems.[9] Admittedly, this change would mean delayed market entry for any new test. However, only a minority of new tests ultimately prove beneficial when rigorously assessed. Commercial and political pressures continue to drive public uptake. Greater expedience and transparency regarding full results, not just those that place the product in the best light, are needed. Rigorous, long-term randomised trials with hard endpoints—modelled on drug development standards—are essential to ensure that new cancer detection technologies deliver genuine benefit rather than measurable harm.

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