

New Cancer Screening / Detection

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Screening Outcomes

Cancer screening is often described as finding cancer early, but the clinical goal is more demanding: screening should reduce cancer mortality or serious morbidity without causing excessive harm to people who do not have symptoms. A screening test is used in an apparently healthy population, while diagnostic testing is used after symptoms, an abnormal examination, or a positive screening result. This distinction matters because most people entering a screening program do not have cancer. A test can detect more tumors and still fail to improve survival if it mainly identifies indolent disease, produces many false positives, or moves the date of diagnosis earlier without changing the date of death. The National Cancer Institute therefore emphasizes both benefits and harms when evaluating screening, including false-positive results, false negatives, overdiagnosis, overtreatment, and complications from follow-up procedures (NCI, 2023a). New technologies such as artificial intelligence, circulating tumor DNA, and multicancer blood tests are scientifically promising, but they should be judged by the same standard as established screening: do they improve outcomes in the population in which they are offered?

Established Screening

Some cancer-screening approaches already have strong evidence and are recommended for defined populations. NCI identifies mammography for breast cancer, HPV and Pap testing for cervical cancer, colorectal screening using stool-based or structural examinations, and low-dose CT for selected people at high risk of lung cancer as examples of established screening strategies (NCI, 2024a). These programs do more than produce a result. They define who should be screened, how often testing should occur, what happens after an abnormal result, and which treatment or preventive intervention follows. Cervical screening can identify precancerous changes that can be treated before invasive cancer develops. Colorectal screening can detect cancer but can also prevent cancer when precancerous polyps are found and removed. Lung screening is targeted to people whose smoking history places them at sufficiently high risk that the benefits of low-dose CT outweigh harms from false positives and radiation.

The screening pathway is therefore as important as the test. A highly accurate screening test has limited value if patients cannot obtain diagnostic follow-up, biopsy, treatment, or repeat surveillance. Systems also need reminders, navigation, quality assurance, and reliable reporting. Screening

programs can fail through underuse as well as overuse. People who are uninsured, geographically isolated, unable to take time off work, or distrustful of healthcare may receive less evidence-based screening even while lower-risk people undergo tests unlikely to help them. The future of early detection depends partly on improving access to proven screening before assuming that a new technology will solve existing delivery failures.

Overdiagnosis and Lead-Time Bias

Lead-time bias occurs when screening identifies a cancer earlier but does not extend the person's life. If a cancer would ordinarily be diagnosed at age 68 and a patient dies from it at 70, measured survival after diagnosis is two years. If screening finds the same cancer at 64 and death still occurs at 70, survival appears to rise to six years even though the patient lived no longer. This is why survival time after diagnosis is a poor measure of whether a screening program saves lives. Randomized trials and population studies instead examine cancer mortality, all-cause mortality where appropriate, advanced-stage disease, and harms.

Overdiagnosis is different. It occurs when screening detects a cancer that would never have caused symptoms or death during the person's lifetime. Once such a cancer is found, clinicians and patients may feel compelled to treat it, exposing the person to surgery, radiation, medication, anxiety, cost, and long-term side effects without clinical benefit. NCI's current screening overview identifies overdiagnosis and resulting overtreatment as central harms that must be considered alongside false-positive and false-negative results (NCI, 2023a). These principles are especially important when evaluating new molecular tests because increasingly sensitive technology can find smaller biological abnormalities without automatically proving that intervention improves health.

Multicancer Blood Tests

Multicancer detection tests attempt to detect signals from several cancers using one blood sample. Depending on the platform, they may analyze cell-free DNA, methylation patterns, proteins, fragments of genetic material, or combinations of biomarkers and machine-learning algorithms. The idea is attractive because many lethal cancers currently lack population-screening programs. A single blood draw that detects pancreatic, ovarian, liver, or other cancers before symptoms could potentially change outcomes. NCI has therefore created the Cancer Screening Research Network and is using the Vanguard Study to develop the infrastructure needed for larger randomized trials of multicancer detection (NCI, 2025a).

The evidence, however, does not yet justify treating these tests as proven population screening. An Agency for Healthcare Research and Quality systematic review published in 2025 found no completed controlled studies showing that blood-based multicancer screening reduces cancer deaths, advanced-stage cancer, or improves quality of life. The review evaluated 20 studies covering more than 109,000

participants and found that accuracy varied widely, while the strength of evidence remained insufficient because many studies had serious methodological limitations (Kahwati et al., 2025a). A companion systematic review in *Annals of Internal Medicine* reached the same conclusion: no completed controlled trial had demonstrated benefit, and evidence on harms remained insufficient (Kahwati et al., 2025b). These tests may eventually become important, but their current status is investigational rather than equivalent to established mammography, cervical, colorectal, or lung screening.

The challenge with a blood-based cancer signal is that the patient may feel healthy and the location of the suspected cancer may be uncertain. A positive result can lead to imaging, endoscopy, biopsy, specialist referral, or repeated testing. If no cancer is found, the patient may experience prolonged anxiety and incur substantial cost. If an indolent cancer is detected, overdiagnosis becomes possible. False-negative results can also create misplaced reassurance, especially if patients incorrectly believe one blood test replaces established screening.

For these reasons, the American Cancer Society–associated 2025 consensus guidance states that currently available multicancer early detection tests are not FDA-approved for population screening and have not been shown in randomized trials to reduce cancer mortality. Clinicians are advised to discuss benefits, uncertainties, follow-up implications, and the continued need for standard age- and risk-appropriate screening when patients ask about these tests (Hoffman et al., 2025). A 2026 clinical review similarly emphasizes potential harms including false positives, overdiagnosis, unclear diagnostic pathways, psychological distress, and healthcare-resource use (Snead et al., 2026). The practical lesson is that the simplicity of the blood draw should not be confused with simplicity of the clinical pathway.

Artificial Intelligence

Artificial intelligence is increasingly used to assist interpretation of mammograms, CT scans, pathology images, skin lesions, and other screening-related data. AI systems may highlight suspicious regions, prioritize cases, estimate risk, or integrate large amounts of imaging and clinical information. These tools can improve efficiency and potentially increase sensitivity or reduce workload, but their performance depends on training data, population characteristics, image quality, and how they are integrated with clinician judgment. A model that performs well in one hospital or demographic group may perform differently elsewhere.

AI therefore should be evaluated as part of a screening system rather than as a stand-alone accuracy competition. The relevant questions are whether it reduces missed cancers, increases unnecessary recalls, changes biopsy rates, creates automation bias, and ultimately improves patient outcomes. NCI's screening-research program continues to support imaging biomarkers and AI-based approaches while emphasizing validation in real screening populations (NCI, 2025a). The same caution applies to radiomics and other high-dimensional methods: discovering a pattern associated with cancer is only

the beginning. The pattern must be reproducible, clinically interpretable, and useful enough to change management in a way that benefits patients.

Risk-Based Screening

Age remains one of the strongest cancer-risk factors, but inherited mutations, family history, smoking exposure, prior radiation, certain medical conditions, and other factors can place some people at substantially higher risk than the general population. Risk-based screening attempts to match the intensity and modality of screening to that underlying risk. People with hereditary cancer syndromes may need earlier or more frequent imaging, endoscopy, or specialized surveillance. The related Academic Master discussion of [genetic testing](#) is relevant because genetic information can help identify high-risk families but also raises questions about consent, privacy, uncertainty, and the psychological effects of learning about inherited risk.

Risk-based approaches could also reduce unnecessary screening among people unlikely to benefit, but they require accurate risk models and equitable access to assessment. A model that depends heavily on family history can underestimate risk in people who lack information about relatives. Genomic datasets can also underrepresent some populations. The future of screening may therefore involve combinations of age, family history, genetics, imaging, lifestyle exposure, and molecular biomarkers, but personalization should be tested carefully rather than assumed to be superior simply because it is more technologically complex.

New screening technologies attract attention because they promise dramatic change, but large benefits can also come from ensuring that people complete existing evidence-based screening and receive timely follow-up after abnormal results. NCI's current research agenda explicitly includes both new tests and improvements in implementation, biomarkers, trial design, and equitable participation (NCI, 2025a). A screening program fails when a positive stool test is never followed by colonoscopy, an abnormal mammogram is not resolved, or a high-risk smoker is never offered low-dose CT.

Equity should therefore be built into screening innovation from the beginning. Trials should include populations that reflect the people who will use the test, and screening systems should measure follow-up completion rather than only initial test uptake. Cost, insurance coverage, rural access, language, disability, trust, and transportation can determine whether early detection actually leads to earlier treatment. A technology that improves accuracy but widens access gaps may increase rather than reduce disparities.

Conclusion

Cancer screening is successful when it improves patient outcomes, not merely when it finds more abnormalities. Established screening programs for selected cancers have evidence supporting their use in defined populations, but even proven screening involves trade-offs involving false positives,

false negatives, overdiagnosis, invasive follow-up, anxiety, and cost. Emerging technologies such as multicancer blood tests, circulating tumor DNA, radiomics, and artificial intelligence may eventually expand early detection, especially for cancers without current screening options. The strongest current evidence, however, does not yet show that multicancer blood testing reduces cancer mortality, and major randomized studies are still being developed. New tools should therefore supplement research and shared decision-making rather than displace proven screening prematurely. The future of cancer detection will likely combine better risk assessment, molecular biomarkers, imaging, AI, and more efficient care pathways. The central scientific standard should remain unchanged: a screening technology is valuable only when the benefits of finding disease earlier outweigh the physical, psychological, and financial harms created by testing healthy populations.

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