MCED Care Delivery Screening Guidance: Frequently Asked Questions (FAQ)

This Frequently Asked Questions document aims to complement the MCED Care Delivery Workgroup's paper, *Multicancer Early Detection (MCED) Screening Guidance:* A Recommended Care Pathway for Clinical Use of MCED Tests, and serve as a quick reference for providers to understand the current state of MCED technologies.

1. What is an MCED?

Multicancer Early Detection (MCED) refers to an emerging set of laboratory technologies that can enable clinicians to rapidly screen for multiple cancer types from the same specimen source, typically a blood draw.

2. Why is there so much interest in the potential of MCEDs to screen for cancer in people without symptoms of cancer? Is it likely that a patient of mine will ask me whether they should have an MCED or not?

Some national organizations currently recommend screening tests for five cancers: breast, colorectal, cervix, lung, and prostate. Together, these five cancers account for about 30% of all malignancies. Except for screening in a small number of people who are at very high risk for one or more of the remaining 70% of cancers, no other cancer screening is recommended at the population level. When added to existing approaches to single cancer screening, MCED tests could provide clinicians with the opportunity to identify a broader range of cancers earlier in the course of the disease, raising the potential to treat them more effectively. These new technologies may have the potential as screening tests to be used in the population broadly or as specific tools for clinicians to help diagnose cancer in the clinical setting.

Yes, it's likely that one or more patients will ask you in the near future about whether they should have an MCED. These new tests have received much attention in the lay and scientific press. The concept of screening for over 50 cancers through one blood test will undoubtedly stimulate interest in a lot of patients.

3. Does this test determine if someone has a predisposition to cancer – like BRCA, or is it something completely different?

MCEDs are designed to detect cell-free DNA from cancer cells that have broken down and are circulating in the blood. Although an MCED may lead to the diagnosis of cancer for which a person has an inherited risk, the MCED itself does not assess inherited genetic changes or provide any information about a person's genetic predisposition to developing cancer.

4. Are MCEDs recommended by any authoritative guideline group like the USPSTF or the ACS?

No. To date, no medical society or authoritative guideline group has made recommendations to use MCED tests for cancer screening.

5. Are these tests being studied? Is it possible that they will be included in screening guidelines?

Yes, these tests are currently being studied in multiple, large-scale clinical trials to demonstrate clinical benefit further. Additional regulatory approvals by the Food and Drug Administration (FDA) are needed before MCED tests are included in future screening guidelines.

6. Are MCED tests considered standard of care or included in quality measures at this time?

No, MCEDs are not considered standard of care. Committing to screening all eligible patients with the currently recommended screening tests defines the current standard of care, and many are included in quality measures.

7. What MCED tests are currently available?

The Galleri® test is the only *commercially* available in some locations/practices/health systems in the U.S. and costs $949/test. It is offered as a laboratory-developed test (LDT), which means the tests and the laboratories have been evaluated for analytical validity under Clinical Laboratory Improvement Amendments (CLIA) or College of American Pathologists (CAP) guidelines. MCEDs are not currently offered for clinical use in the U.K. but are the subject of ongoing randomized trials.[1]

The Exact Sciences MCED test and OverC MCDBT are not yet offered to the public outside of clinical research studies. While our paper primarily highlights data points on MCED tests from Grail Bio and Exact Sciences, additional MCED tests are expected to be developed and released in the coming years.

8. Are MCEDs likely to be paid for by a patient's insurance? If not, how much can the patient expect to pay?

No, MCEDs are not currently covered by Medicare or the vast majority of commercial insurance companies. The Galleri® test is the only one currently *commercially* available in some locations/practices/health systems in the U.S. and costs $949/test.

[1] https://pubmed.ncbi.nlm.nih.gov/36230741/

9. If the patient has a positive result and receives additional testing, are these tests likely to be covered by the patient's health insurance?

Although most payers will cover many follow-up tests, coverage will likely vary depending on the payer and the test. Providers are encouraged to work with care coordinators and their patient's health plans to ensure that any necessary follow-up tests are covered before starting the evaluation. Prior to receiving an MCED, patients should be fully informed about the potential need for follow-up tests and that out-of-pocket expenses may be incurred.

10. What does a positive test result mean? Does a positive MCED test give information about the potential cancer site?

MCED tests are meant to target if a cancer signal is present but are not a diagnosis of cancer because false positives may occur. Depending on the test, an MCED may also provide information about the possible organ to suspect. They also may list more than one option – the most likely organ where the cancer started, as well as a second choice for the originating organ. Other tests may instead recommend follow-up via imaging.

11. If the test is positive, how likely is it that the patient actually has cancer? How accurate is the information about the likely organ where the cancer started (organ of origin)? If the patient requires additional testing, how do I know what tests to order to find the cancer? As a primary care clinician, am I responsible for ordering these tests, or should I consult specialists?

A positive test indicates that a molecular signal associated with cancer was detected, and the patient should receive additional tests/workup to determine if cancer can be found. An organ of origin report is intended to guide the sequence of appropriate testing (organ-specific workup, C.T. scan, etc.). As a primary care clinician, you have the option to guide the workup yourself in consultation with appropriate specialists. Some centers may develop a specialized team to aid in the diagnostic workup.

12. If the test is negative, how confident can I be that the patient does not have cancer?

While a negative test provides some reassurance that the patient does not have advanced cancer, current MCED tests do not detect all cancers and are less likely to be positive for early cancers or pre-cancers. We recommend that your patients attend their regularly scheduled screening appointments (e.g., mammogram, low-dose C.T., etc.).

13. Can this test replace other recommended screening tests, like the tests we do to screen for breast, colorectal, cervix, lung, and prostate cancer?

No. MCED tests should not replace currently recommended cancer screening tests.

14. What is the regulatory status of MCED tests?

Three MCED tests have been designated as Breakthrough Devices by the US FDA, allowing for expedited review of the tests. The three tests are the Galleri® from GRAIL Bio U.K., Exact Sciences MCED Test, and the OverC Multi-Cancer Detection Blood Test (MCDBT). It is important to note that while all three tests have been granted FDA Breakthrough Designation, they have not been officially approved by the FDA.

15. What are the health equity considerations for MCED tests?

There are longstanding disparities in cancer screening, treatment, and outcomes in both the United States and the United Kingdom. Individuals with low incomes, poor education, or certain disabilities, and those from racial/ethnic minority groups often face challenges accessing health care services, leading to worse outcomes. Low patient awareness, knowledge, health literacy, and negative attitudes, including stigma, provider bias, and miscommunication between patients and providers, are important factors that may contribute to low screening and diagnostic rates among adults in those populations.

MCED tests hold the opportunity to reduce health inequities as well as the potential to exacerbate them. MCED tests may help reduce health disparities by increasing participation rates through improved access to screening. Still, if tests are not widely available, affordable, and acceptable to minority groups, inequities will increase. While the Galleri® test is available in the U.S. with a clinician's approval, most insurers do not currently cover MCED testing as many consider the tests experimental until FDA approval. This broadly and differentially restricts the population that can access them. Additionally, the National Health Service (NHS) has not yet made MCED tests available until further evaluation is complete. For more information on building health equity through research study design, please see the Health Equity Work Group's white paper here.