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The Promise of Multi-Cancer Early Detection Technologies in Encouraging Research & Development

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ABOUT US

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FasterCures, a center of the Milken Institute, is working to build a system that is effective, efficient, and driven by a clear vision: patient needs above all else. We believe that transformative and life-saving science should be fully realized and deliver better treatments to the people who need them.

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INTRODUCTION

Cancer is a leading cause of death worldwide and second only to heart disease in the United States in 2020.¹

Despite shifting trends in mortality for leading causes of death due to the COVID-19 pandemic, cancer remains one of the top causes of death globally.²

Significant advances have occurred in the treatment of cancer, with a range of interventions providing essential options for patients. The likelihood of treatment success is the highest when cancer is found early, which has elevated early detection as a key goal in cancer care and management.³ However, in the United States, routine provider-based screenings occur for only five types of cancer: breast, cervical, colorectal, prostate, and lung.⁴ Other cancers—which combined are responsible for nearly 71 percent of cancer deaths—have no recommended method for provider-based screening.⁵

New blood-based technologies, known as multi-cancer early detection (MCED) tests, are entering the market and can identify multiple cancers early and simultaneously. These tests detect signals found in DNA that cancer cells shed into the bloodstream.⁶ Interest in MCED tests is growing because of their potential to detect more cancers earlier and lead to better patient outcomes.⁷

In this report, we examine how early detection of cancer through MCED tests may change the landscape for cancer research and treatments. The exploration of MCED technology builds on FasterCures' work to define and measure the performance of the biomedical ecosystem to address patient needs and improve outcomes. This specific focus on oncology allows for deeper analysis of a relatively mature segment of the ecosystem to identify solutions to persistent challenges.

BACKGROUND

Detecting cancer early, before it spreads or becomes metastatic, has been shown to reduce mortality. When cancer is found early, treatment options can potentially be curative or increase long-term survival.⁸

Localized cancer is found only in the tissue or organ where it began and has not spread to nearby lymph nodes or to other parts of the body. Some localized cancers can be completely removed by surgery. For example, in breast cancer, the five-year survival rate for women with localized cancer is 99 percent compared with 29 percent when the cancer has metastasized.⁹ Similarly, in colon cancer, the five-year survival rate for localized cancer is 90.6 percent versus 14.7 percent when cancer is diagnosed when it has metastasized.¹⁰ Conversely, pancreatic cancer, for which there is no recommended screening, has a five-year survival rate of 41 percent when localized and only 3 percent after the cancer metastasizes.¹¹

In the US, routine provider-based screenings are currently recommended and available for five cancers: breast, cervical, colorectal, prostate, and lung (for people with a specified smoking history).

These screenings include mammography, pap smear, colonoscopy, prostate-specific antigen test, and low-dose computed tomography scans. In addition, providers are encouraged to incorporate shared decision making into interactions with patients about screening.¹² However, cancers with no recommended routine screening options—such as liver, ovarian, and pancreatic cancers—are responsible for almost three-quarters of cancer deaths.¹³

New early detection technologies offer the potential to identify cancers that lack screening tests. MCED tests rely on circulating tumor cell-free DNA to identify signals of early cancer in the blood without biopsy.¹⁴ Through a single blood draw, MCED tests can simultaneously detect and localize multiple cancers in parts of the body that are not easily accessible for physical exam or surgical biopsy. MCED tests may also lower access-related barriers to traditional screenings. Liquid biopsies, the technology on which many MCED tests rely, can be administered without highly specialized equipment or facilities. They are noninvasive and test multiple cancers simultaneously. Challenges related to accessing the right facility, traveling to appointments, or taking time off from work could be mitigated with a blood-based test that screens for multiple cancers simultaneously. Tests in development and currently available, however, are intended to complement existing screenings.

If new screening technologies such as MCED tests can identify more individuals with earlier stage cancers, how might cancer research and development change? Could it spur greater biomedical innovation?

To help answer these and related questions, FasterCures analyzed the peer-reviewed and grey literature to identify articles relevant to the topic. The grey literature included sources of non-peer-reviewed or academic literature such as articles published in public media and publicly available government and non-government organization data through the National Cancer Institute, the US Food and Drug Administration (FDA), and the World Health Organization. We also conducted 12 interviews with leaders and subject matter experts representing providers, patient advocates, the biopharma industry, and academia.

FINDINGS

Because MCED screening tests could lead to earlier diagnosis of more individuals with earlier stages of cancer, several experts predict the following impacts on the research ecosystem:

- **STIMULATE RESEARCH ON THE BIOLOGY OF EARLY-STAGE CANCER AND PROGRESSION PATTERNS.** There are many unknowns about early-stage cancers and their progression to metastatic, lethal disease. Biological complexity and lack of early-stage samples are among the reasons cited for the historical under-prioritization of early cancer research.¹⁵ Based on the current structure of clinical trials, identifying more individuals with early-stage cancer would enable more research into cancer biology and the progression of early cancer to a malignant and metastatic state. Some experts believe that more widespread early detection will promote investments in research in earlier stages of cancers, including the conduct of longitudinal studies of individuals with specific types of early cancer. These studies could help

identify factors that predict progression to advanced disease and support the development of diagnostic and prognostic technologies, as well as potential interventions.

“The more we understand what’s going on in a particular person’s cancer, the more we can understand the intervention that will be effective in treating that cancer.”

—An Academic Oncologist and Cancer Prevention Expert

- **SPARK RESEARCH TO SUPPORT TREATMENT OF EARLY-STAGE DISEASE.** New drugs in cancer have generally focused on late-stage disease. In fact, of the 39 novel drugs and new indications that the FDA approved for use in oncology in 2020, almost 70 percent are for late-stage or refractory disease.¹⁶ Experts indicate that if more early-stage patients were present in clinical care, we would see a greater focus on early-stage disease. But in the absence or dearth of those patients, that shift is less likely to occur.

“New early detection technology can most notably identify previously untreatable cancers that could have a more successful trajectory. For example, pancreatic cancer is diagnosed when advanced. It’s one reason why treatments have been marginal at best (although there are also biological reasons why it’s more difficult to treat). Still, one challenge is that there is no effective treatment modality until there are more adverse symptoms. If we think there can be better treatment, we need to identify those people first before even getting to that part.”—Head of Cancer Research Organization

- **LEAD TO MORE RESEARCH IN NOVEL NEO-ADJUVANT AND ADJUVANT THERAPIES.** Neo-adjuvant therapies are treatments administered as a first step to shrink a tumor before the main treatment (usually surgery). In contrast, adjuvant therapies are additional treatments administered after a primary treatment to lower the risk that the cancer will return.¹⁷ Neo-adjuvant and adjuvant therapeutic options exist for many cancers, but they require continued refinement to reduce their side effects and increase their effectiveness in extending life and improving quality of life.¹⁸ In addition, complications such as resistance to chemotherapy further highlight the need for early detection in concert with novel therapeutics.¹⁹ Researchers and biopharmaceutical companies have strong interest in evaluating new therapies in the neo-adjuvant and adjuvant settings, particularly in cancers such as lung cancer, for which the risk for recurrence in distant sites (metastasis) after surgical resection is high.²⁰ However, many neo-adjuvant and adjuvant trials in lung cancer have not met accrual goals for myriad reasons, including a smaller patient pool than in the metastatic setting.²¹ Identifying more patients with early-stage cancer across multiple cancer types will facilitate additional investigation of these therapies.

“In pancreatic cancer, only 10–15 percent of individuals diagnosed go to surgery. If we start to diagnose people earlier, that percentage would increase, which will spur efficiency within the surgical community; we would get better at doing [surgeries]

because we have more cases, it would be more routine ... That would then probably drive an increase in clinical trials for adjuvant therapy. Right now, there are a few but not very many for adjuvant therapies ... It would change the clinical trial landscape."

—A Chief Science Officer of a Cancer Advocacy Organization

- **ACCELERATE RESEARCH ON THE POTENTIAL APPLICATION OF CURRENTLY AVAILABLE THERAPIES FOR EARLIER-STAGE PATIENTS.** Experts anticipate increased numbers of clinical trials to evaluate the efficacy of established anti-cancer therapies indicated for late stage or metastatic disease in earlier stages of disease. As a notable example, Herceptin (trastuzumab) was originally developed as a targeted therapy to treat metastatic disease but was later approved for use in both neo-adjuvant and adjuvant settings.²² Similarly, in melanoma, new immunotherapy agents have improved survival for patients with advanced stage melanoma from a few months to greater than five years for nearly half of patients. Studies are ongoing to determine whether these game-changing immunotherapy drugs when provided to earlier stage or localized melanoma patients, as either neo-adjuvant or adjuvant therapy, can improve survival even further.²³

"The focus has been on lung, breast, colorectal, and prostate cancer. But what about all the others? ... We could really cure melanoma with the complements of treatment and early detection of cancer. That could be the same for bone cancer or deep tissue sarcoma, which become problematic very quickly and in later stages become very symptomatic, and then surgery becomes challenging, and not a lot of treatments are available. In the future, we will be able to identify more of these patients earlier and be able to apply new treatments."—Head of Oncology at a Biopharmaceutical Company

- **CHANGE THE WAY PATIENT BENEFIT IN EARLY-STAGE CANCERS IS MEASURED OR EVALUATED.** Traditional clinical trial endpoints, such as overall survival, which have been viewed as the gold standard for evaluating therapies, cannot always be assessed in cancer. Further, in trials with patients with early-stage cancers, in particular, it could be decades before impact on survival can be directly assessed. Experts anticipate greater use of surrogate endpoints. Surrogate endpoints, such as progression-free survival and objective response rate, are already used in both clinical and regulatory decision making for certain cancers.²⁴ Other surrogate endpoints such as pathologic complete response are emerging as acceptable endpoints in neo-adjuvant trials.²⁵ In addition to surrogate endpoints, the opportunity exists to measure different outcomes to assess the impact of treatments in early-stage patients outside of survival, such as patient-reported outcomes, quality of life, and the ability to work. Experts also anticipate that identification of early-stage cancer will necessitate consensus on the goals for treatment at earlier stages. Consensus among patients, providers, industry, regulators, and payers would drive greater efficiencies in clinical trials that could shorten the development timeline and thereby incentivize drug development.

DISCUSSION

Our research suggests that early detection technologies such as MCED tests may propel additional research and development activities in early-stage cancer. An important caveat is that our research did not examine MCED technology performance or regulatory oversight. Therefore, this report does not address those issues.

Although its feasibility is difficult to predict given competing priorities for R&D dollars, the identification of more patients with different types of cancers, as facilitated by technologies such as MCED tests, may stimulate greater investment in research on the biology of early cancers that can lead to the development of prognostic technologies, novel neo-adjuvant and adjuvant therapies, and efficacy and safety of existing therapies in earlier-stage populations. Our research also indicates that a key area of debate will center on the right endpoints to assess patient benefit and risk in clinical trials for therapies to treat early-stage cancer. As more people are identified with early-stage cancer, answering this question will become more urgent.

CONCLUSION

FasterCures sought to understand how the availability of new early detection technologies, such as MCED tests, would affect biomedical research activities. As outlined in this report, experts across the cancer ecosystem see the potential for MCED tests to stimulate cancer research that can lead to the development of more treatment options for early-stage patients. The provider community and other stakeholders must evaluate questions on the clinical utility of MCED tests and weigh their benefits and risks. Many of the findings in this report were also reflected in a panel discussion held at the Milken Institute's Future of Health Summit in June 2021, [The Promise of Earlier Detection in Shifting Cancer Research and Spurring Innovation](#).

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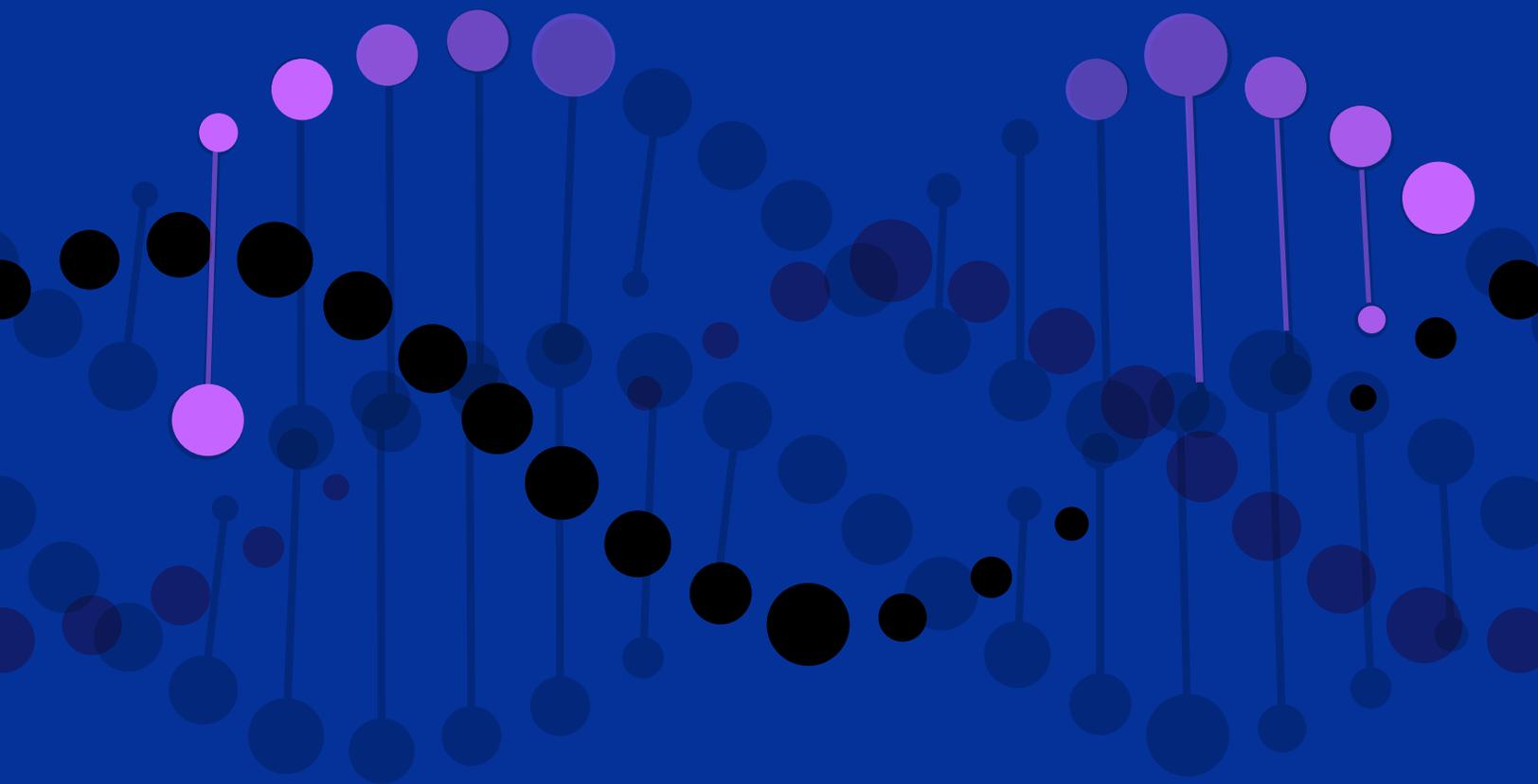
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