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# Real-World Data and Clinical Experience From Over 100,000 Multi-Cancer Early Detection Tests

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## INTRODUCTION

- Only 4 cancers—breast, colorectal, cervical, and lung (in high-risk individuals)—have United States Preventive Services Task Force (USPSTF) grade A/B screening recommendations[1-4]
- In the US, an estimated 83% of cancer-related deaths result from cancers diagnosed outside of recommended screening[5]
- Blood-based multi-cancer early detection (MCED) tests have the potential to simultaneously screen for multiple deadly cancers with high positive predictive value (PPV)
- A commercially available MCED test (Galleri®, GRAIL, Inc.) detects a shared cancer signal and predicts cancer signal origin (CSO) by analyzing methylation patterns in cell-free DNA isolated from peripheral blood
  - This MCED test was evaluated in a multi-center interventional study (PATHFINDER)[6] that included individuals aged ≥50 years, where it demonstrated a PPV of 43.1%
- Examining the real-world experience of this MCED test is important to understand how it performs in clinical practice

## OBJECTIVE

- Report the real-world clinical experience with >100,000 MCED tests ordered and processed from April 19, 2021 through October 14, 2023

## METHODS

### Data Collection

- This analysis includes de-identified MCED test result data from 111,080 MCED tests returned to individuals aged ≥22 years from sites in the US (and Puerto Rico)
- This analysis also includes de-identified data regarding clinical cancer outcomes for cancer signal detected (positive) MCED test results (N=411) that were collected as part of GRAIL's Quality Assurance Program intended to monitor the implementation and safety of the MCED test in clinical practice
  - Clinical cancer outcomes are voluntarily provided from ordering providers in compliance with the requirements of the US Health Insurance Portability and Accountability Act (HIPAA) of 1996 and its implementing regulations
  - For true positives, when possible, details on time to diagnosis (time from test return to cancer diagnosis), diagnostic workup, cancer type, and cancer stage are obtained
  - False positives are determined when the healthcare provider reports that no further workup is planned in the absence of a cancer diagnosis

### Data Analysis

- The CSDR was defined as the number of MCED tests with a positive result divided by all tests
  - CSDR doubling time was determined by logistic regression of CSDR against age for 40- to 80-year-old individuals
- The empirical positive predictive value (ePPV) is the cancer diagnosis rate in the population of patients who had a positive MCED test, a completed diagnostic workup, and clinical follow-up reported by their healthcare provider
  - Patients with a known active cancer at the time of ordering the test were not included in ePPV calculations
  - For this population, ePPV was computed as the number of patients with an invasive cancer diagnosis divided by the total number of patients within this population
- Individual CSO prediction accuracies were calculated among positive MCED tests with an invasive cancer diagnosis; individuals without reported cancer types were excluded
  - For each CSO, the prediction accuracy was the fraction of CSO predictions with a matching clinical diagnosis

## SUPPORTING DATA

### Implementation and Population Characteristics

- 111,080 MCED tests were ordered, processed, and had results returned to 9,136 healthcare providers across all US states
- A similar number of female (n=49,415; 44%) and male (n=61,665; 56%) individuals took the MCED test, both with a median age of 58 years (IQR 51-67 female; 50-67 male)
- Results were returned for >98% of tests with a mean turnaround time of 6.1 business days

### Cancer Signal Origin Prediction

- The real-world CSO prediction distribution was largely aligned with the modeled distribution (Spearman r=0.85), showing more frequent predictions for relatively common cancers (eg, colon/rectum, breast, lung) and less frequent predictions for uncommon cancers (eg, kidney, anus, cervix)

## IN REAL-WORLD EXPERIENCE, THE MCED TEST FACILITATED DIAGNOSIS ACROSS A BROAD SPECTRUM OF CANCERS, INCLUDING CASES IN EARLY STAGES AND WITHOUT RECOMMENDED SCREENING

### Cancer Signal Detection Rate (CSDR)

- The overall real-world CSDR was 0.91% (1011/111,080) and increased with age, doubling every 9.5 years for individuals between ages 40 to 80 years
- The real-world CSDR was slightly higher in males than females (0.98% vs 0.82%) and was consistent with PATHFINDER[6] CSDRs; neither observation had statistically significant differences (**Table 1**)

**Table 1. The Real-World CSDR was Consistent With Prior Clinical Study.**

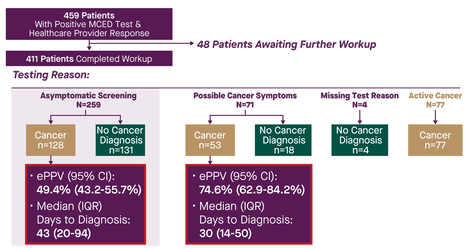
| | Real-World CSDR, 95% CI (n/N) | PATHFINDER[6] CSDR, 95% CI (n/N) |
|---|---|---|
| Overall | 0.91%, 0.86-0.97% (1011/111,080) | 0.88%, 0.67-1.1% (58/6578) |
| Female | 0.82%, 0.74-0.90% (405/49,415) | 0.72%, 0.48-1.0% (30/4183) |
| Male | 0.98%, 0.91-1.1% (606/61,665) | 1.2%, 0.78-1.7% (28/2395) |

CI, confidence interval; CSDR, cancer signal detection rate.

### Clinical Cancer Outcomes

- Clinical follow-up was reported by healthcare providers for 459 individuals with a positive MCED test result; follow-up rate was 45% (459/1011)
- In this real-world population, the reasons for undergoing MCED testing varied (**Figure 1**)

**Figure 1. Clinical Cancer Outcomes Reported After a Positive MCED Test Result.**




Of the 1011 positive MCED tests reported in this real-world dataset, 459 had follow-up information provided by the ordering healthcare providers. Excluding 48 patients who were awaiting further workup, clinical cancer outcomes were available for 411 patients. The ePPV was calculated as the cancer diagnosis rate in the population of patients with a positive MCED test, a completed diagnostic workup, and clinical follow-up reported by their healthcare provider.
CI, confidence interval; ePPV, empirical PPV; MCED, multi-cancer early detection; IQR, interquartile range.

- The intended use of this MCED test is for screening in an asymptomatic population, for which the empirical PPV (ePPV) was 49.4% (95% CI: 43.2-55.7%) and the median time to diagnosis was 43 days (IQR: 20-94) in this analysis (**Figure 1**)
  - For this real-world dataset where the status of some patients remains unknown, ePPV is reported in place of a formal, clinical PPV
- A wide range of distinct cancer types (N=32) were diagnosed (**Figure 2**)
- The majority of cancers diagnosed (74% [182/247]) have no USPSTF grade A/B–recommended screening (ie, cancer types other than breast, colon/rectum, cervix, or lung)
- Clinically significant cancers were diagnosed, with cancer stage information reported in 124 cancers from 122 patients (**Table 2**)
  - Some individuals had cancer-associated symptoms when they took the MCED test, which biases toward late-stage detection
  - The current data reflect individuals undergoing their first MCED screening (prevalence round), where later-stage cancer diagnoses are likely to be more common because no previous screening has been done; for example, a preliminary analysis of patients with year-over-year MCED testing found a higher percentage of stage I diagnoses compared with patients taking their first test[7]

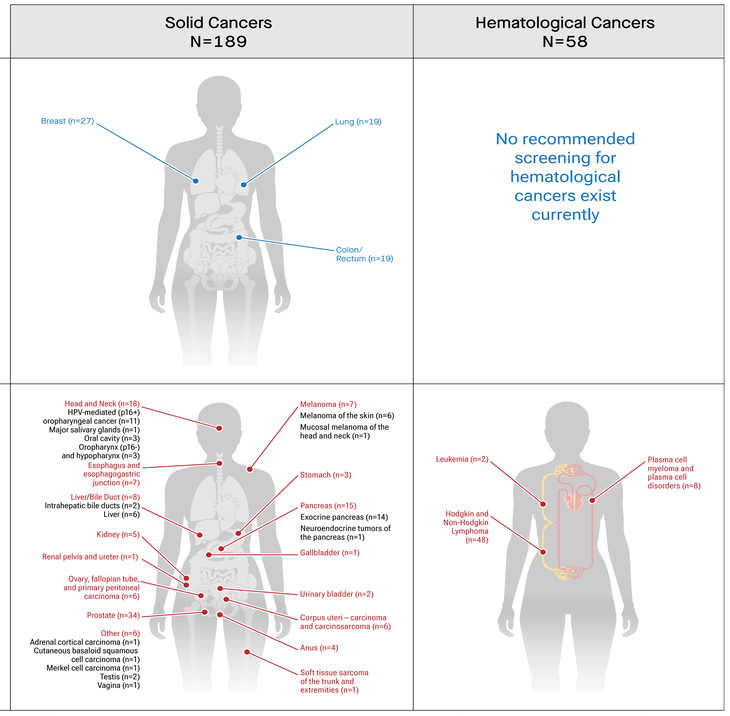
**Table 2. Cancer Stage at Diagnosis Differed Between Patients With and Without Cancer-Associated Symptoms at the Time of MCED Testing.**

| | Asymptomatic (n/N) | Symptomatic (n/N) | All Patients[a] (n/N) |
|---|---|---|---|
| Stages I to III | 63% (43/68) | 38% (9/24) | 52% (65/124) |
| Stage IV | 37% (25/68) | 62% (15/24) | 48% (59/124) |

Cancer stage information was voluntarily reported by healthcare providers. For patients with an available cancer type, cancer stage was reported for 124 cancers.
[a]Including patients with active cancer.

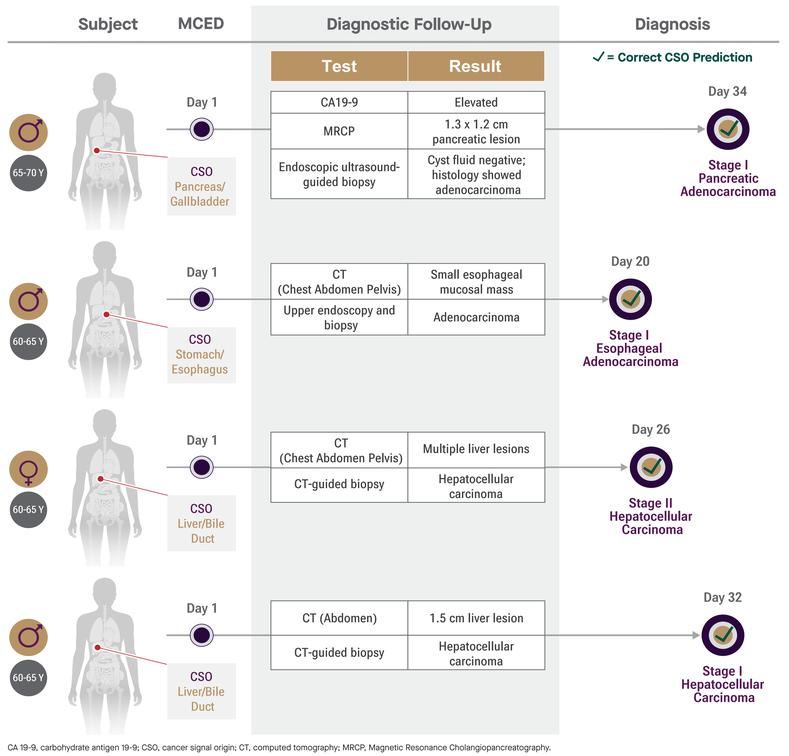
- The overall real-world CSO prediction accuracy was 87% (207/237) across the 19 different CSO categories in this dataset, comparable to previous clinical studies (CCGA: 88.7% [1273/1435][8]; PATHFINDER: 84% [21/25][6])
- The prediction accuracy of individual CSOs (ie, the proportion of each CSO prediction with a matching clinical diagnosis) ranged between 82% and 97%
- In this real-world dataset, detailed information on diagnostic workups was not typically available; however, examples of patient diagnostic journeys following a positive MCED test with CSO prediction are illustrated in **Figure 3**

**Figure 2. 32 Distinct Cancer Types were Diagnosed Following a Positive MCED Test Result, Most Without Recommended Screening Options.**




Among the 258 patients with a positive MCED test and cancer diagnosis, 247 cancers had sufficient clinical detail to identify cancer type as defined by AJCC. Cancers are indicated by organ location and AJCC notation. When multiple AJCC types correspond to the same organ location, each type is listed in black under the location header. Cancers with existing USPSTF grade A/B screening recommendation are denoted in blue, and cancers without existing USPSTF grade A/B recommended screening are denoted in red.
AJCC, American Joint Committee on Cancer; USPSTF, HPV, Human Papillomavirus; United States Preventive Services Task Force.

**Figure 3. Clinical Workup Examples: Patients With Early-Stage Cancer and Rapid Diagnosis Following a Positive MCED Test Result.**




CA 19-9, carbohydrate antigen 19-9; CSO, cancer signal origin; CT, computed tomography; MRCP, Magnetic Resonance Cholangiopancreatography.

## CONCLUSIONS

- These real-world data illustrate the MCED test's capacity to identify cancer in asymptomatic and symptomatic individuals, already detecting cancer across 32 distinct cancer types in this early phase of commercial clinical use
  - Many late-stage cancers are expected to be found during the first round of MCED screening, as there was no previous screening that would have caught these cancers early; despite this, many early-stage, unscreened for cancers were detected in the real-world population
- The MCED test facilitated clinically significant cancer diagnoses, supported by accurate CSO predictions, which were correct 87% of the time and enabled prompt and efficient diagnostic evaluations
- For asymptomatic screening, 49% of the positive MCED test results led to a confirmed cancer diagnosis following a comprehensive diagnostic workup; for patients with possible cancer symptoms, this rate increased to 75%, consistent with the PPV reported in the SYMPLIFY study of this MCED test in symptomatic patients[9]
  - These diagnostic rates for patients with provider-reported clinical outcomes reveal a PPV that is 7 to 10 times higher than the PPV reported for approved single-cancer screening tests for asymptomatic, recommended populations in the US, such as mammography, fecal immunochemical test, and low-dose computed tomography[10-13]
- Collectively, this real-world experience underscores the potential of MCED testing to broaden the spectrum of cancers detected earlier than the onset of symptoms, while maintaining a low false positive rate when integrated with existing recommended screening protocols in clinical practice

### References

1. Siegel RL et al. *CA Cancer J Clin*. 2024;74(1):12-49.
2. Siu AL et al. *Ann Intern Med*. 2016;164(4):279-296.
3. US Preventive Services Task Force et al. *JAMA*. 2016;320(7):674-686.
4. US Preventive Services Task Force et al. *JAMA*. 2021;325(10):962-970.
5. Oman J et al. *Cancer Biomark*. 2025;42(1).
6. Schrag D et al. *Lancet*. 2023;402(10409):1251-1260.
7. Abrams R et al. *Cancer Res*. 2024;84(6_Supplement):3891.
8. Klein EA et al. *Ann Oncol*. 2021;32(9):1167-1177.
9. Nicholson BD et al. *Lancet Oncol*. 2023;24(7):733-743.
10. Lehman CD et al. *Radiology*. 2017;283(1):49-58.
11. Pinsky PF et al. *Ann Intern Med*. 2015;162(7):485-491.
12. Pickhardt PJ et al. *Am J Roentgenol*. 2021;217(4):817-830.
13. Bakey SER et al. *Br J Cancer*. 2021;124(7):1231-1236.

### Disclosures

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