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Impact of Multicancer Early Detection (MCED) Test on Participant-Reported Outcomes and Behavioral Intentions by Cancer Risk

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INTRODUCTION

- Despite its benefits, cancer screening may be associated with adverse psychosocial patient impacts[1]
- Individuals with a higher risk of cancer may experience greater levels of anxiety, distress, or worry during or after cancer screening[1,2]; these negative feelings may impact adherence to future screening[3]
- Newly developed multi-cancer early detection (MCED) tests can detect a cancer signal shared across multiple cancer types using a single blood test, potentially allowing for the diagnosis of cancers with no routine screening at earlier stages, when treatment is more effective[4]
- However, the value of MCED tests may be affected by perceptions and behavioral intentions following MCED testing, which may lead patients to avoid or delay routine screening
- The recent PATHFINDER study evaluated the implementation of an MCED test[5] and assessed the impact of MCED testing on participants' mental well-being and their intentions to undergo future cancer screening

OBJECTIVE

- Assess the impact of MCED testing on patient-reported outcomes and intention to undergo future screening in the PATHFINDER study population stratified by cancer risk

CONCLUSIONS

- Overall, participants reported high test satisfaction and there was a low impact of MCED testing on levels of distress and uncertainty
- No significant difference in the impact of MCED testing on mental health was observed between participants with or without additional cancer risk
- While levels of psychological distress were higher in those with a cancer signal detected relative to those without a signal detected, the level of impact was low for both groups
- As participants were part of a clinical trial, the MCED test was made available at no cost; out-of-pocket costs may impact participants' willingness to undergo MCED testing in a real-world setting
- Regardless of cancer risk status, the vast majority of participants indicated their intention to follow their healthcare provider's cancer screening recommendations following MCED testing, even with a no cancer signal detected result, as well as a willingness to undergo subsequent MCED testing

References

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Disclosures

CHM is a consultant for GRAIL, Inc; EAK is an employee of GRAIL, Inc; CRM serves an advisory role with Exact Sciences and is a consultant with Natera; LN owns stock in Culmination Bio; KCC owns stock in Illumina, Bristol Myers Squibb, Gilead, Baxter, and Bayer, and is a former employee of GRAIL, Inc. ETF and ML own stock in Illumina and are employees of GRAIL, Inc. DS acts in an uncompensated advisory role and is a study investigator at the Dana Farber Cancer Institute (GRAIL, Inc) and receives fees for editorial service (*JAMA*). All other authors declare no competing interests. Presenting author email: dilaveri.christina@mayo.edu

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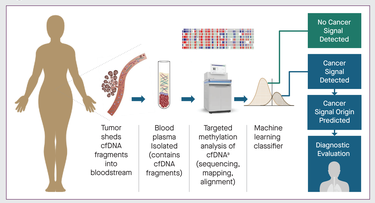
METHODS

- The prospective PATHFINDER study (NCT04241796) enrolled 6662 adults aged ≥50 years into 2 cohorts:
  1. Without additional cancer risk
  2. With additional cancer risk
- Additional cancer risk participants had ≥1 factor:
  - ≥100 cigarette smoking history
  - Germline/hereditary cancer high risk
  - Prior cancer ≥3 years before enrollment
- After the blood draw and processing, participants were notified whether or not a cancer signal was detected (**Figure S1**)
- To assess patient-reported outcomes, participants were asked to complete a variety of questionnaires, including the following:
  - Adapted Multidimensional Impact of Cancer Risk Assessment (MICRA) assessed at test result disclosure
    - The MICRA is a previously validated instrument that assessed different levels of impact of genetic test result disclosure[6,8]
    - The MICRA was adapted to measure the impact of result disclosure after MCED testing (instead of genetic testing) and consisted of 21 items addressing 3 domains (distress, uncertainty, and positive experience) and a total score
    - Score ranges are:
      - Total 0–95: a total score of 19 corresponds to an average response of 1 (rarely experiencing a negative emotion) on the MICRA (higher scores reflect increased psychological distress, uncertainty, or less positive experience)
      - Distress 0–30
      - Uncertainty 0–45
      - Positive experience 0–20
  - The Short Form 12-Item Health Survey (SF-12v2) Mental Component Summary assessed mental health
  - A 3-item questionnaire measured satisfaction:
    - Overall, how confident are you that this MCED test is a good thing for you?
    - How certain are you that the good things about the MCED test outweigh the bad things?
    - Taking all things into account, how satisfied are you with the MCED test?
  - Two de-novo single-item questions assessing intention towards future testing (listed in Results)
- Assessments were administered at 4 timepoints:
  - Baseline - Pre-test
  - Return of results - Within 2 months (or 61 days) of baseline assessment and before diagnostic resolution in those with a cancer signal detected
    - Attitude towards adherence to guideline-recommended screening was assessed only in participants with no cancer signal detected results at this timepoint
  - Diagnostic resolution - Within 2 months (or 61 days) of diagnostic resolution in those with a cancer signal detected or within 3 months of the end of study time point
  - End of study - 12 months after MCED test
- Descriptive statistics were generated for patient-reported outcome endpoints; *p*-values after Hochberg adjustment were reported for descriptive purposes

Figure S1. MCED Test Work Flow and Output



cfDNA, cell free DNA; MCED, multi-cancer early detection.
*Bisulfite treatment, targeted probes pull out fragments matching regions of interest.
Adapted from Liu MC, et al. Ann Oncol. 2020;31(6):745-759.

KEY RESULTS: PARTICIPANTS REPORTED LOW IMPACT OF MCED TESTING ON MENTAL HEALTH REGARDLESS OF SIGNAL DETECTION STATUS OR CANCER RISK AND INDICATED A HIGH LIKELIHOOD OF FOLLOWING THEIR HEALTHCARE PROVIDER'S CANCER SCREENING RECOMMENDATIONS

Patient Population

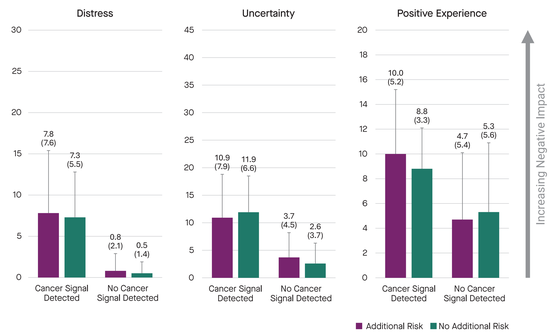
- Just over half of the 6621 evaluable participants in the PATHFINDER study were female and a majority identified as White (**Table 1**)
  - The MCED test detected a cancer signal in 1.4% (92/6621) of PATHFINDER participants, 60.9% (56/92) had additional risk for cancer
  - 44.5% (2904/6529) of participants with no cancer signal detected had additional cancer risk

Table 1. PATHFINDER Study Population Demographics

	Cancer Signal Detected		No Cancer Signal Detected	
	Additional Risk (n=56)	No Additional Risk (n=36)	Additional Risk (n=3625)	No Additional Risk (n=2904)
Median age, years (IQR)	69.0 (63.0, 76.2)	68.0 (60.5, 72.2)	64.0 (58.0, 71.0)	60.0 (55.0, 67.0)
Sex, female (%)	29 (51.8)	20 (55.6)	2364 (65.2)	1791 (61.7)
BMI, mean (SD)	28.8 (5.8)	29.2 (7.0)	28.7 (6.2)	28.1 (6.0)
Race/Ethnicity, n (%)				
American Indian or Alaska Native	0	0	5 (0.1)	5 (0.2)
Asian, Native Hawaiian or Pacific Islander, non-Hispanic	0	0	39 (1.1)	90 (3.1)
Black, non-Hispanic	0	0	44 (1.2)	46 (1.6)
Hispanic	2 (3.6)	2 (5.6)	64 (1.8)	66 (2.3)
White, non-Hispanic	54 (96.4)	31 (86.1)	3387 (93.4)	2599 (89.5)
Other/unknown/missing	0	3 (8.3)	86 (2.4)	98 (3.4)
Prior cancer history, n (%)	33 (58.9)	0	1589 (43.8)	0
Smoking history, n (%)	32 (57.1)	0	2465 (68.0)	0
Genetic cancer predisposition, n (%)	2 (3.6)	0	423 (11.7)	0

Patient-Reported Outcomes

Figure 2. Adapted MICRA Results by MCED Signal Detection Status and Cancer Risk at Results Disclosure

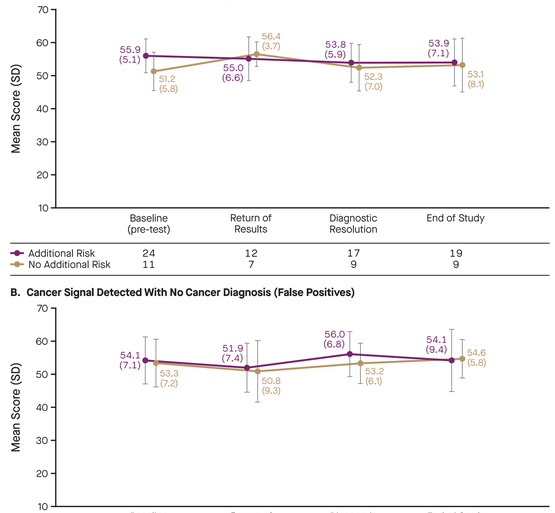


MICRA scores are reported as mean (SD).
For MICRA, Distress/uncertainty scores of 6/8 = "rarely" experiencing negative emotion; scores of 18/24 = "sometimes" experiencing negative emotion.
MCED, multi-cancer early detection; MICRA, Adapted Multidimensional Impact of Cancer Risk Assessment; SD, standard deviation.

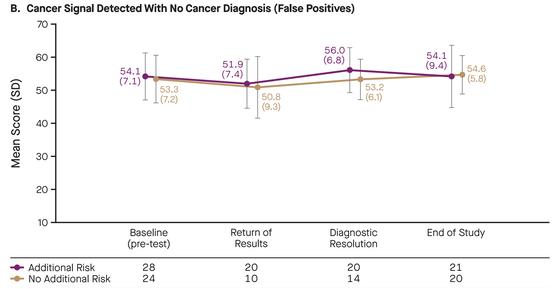
- Among participants with a cancer signal detected, those with additional cancer risk did not report significantly different levels of distress (adjusted *p*=0.825), uncertainty (adjusted *p*=0.825), or positive experience (adjusted *p*=0.825) following MCED test result disclosure compared to those with no additional cancer risk (**Figure 2**)
- Across all three MICRA domains for participants with no cancer signal detected, the differences among those with or without additional cancer risk were relatively small in magnitude but statistically significant (adjusted *p*<0.001 for each domain; **Figure 2**) due to large sample size in these subgroups

Figure 3. Mental Health Impact of MCED Testing by Risk Cohort (SF-12v2 Mental Component Summary Score)

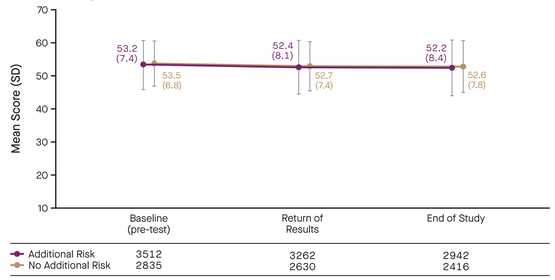
A. Cancer Signal Detected With Cancer Diagnosis (True Positives)



B. Cancer Signal Detected With No Cancer Diagnosis (False Positives)



C. No Cancer Signal Detected



SF-12v2 Mental Component Summary Scores reported as mean (SD).
Higher scores indicate better health in SF-12v2.
SD, standard deviation.

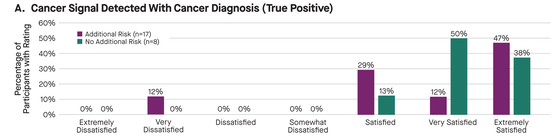
- No notable differences were observed in mental health impact between cancer risk cohorts by cancer signal detection status, regardless of whether cancer was diagnosed at resolution (**Figure 3**)

Satisfaction and Future Intention Toward Screening

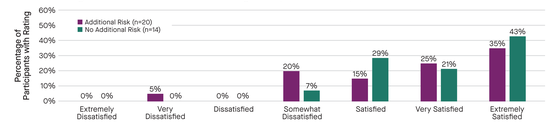
- Among participants with a cancer signal detected, mean total satisfaction scores were comparable between participants with additional cancer risk (74.0, SD=28.4 [n=22]) and those without additional risk (80.8, SD=21.3 [n=37]; adjusted *p*=0.3)
- Conversely, for participants with no cancer signal detected, the mean total satisfaction score was slightly lower for participants with additional cancer risk (82.9, SD=16.9 [n=3243] compared to those without additional cancer risk (84.0, SD=16.5 [n=2618]; adjusted *p*=0.026)

Figure 4. Distribution by Signal Detection Status and Cancer Risk for Responses to the Question *"Taking all things into account, how satisfied or dissatisfied are you with the MCED test?"*

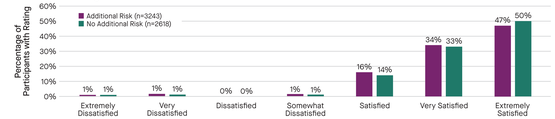
A. Cancer Signal Detected With Cancer Diagnosis (True Positive)



B. Cancer Signal Detected With No Cancer Diagnosis (False Positive)



C. No Cancer Signal Detected



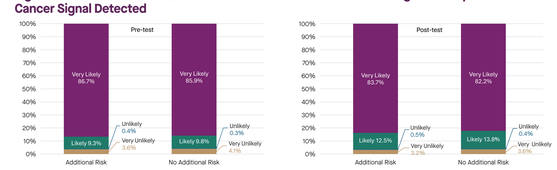
- The majority of participants were satisfied with the MCED test, regardless of signal detection or cancer risk status (**Figure 4**)

Table 2. Percentage of Participants Responding "Likely/Very Likely" to the Question "*How likely are you to follow your healthcare provider's cancer screening recommendations?*" at End of Study

	Additional Risk	No Additional Risk
True Positives[a]	19/19 (100%)	9/9 (100%)
False Positives[b]	21/21 (100%)	20/20 (100%)
No Cancer Signal Detected	2812/2937 (95.7%)	2301/2412 (95.4%)

[a]Participants with a cancer signal detected and cancer diagnosis at resolution. [b]Participants with a cancer signal detected but no cancer diagnosis at resolution.
Results are reported for participants who responded to the questionnaire within the analysis window ≤3 months (91 days) after the questionnaire release for the end of study time point.

Figure 5. Pre- and Post-MCED Test Intentions Toward Future Screening in Participants With No Cancer Signal Detected



- Across both cancer risk cohorts, 95-100% of participants reported that they were likely/very likely to follow their healthcare provider's recommendations (**Table 2**)
- Regardless of cancer risk status, >95% of participants who received a no cancer signal detected result reported that they were likely/very likely to adhere to screening recommendations from their health care providers, both pre-test and after receiving their MCED test result (**Figure 5**)

Table 3. Percentage of Participants who Responded "Likely/Very Likely" to the Question "*How likely are you to undergo a subsequent MCED test?*" post test/diagnostic resolution

	Additional Risk	No Additional Risk
True Positives[a]	16/17 (94.1%)	8/8 (100.0%)
False Positives[b]	18/20 (90.0%)	13/14 (92.9%)
No Cancer Signal Detected	3125/3243 (96.4%)	2499/2616 (95.6%)

[a]Participants with a cancer signal detected and cancer diagnosis at resolution. [b]Participants with a cancer signal detected but no cancer diagnosis at resolution.

- The majority of participants (90-100%) responded that they were likely/very likely to undergo future MCED testing, regardless of signal detection or cancer risk status (**Table 3**)