Effect of Multi-Cancer Early Detection (MCED) Testing on Participant-Reported Outcomes for Mental Health–Related Quality of Life (MHRQoL) in PATHFINDER 2

PCR76

Charles H. McDonnell III,[1] Dax Kurbegov,[2] Karthik V. Giridhar,[3] Kevin C. Oeffinger,[4] Marc R. Matrana,[5] Benjamin Rybicki,[6] Cora N. Sternberg,[7] Raymond H. Kim,[8] Roland Matthews,[9] Alan R. Roth,[10] Raevti Bole,[11] Philip A. Kovoor,[12] Margaret McCusker,[13]* Margarita Lopatin,[13] Anuraag Kansal,[13] Nima Nabavizadeh[14]

[1]Sutter Health Research Institute, Sacramento, CA, USA; [2]HCA Healthcare Sarah Cannon Cancer Network, Nashville, TN, USA; [3]Mayo Clinic, Rochester, MN, USA; [4]Duke University Health System, Durham, NC, USA; [5]Ochsner Clinic Foundation, New Orleans, LA, USA; [6]Henry Ford Health, Detroit, MI, USA; [7]Englander Institute for Precision Medicine, Weill Cornell Medicine, New York, NY, USA; [8]University Health Network, Princess Margaret Cancer Centre, Toronto, Ontario, Canada; [9]Morehouse School of Medicine, Atlanta, GA, USA; [10]Jamaica Hospital Medical Center, Queens, NY, USA; [11]Cleveland Clinic, Cleveland, OH, USA; [12]Texas Oncology-Plano West, Dallas, TX, USA; [13]GRAIL, Inc., Sunnyvale, CA, USA; [14]Oregon Health & Science University, Portland, OR, USA
*At the time of study.

International Society for Pharmacoeconomics and Outcomes Research (ISPOR) Europe
8-11 November 2026
Vienna, Austria

INTRODUCTION

- Multi-cancer early detection (MCED) tests screen for multiple cancer types with a single, minimally invasive test, potentially detecting cancers at early stages when treatment is more effective and potentially curative[1]
- The performance and safety of one blood-based MCED test, which utilizes methylation patterns on cell-free DNA to both detect a shared cancer signal and provide a predicted cancer signal origin,[2,3] has been validated in case-control, interventional, and randomized controlled studies[2-5]
- Although cancer screening tests can be associated with anxiety, distress, and worry, there is evidence that these negative psychological impacts are generally minimal and transient[6]
  - This is consistent with results from the first PATHFINDER study,[7] which found that MCED testing had minimal negative psychological impact as assessed by participant-reported outcomes (PROs)[8]
- The PATHFINDER 2 study (NCT05155605) is a prospective, interventional study evaluating performance and safety of this MCED test[9] and includes PROs to expand the assessment of the psychological impacts of MCED testing
  - A previously published report described a temporary rise in participant-reported anxiety for those with a true-positive MCED test result that returned to baseline levels at the 12-month follow-up timepoint[9]

OBJECTIVE

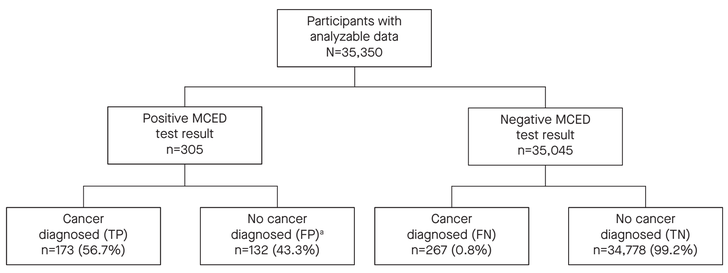
- To investigate participant-reported mental health–related quality of life (MHRQoL) and perceptions of an MCED test following MCED testing in the PATHFINDER 2 study

RESULTS

Demographics and Baseline Characteristics

- A total of 35,350 participants enrolled in PATHFINDER 2 had analyzable data (**Figure 1**)
  - Demographics were generally representative of adults aged 50 years and older in the US population[10] (**Table 1**)

Figure 1. Participant Flow Diagram.



[a]Participants with no 12-month cancer status assessment are included in this count.
FN, false negative; FP, false positive; MCED, multi-cancer early detection; TN, true negative; TP, true positive.

Table 1. Participant Demographics and Baseline Characteristics.

Characteristic	Positive MCED test result n=305	Negative MCED test result n=35,045	Total N=35,350
Age, years, median (IQR)	69.0 (63.0, 75.0)	64.0 (58.0, 70.0)	64.0 (58.0, 70.0)
Age group, years, n (%)			
50-59	34 (11.1)	10,019 (28.6)	10,053 (28.4)
60-69	134 (43.9)	15,415 (44.0)	15,549 (44.0)
70-79	106 (34.8)	8658 (24.7)	8764 (24.8)
≥80	31 (10.2)	953 (2.7)	984 (2.8)
Sex, n (%)			
Female	136 (44.6)	19,741 (56.3)	19,877 (56.2)
Male	169 (55.4)	15,304 (43.7)	15,473 (43.8)
Race (self-reported),[a] n (%)			
American Indian or Alaska Native only	3 (1.0)	243 (0.7)	246 (0.7)
Asian only	19 (6.2)	2072 (5.9)	2091 (5.9)
Black or African American only	31 (10.2)	3074 (8.8)	3105 (8.8)
Native Hawaiian or other Pacific Islander only	0	80 (0.2)	80 (0.2)
White only	241 (79.0)	28,080 (80.1)	28,321 (80.1)
>1 race reported	4 (1.3)	470 (1.3)	474 (1.3)
Missing	7 (2.3)	1026 (2.9)	1033 (2.9)
Ethnicity, n (%)			
Hispanic or Latino	22 (7.2)	2,610 (7.4)	2,632 (7.4)
Not Hispanic or Latino	281 (92.1)	31,993 (91.3)	32,274 (91.3)
Missing	2 (0.7)	442 (1.3)	444 (1.3)
Bachelor's degree or higher, n (%)	153 (50.2)	20,650 (58.9)	20,803 (58.8)
Prior cancer history,[b] n (%)	62 (20.3)	3202 (9.1)	3264 (9.2)
Smoking history, n (%)			
Never smoker	176 (57.7)	24,316 (69.4)	24,492 (69.3)
Former smoker	104 (34.1)	9446 (27.0)	9550 (27.0)
Current smoker	25 (8.2)	1283 (3.7)	1308 (3.7)
BMI category, n (%)			
<25 kg/m^2	95 (31.1)	11,643 (33.2)	11,738 (33.2)
25 to <30 kg/m^2	108 (35.4)	12,648 (36.1)	12,756 (36.1)
≥30 kg/m^2	100 (32.8)	10,657 (30.4)	10,757 (30.4)
Missing	2 (0.7)	97 (0.3)	99 (0.3)
Presence of genetic cancer predisposition, n (%)	17 (5.6)	2030 (5.8)	2047 (5.8)

[a]Race categories that are reported alone or as part of multiple race categories (not mutually exclusive).
[b]Non-metastatic basal cell carcinoma and squamous cell carcinoma of the skin are not included.
IQR, interquartile range; MCED, multi-cancer early detection.

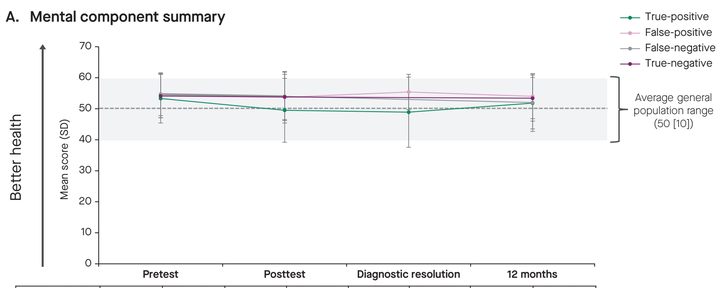
KEY RESULTS: MCED TESTING HAS MINIMAL AND TRANSIENT NEGATIVE PSYCHOLOGICAL IMPACTS ON PARTICIPANTS

Short Form 12-Item Health Survey Version 2 (SF-12v2) Mental Component Summary (MCS) Scores

- All mean SF-12v2 MCS and MCS subscale scores remained within the average general population range at all timepoints analyzed regardless of MCED test result status (**Figure 2**)
  - Among participants with true-positive MCED test results, mean scores were lower posttest and at the time of diagnostic resolution compared with pretest and increased toward baseline levels by 12 months

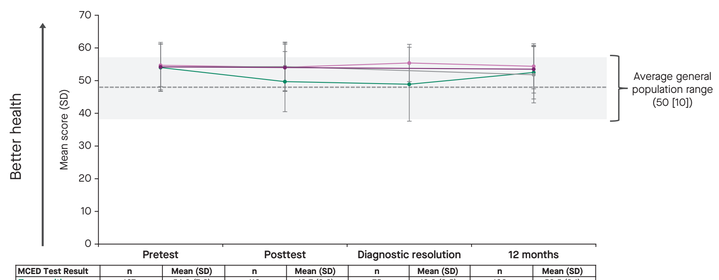
Figure 2. Short Form 12-Item Health Survey (SF-12v2) Mental Component Summary and Subscale Scores.

A. Mental component summary



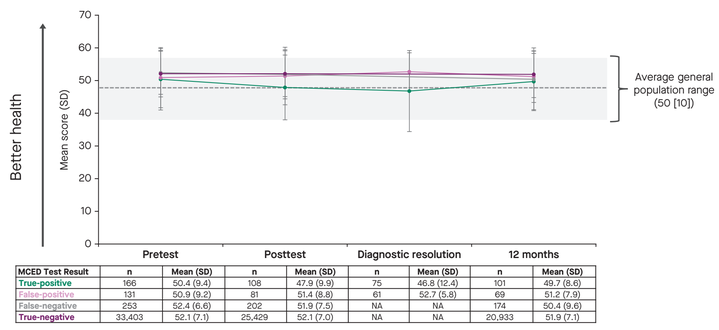
MCED Test Result	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)
True-positive	166	53.3 (7.9)	108	49.5 (10.3)	74	48.9 (11.3)	101	51.8 (8.3)
False-positive	129	54.2 (7.1)	81	53.7 (8.3)	61	55.4 (5.7)	69	54.0 (7.2)
False-negative	250	54.7 (6.9)	201	54.0 (7.8)	NA	NA	173	52.0 (9.3)
True-negative	33,218	54.1 (7.0)	25,334	53.8 (7.3)	NA	NA	20,849	53.4 (7.4)

B. Mental Health Subscale



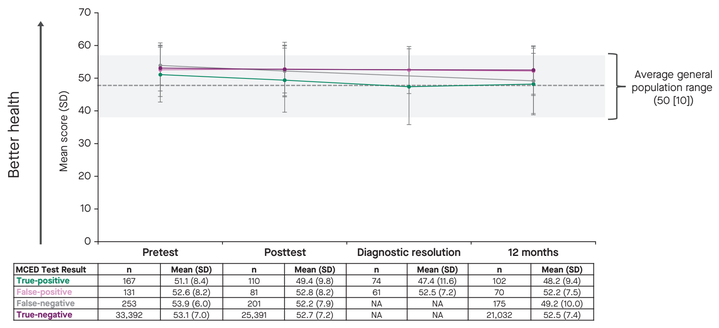
MCED Test Result	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)
True-positive	167	54.0 (7.2)	110	49.7 (9.2)	75	49.9 (9.5)	102	52.5 (8.1)
False-positive	131	54.7 (6.5)	81	54.1 (7.4)	61	55.4 (6.5)	69	54.4 (6.9)
False-negative	253	54.2 (7.5)	202	54.3 (7.5)	NA	NA	175	51.8 (8.6)
True-negative	33,391	54.2 (7.0)	25,393	54.0 (7.1)	NA	NA	21,029	53.5 (7.3)

C. Role-Emotional Subscale



MCED Test Result	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)
True-positive	166	50.4 (9.4)	108	47.9 (9.9)	75	46.8 (12.4)	101	49.7 (8.6)
False-positive	131	50.9 (9.2)	81	51.4 (8.8)	61	52.7 (5.8)	69	51.2 (7.9)
False-negative	253	52.4 (6.6)	202	51.9 (7.5)	NA	NA	174	50.4 (9.6)
True-negative	33,403	52.1 (7.1)	25,429	52.1 (7.0)	NA	NA	20,933	51.9 (7.1)

D. Social Functioning Subscale



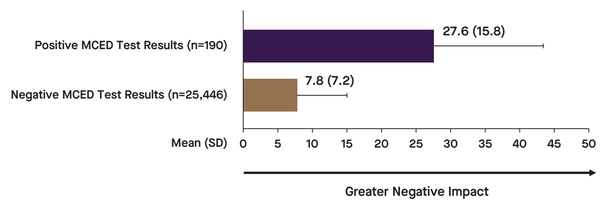
MCED Test Result	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)
True-positive	167	51.1 (8.4)	110	49.4 (9.8)	74	47.4 (11.6)	102	48.2 (9.4)
False-positive	131	52.6 (8.2)	81	52.8 (8.2)	61	52.5 (7.2)	70	52.2 (7.5)
False-negative	253	53.9 (6.0)	201	52.2 (7.9)	NA	NA	175	49.2 (10.0)
True-negative	33,392	53.1 (7.0)	25,391	52.7 (7.2)	NA	NA	21,032	52.5 (7.4)

The average score (with standard deviation) for the general population is noted with a dashed line and the general population range is noted in grey. The n values for each group at each timepoint are provided in the table below the graph. As participants with negative MCED test results did not undergo a diagnostic workup triggered by the MCED test, an assessment at diagnostic resolution was not completed for participants with false-negative or true-negative MCED test results.
MCED, multi-cancer early detection; NA, not assessed; SF-12v2, Short Form 12-Item Health Survey.

Multidimensional Impact of Cancer Risk Assessment (MICRA) Scores

- Posttest MICRA scores were higher for participants with positive versus negative MCED test results, indicating that disclosure of a positive MCED test result had a greater negative psychosocial and emotional impact (**Figure 3**)
  - For context, scores for participants with positive MCED test results were similar to those of individuals who had pathogenic variants detected during germline genetic testing; scores for participants with negative MCED test results were lower than those of individuals with no genetic variants identified[11]

Figure 3. Adapted MICRA Scores Posttest, Mean (SD).



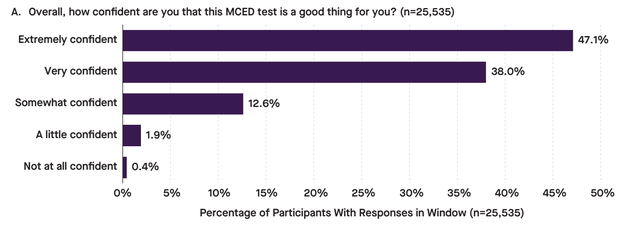
MCED, multi-cancer early detection test; MICRA, Multidimensional Impact of Cancer Risk.

MCED Test Satisfaction and Attitudes Toward Future MCED Testing

- Among participants with responses within the analysis window, the majority were confident that the MCED test was a good thing for them (**Figure 4A**) and were certain that the good things about the MCED outweighed the bad (**Figure 4B**)
- Over 95% of participants were satisfied with MCED testing (**Figure 4C**), and 94.6% indicated they were likely/very likely to undergo subsequent MCED testing (**Figure 4D**)

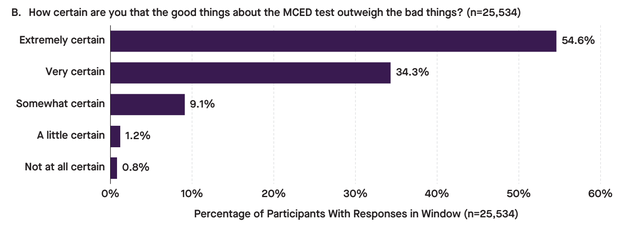
Figure 4. Single-Item Questions Measuring MCED Test Satisfaction and Attitudes Toward Testing.[a]

A. Overall, how confident are you that this MCED test is a good thing for you? (n=25,535)



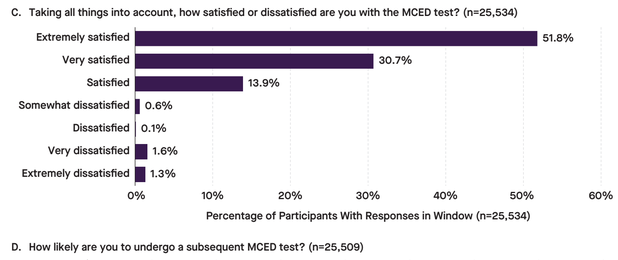
85.1% of participants felt extremely/very confident that the MCED test was a good thing for them

B. How certain are you that the good things about the MCED test outweigh the bad things? (n=25,534)



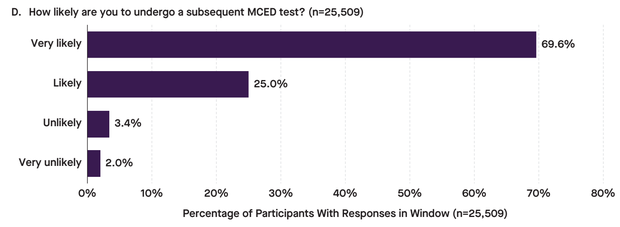
88.9% of participants felt extremely/very certain that the good things about the MCED test outweighed the bad

C. Taking all things into account, how satisfied or dissatisfied are you with the MCED test? (n=25,534)



96.4% of participants were satisfied with MCED testing

D. How likely are you to undergo a subsequent MCED test? (n=25,509)



94.6% of participants indicated they were likely/very likely to undergo subsequent MCED testing

[a]Single-item questionnaires measuring MCED test satisfaction and attitudes toward future testing were administered posttest for participants with a negative MCED test result and at diagnostic resolution for those with a positive MCED test result. Questionnaires were required to be filled out within 2 months (61 days) after questionnaire release. Questionnaires completed outside of these windows are considered to be 'out of window' and not included in the analysis. Questionnaires will be considered to be filled out at a 'Different timepoint' and not included in the analysis if they were completed in the time interval not intended for a given timepoint, for example, if a pretest questionnaire was filled out after the test result was communicated.
MCED, multi-cancer early detection test.

CONCLUSIONS

- MCED testing had a generally minimal impact on the MHRQoL of participants in the PATHFINDER 2 study, with all SF12-v2 MCS mean scores remaining within the average general population range
  - Participants with true-positive MCED test results experienced a small decrease in SF12-v2 MCS mean scores, which improved by 12 months in a pattern consistent with published studies of single-cancer screening program participants
- Although posttest MICRA scores of participants with a positive MCED test result indicated a greater negative psychological impact compared to participants with a negative MCED test result, it is impossible to separate out the impact of the MCED test result from the impact of a cancer diagnosis
- Approximately 95% of participants indicated they were satisfied with MCED testing and were likely to undergo subsequent MCED testing in the future
- An important limitation of these findings is that questionnaire completion rates for all of these instruments tended to decrease over time and were generally lower in participants with a positive MCED test result; however, these patterns are consistent with previously published reports[12]
- Overall, PRO data from the PATHFINDER 2 study support the minimal and transient nature of negative psychological impacts as a result of MCED testing

References

1. Loud JT, et al. *Semin Oncol Nurs.* 2017;33(2):121-128. **2.** Klein EA, et al. *Ann Oncol.* 2021;32(9):1167-1177. **3.** Liu MC, et al. *Ann Oncol.* 202031(6):745-759. **4.** Jamshidi A, et al. *Cancer Cell.* 2022;40(12):1537-1549.e12. **5.** Neal, RD. et al. *Cancers.* 2022;14(19):4818. **6.** Kim A, et al. *BMC Cancer.* 2022;22(1):223. **7.** Schrag D, et al. *Lancet Oncol.* 2023;402(10409):1251-1260. **8.** Nadauld L, et al. *Lancet Oncol.* 2025;26(2):165-174. **9.** Nabavizadeh N et al. *Nat Med.* 2026; https://doi.org/10.1038/s41591-026-04618-w. **10.** Gadgeel S, et al. *Cancer Epidemiol Biomarkers Prev.* 2025;34(9_Supplement):C145-C145. **11.** Culver JO, et al. *Cancer.* 2021;127(8):1275-1285. **12.** Wang K, et al. *BMJ Open.* 2020;10(8):e030808. **13.** Bhandari NR, et al. *Res Social Adm Pharm.* 2018;14:1080-1084. **14.** MICRA: Multidimensional Impact of Cancer Risk Assessment. FACIT group. Accessed September 1, 2026. https://www.facit.org/measures/micra. **15.** Atkinson MJ, et al. *Health Qual Life Outcomes.* 2004;2:12.

Disclosures

Study funded by GRAIL, Inc. **MM**, **ML**, and **AK** are current or former employees of GRAIL, Inc., with equity in the company. **CM** has served in a consulting/advisory role for GRAIL. DK is an employee of HCA Healthcare and holds stock in the company. **KVG** has served in a consulting/advisory role for Lilly, Onviv, Novartis, Medscape, Clinical Education Alliance, Quantum Leap Healthcare Collaborative, GRAIL, Conexiant, and Association for Molecular Pathology and received travel expenses from GRAIL. **KCO** has served in a consulting/advisory and leadership role for Maia Oncology and holds stock in the company. **MRM** is an employee of Ochsner Health; has served in a consulting/advisory role for AstraZeneca and Tempus; and has served on a speakers bureau for Bristol Myers Squibb, AstraZeneca, Merck, Eisai, Genentech, Janssen, Exelixis, Seagen, and Daiichi Sankyo/Lilly. **CNS** reports grants and personal fees from Astellas and Pfizer. **NN** has served in a consulting/advisory role for GRAIL and Exact Sciences and has received honoraria from Roche Diagnostics and MJH Life Sciences. The remaining authors have nothing to disclose.

Acknowledgements

Funded by GRAIL, Inc. Medical writing support was provided by Samantha Watry, PharmD, for Citrus Health Group, Inc. (Chicago, IL) and was funded by GRAIL, Inc.

METHODS

- PATHFINDER 2 is a multicenter, prospective, interventional study that enrolled participants aged ≥50 years without clinical suspicion of cancer
  - A blood sample was drawn from each participant for MCED testing, and participants were actively followed for 3 years to assess cancer status and utilization of standard-of-care cancer screening tests on an annual basis
- Endpoints evaluating MHRQoL included SF-12v2 MCS and subscales,[13] an adapted MICRA questionnaire,[14] and single-item questions[15] (**Table 2**)
- True-positive, false-positive, true-negative, and false-negative MCED test results were defined using cancer status at 12 months after blood draw
- All statistical analyses for endpoints reported in this analysis were descriptive

Table 2. Description of Endpoints and Timepoints Evaluated.

Test	Description	Timepoints Evaluated			
		Pretest	Posttest	Diagnostic resolution	12 months post-enrollment
SF-12v2 MCS and subscales	The SF-12v2 MCS measures overall mental health status and includes the following subscales: vitality, social functioning (i.e., limitations in social functioning), role participation with emotional health problems (role-emotional), and mental health	✓	✓	✓[a]	✓
Adapted MICRA	The MICRA was adapted to measure impacts of MCED test result disclosure and is composed of 21 items addressing 3 domains (distress, uncertainty, positive experience) and a total score; 4 conditional items from the original MICRA relating to parenthood and prior cancer were excluded. A higher score indicated a higher level of distress and uncertainty and a lower level of positive experience		✓		
MCED test satisfaction questionnaires	Single-item questionnaires measuring MCED test satisfaction and attitudes toward future testing		✓[b]	✓[c]	

[a]Only administered at diagnostic resolution for participants with positive MCED test results.
[b]Administered posttest for participants with a negative MCED test result.
[c]Administered at diagnostic resolution for participants with a positive MCED test result.
MCED, multi-cancer early detection; MICRA, Multidimensional Impact of Cancer Risk Assessment; SF-12v2 MCS, Short Form 12-Item Health Survey, Mental Component Summary.

Digital Poster