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# Detecting a Cancer Signal Using a Multi-Cancer Early Detection (MCED) Test

Circulating Cell-free Genome Atlas (CCGA) Substudy 3: Clinical Validation[1]

CCGA: Prospective, observational, case-control study divided into 3 substudies for discovery, training, and validation[2]

**15,254 participants from 142 sites[2]**
56% with cancer
44% without cancer

**Blood samples**
All participants

**Tissue samples**
Participants with cancer only

**MCED Test result**

**Follow-up**
for 5 years
(vitals & cancer status)

## CCGA3: Cancer Signal Detection[1]

### Specificity 99.5%
(95% CI: 99.0–99.8%)

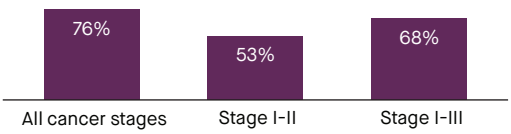
0.5% false-positive rate in participants without cancer

### PPV 44.4%*
(95% CI: 28.6–79.9%)

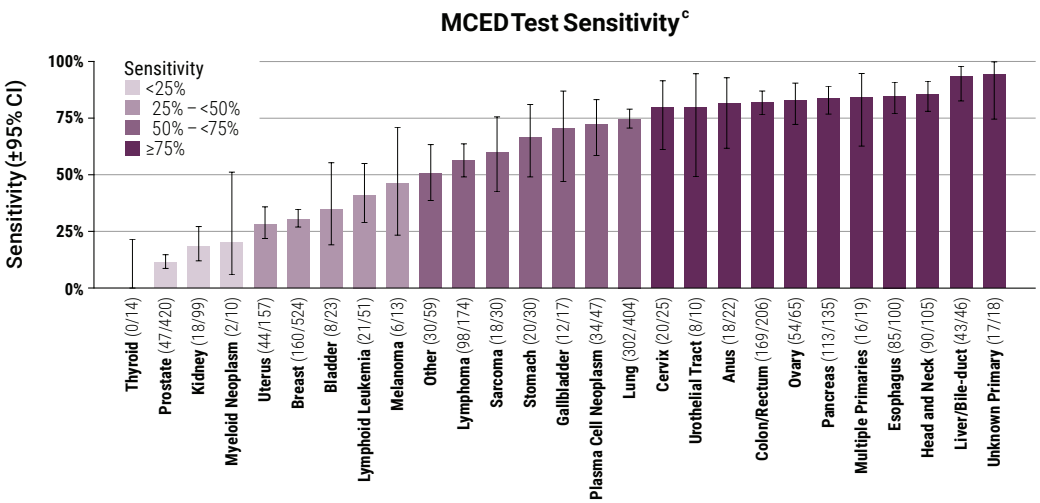
*Estimated value (adjusted to SEER cancer incidence and stage distribution in the 50-79 y age group)[3,a]

### Sensitivity 51.5%
(95% CI: 49.6–53.3%)

Sensitivity of 12 prespecified cancers that account for ~2/3 of US cancer deaths[4,b]



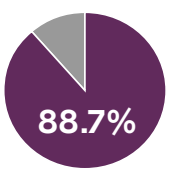

## Diversity of Cancer Signals Detected[1]




### >50 AJCC cancer types[5]

*including a majority* that don't have recommended screenings

## High Accuracy of Predicted Cancer Signal Origin




(95% CI: 87.0–90.2%)

High rate of correctly identified Cancer Signal Origins across multiple cancer types, giving you a roadmap for where to explore further

**Clinical validation supports use of this MCED test in a clinical setting** in addition to single-cancer screening tests in **adults with elevated cancer risk (such as being 50+ years of age.)**

MCED tests do not detect a signal for all cancers and not all cancers can be detected in the blood. False positive and false negative results do occur.

# Adverse Events[1]

**0 serious AEs**

related to blood draw

**0.4%**

participants (20/5309) with AEs related to blood draw


Participants by highest-grade AE

# Overview of CCGA Substudies

## Samples divided among 3 pre-specified CCGA substudies[1]

### CCGA 1

**Discovery[6]**

**Whole Genome Methylation** identified as method for further development (of ten classifiers—using different cfDNA features across three prototype MCED assays)

*Training: n=1785*
*Validation: n=1015*

### CCGA 2

**Assay Refinement and Initial Validation[7]**

**Targeted Methylation** identified key informative methylation regions

**Training and validation of the machine-learning classifier** to differentiate cancer vs non-cancer and predict signal origin

*Training: n=3133*
*Validation: n=1354*

### CCGA 3

**Further Assay Refinement and Clinical Validation[1]**

**Further refined for use** as screening tool

Clinical validation supporting commercial product launch

*n=4077 confirmed status analysis set (cancer=2823; non-cancer=1254)*

[a]Estimated PPV value was adjusted using SEER cancer incidence data[3], as PPV is impacted by population incidence and specificity. PPV in the PATHFINDER study was 43.1%[8].

[b]Anus, Bladder, Colon/rectum, Esophagus, Head and neck, Liver/bile duct, Lung, Lymphoma, Ovary, Pancreas, Plasma cell neoplasm, Stomach.

[c]The graph shows 24 cancer classes plus 3 additional classes (other, unknown primary, and multiple primaries). The 24 cancer classes plus the "other" class used for sensitivity reporting correlate with the >50 AJCC cancer types.

[d]17 participants with 19 mild AEs: dizziness (n=8), bruising (n=2), hematoma and bruising (n=1), lightheaded (n=2), lightheaded and nausea (n=1), feeling warm (n=1). syncope (n=1), multiple attempts for blood draw (n=1).

[e]3 participants with 3 moderate AEs: syncope (n=2) and vasovagal reaction (n=1); 1 participant with syncope also reported a mild AE of vomiting.

Abbreviations: AE: adverse event; AJCC: American Joint Committee on Cancer; CCGA: The Circulating Cell-free Genome Atlas study (1, 2. and 3 indicate substudies); CI: confidence interval; MCED: multi-cancer early detection; PPV: positive predictive value; PSA: prostate specific antigen; SEER: Surveillance, Epidemiology. and End Results Program.

**References**
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