

Efficiency and Safety of Cancer Signal Origin (CSO)-Guided Diagnostic Workups Following Multi-Cancer Early Detection (MCED) Testing: Results from PATHFINDER 2 (PF2)

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DECLARATION OF INTERESTS

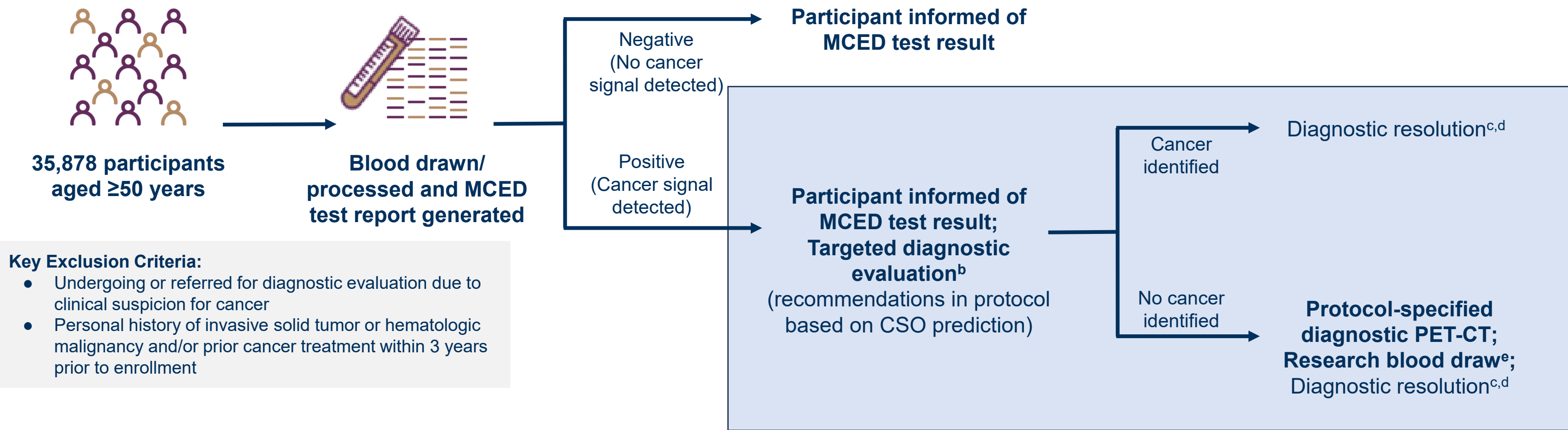
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Presenting author declarations:

- **Employee of HCA Healthcare and holds stock in the company**

PATHFINDER 2^a is the largest prospective, interventional MCED study conducted in North America to date¹



The objective of the present analysis was to describe the efficiency, safety, and resolution of diagnostic evaluations after a positive MCED test result

CSO, cancer signal origin; MCED, multi-cancer early detection; PET-CT, positron emission tomography-computed tomography.

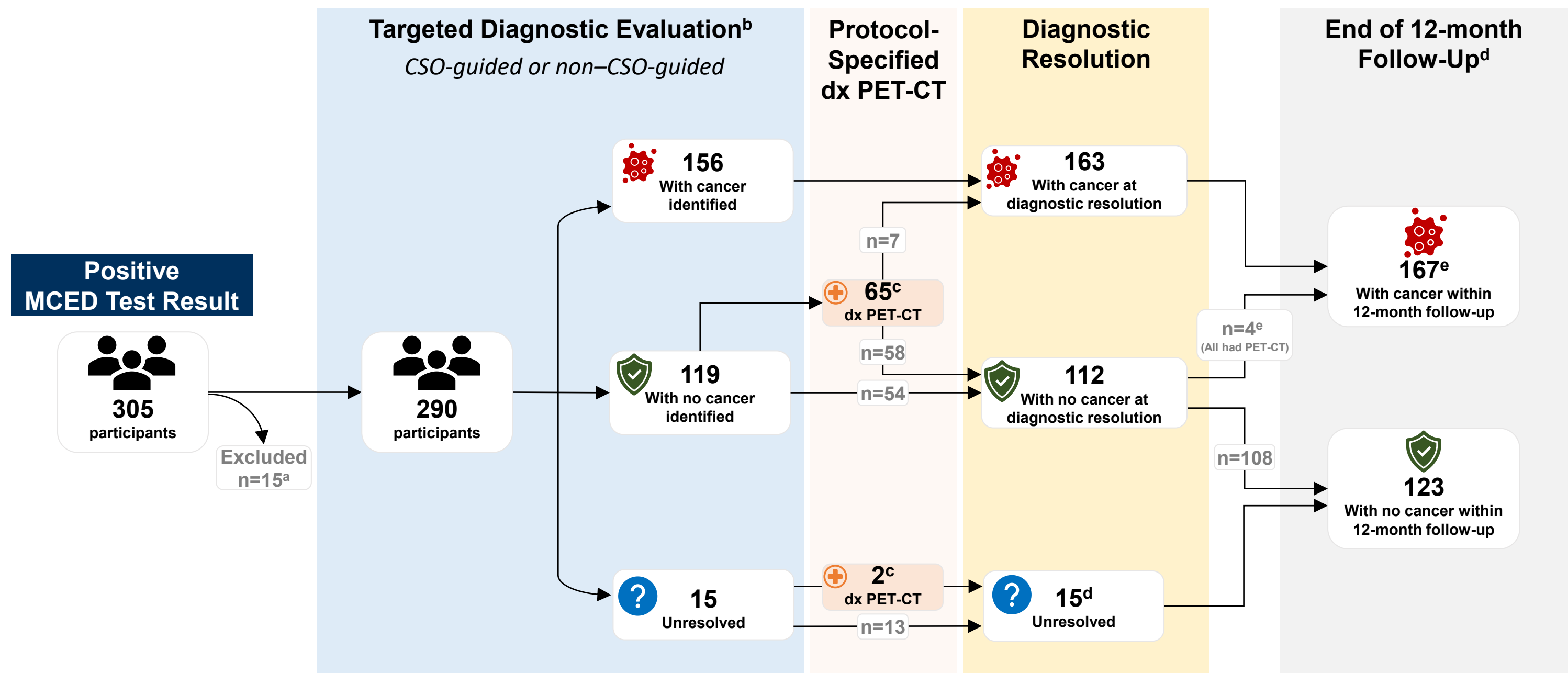
^aNCT05155605. ^bTargeted diagnostic evaluation refers to any initial or subsequent testing performed before the diagnostic PET-CT (if performed) or prior to diagnostic resolution. ^cAll participants are actively followed by enrolling institutions for 3 years to assess cancer status and utilization of cancer screening tests on an annual basis. ^dClinical information including, but not limited to, cancer type, histology, and staging information are collected. ^eResearch blood draw also collected to understand the clinical impact of an MCED retest; results of research blood draw were not returned.

1. Nabavizadeh N, et al. *Nat Med* 2026.

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Of the 305 participants with a positive MCED test result, 290 underwent ≥ 1 diagnostic evaluation

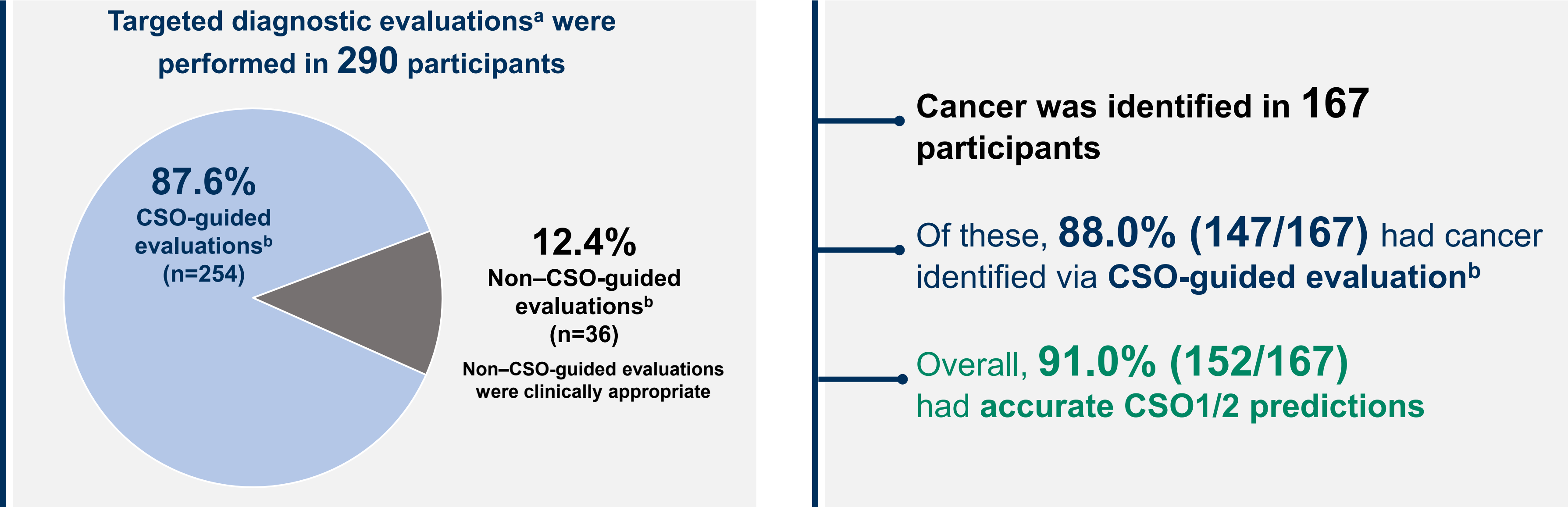


CSO, cancer signal origin top 2 predictions; dx, diagnostic; MCED, multi-cancer early detection; PET-CT, positron emission tomography-computed tomography. ^a15 participants were excluded for either initiation of diagnostic evaluation before communication of MCED test result (11) or no diagnostic evaluation performed after communication of MCED test result, including no communication of test result (4). ^bTargeted diagnostic evaluation refers to any initial or subsequent testing performed before the diagnostic PET-CT (if performed) or prior to diagnostic resolution. ^cDiagnostic PET-CT was performed only after a negative or unresolved targeted diagnostic evaluation. ^dDiagnostic resolution was not achieved within 12 months (Unresolved) for 15 participants, and they were counted in the no cancer within 12-month follow-up group. ^eFour participants had no cancer diagnosis at diagnostic resolution and were subsequently diagnosed with cancer during the remainder of the 12-month follow-up period. All 4 had undergone PET-CT during their diagnostic journey: 2 during targeted diagnostic evaluation and 2 as diagnostic PET-CT after a negative targeted diagnostic evaluation.

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Most evaluations were CSO-guided, most cancers were identified through CSO-guided evaluations, and CSO predictions were accurate



CSO1/2, cancer signal origin top 2 predictions.
^aTargeted diagnostic evaluation refers to any initial or subsequent testing performed before the diagnostic PET-CT (if performed) or prior to diagnostic resolution. ^bEvaluations were classified as CSO-guided when consistent with the diagnostic testing recommended for the predicted CSO(s) in the study protocol, and as non-CSO-guided when inconsistent. The protocol strongly encouraged CSO-guided evaluation unless clinical circumstances dictated otherwise.

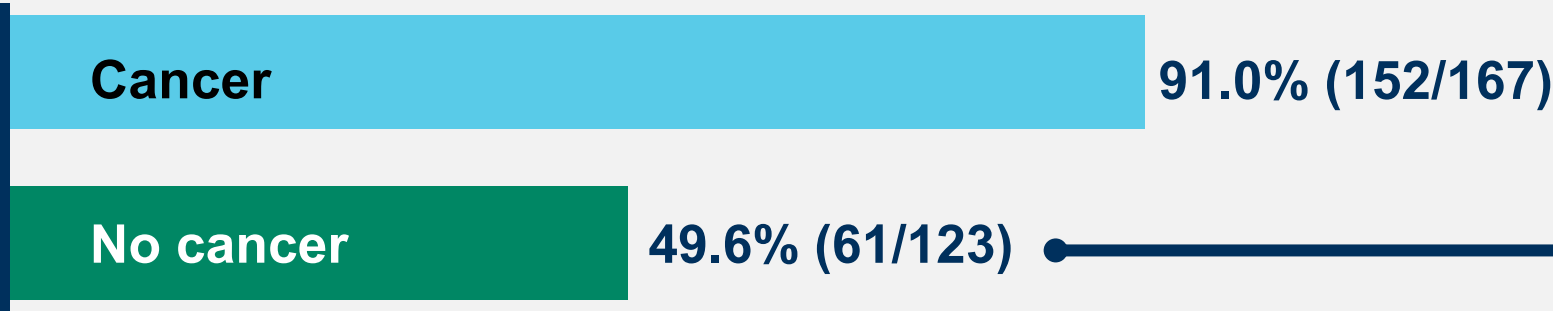
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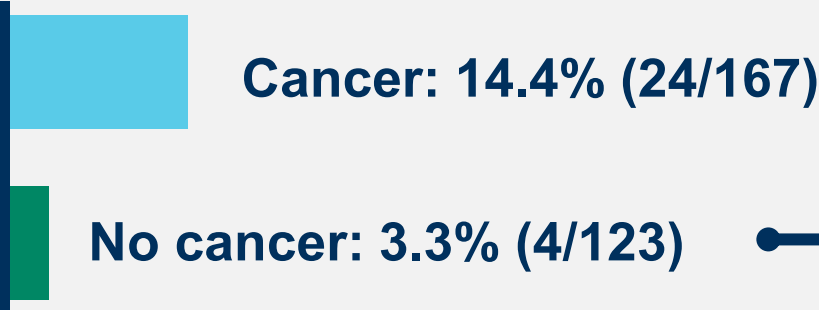
Diagnostic invasive procedures were more common in participants diagnosed with cancer

213 participants had an invasive procedure^a

Invasive procedures were more common in participants with a cancer diagnosis at 12 months



Surgical procedures were more frequent in those with a cancer diagnosis at 12 months^b



- **63.8% (136/213)** had a predicted CSO for which the protocol-recommended evaluation included an **invasive procedure**
- **50.7% (108/213) underwent biopsies**; almost all participants (**98.1%**; 106/108) underwent biopsies only after other diagnostic evaluations
- **80.3% (49/61)** had a predicted CSO for which the protocol-recommended evaluation included an **invasive procedure**
- **70.5% (43/61) underwent endoscopies**
- **29.5% (18/61) underwent biopsies**; all participants (**100%**; 18/18) underwent biopsies after other diagnostic evaluations
- All 4 participants had **benign neoplasms** that warranted **surgical intervention**

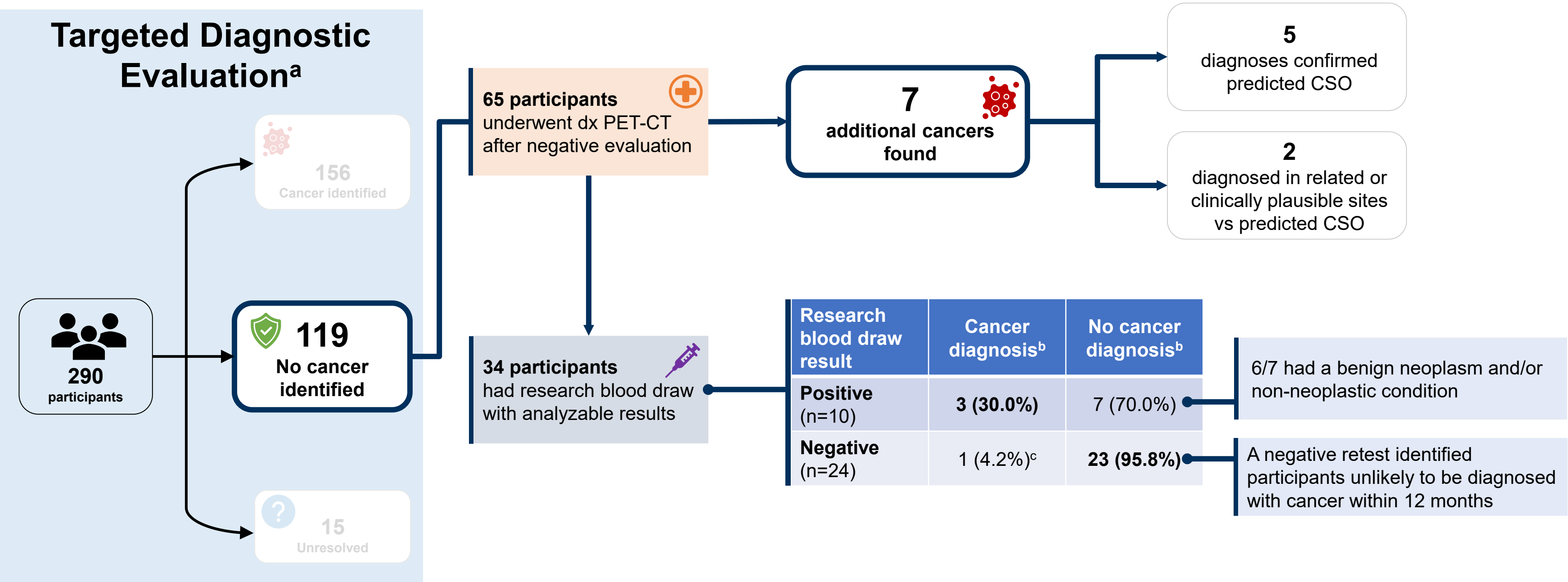
CSO, cancer signal origin.

^aInvasive procedures were categorized as non-surgical invasive procedures, including endoscopy, biopsy, and other non-surgical procedures, or surgical invasive procedures. ^bIncludes participants who had no cancer diagnosed at diagnostic resolution, or participants who are still undergoing diagnostic evaluation at 12 months or have not achieved diagnostic resolution within 12 months.

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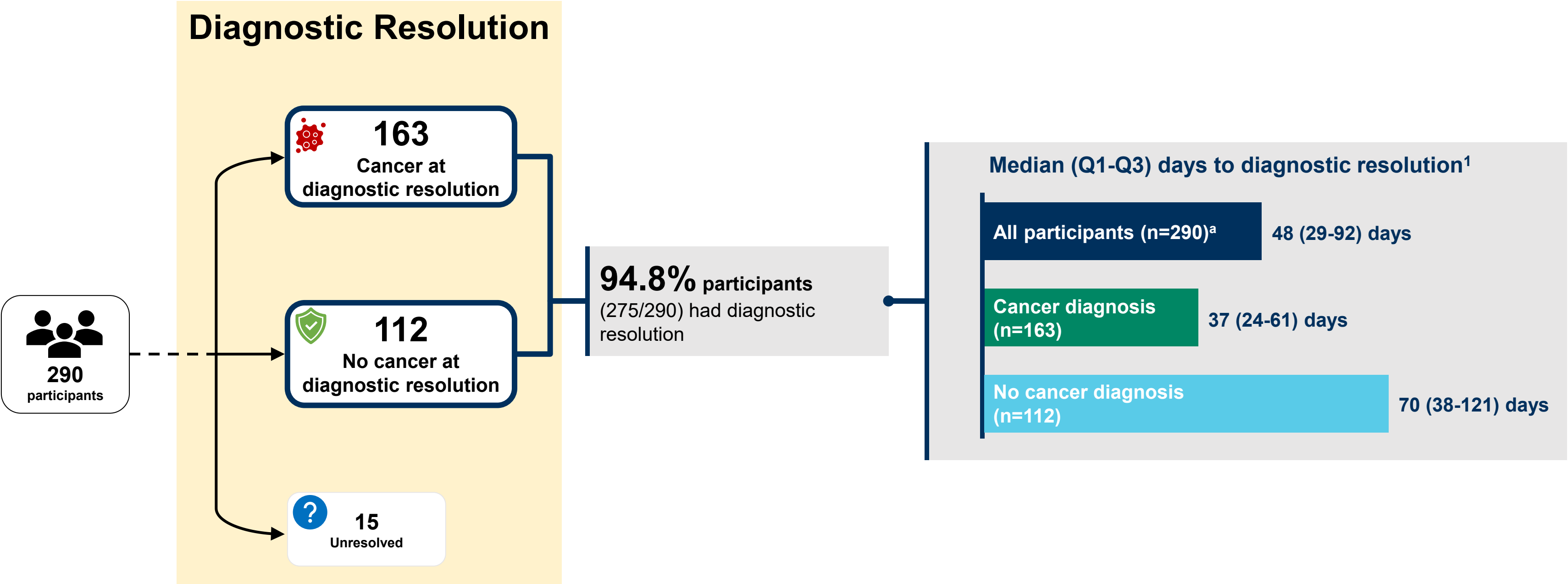
Diagnostic PET-CT provided limited new diagnostic information; persistent MCED positivity was associated with a subsequent cancer diagnosis



CSO, cancer signal origin; dx, diagnostic; MCED, multi-cancer early detection; PET-CT, positron emission tomography-computed tomography.
^aTargeted diagnostic evaluation refers to any initial or subsequent testing performed before the diagnostic PET-CT (if performed) or prior to diagnostic resolution. ^bDiagnosis within 12 months. ^cRecurrent breast cancer was diagnosed approximately 7 months after the research blood draw. The predicted CSOs from the initial test were lung (CSO1) and lymphoid lineage (CSO2).

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95% of participants with a positive MCED test achieved diagnostic resolution



MCED, multi-cancer early detection; PET-CT, positron emission tomography-computed tomography; Q1, first quartile; Q3, third quartile.

^aBased on Kaplan-Meier analysis. Includes 15 participants who did not achieve diagnostic resolution (unresolved).

1. Nabavizadeh N, et al. *Nat Med* 2026.

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Conclusions

1

CSO-guided evaluations identified most cancers after positive MCED test results

2

CSO-guided evaluations were generally focused and safe

3

PET-CT after negative targeted evaluation provided limited new information

4

Persistent MCED positivity on second blood draw may identify participants who warrant continued follow-up

CSO, cancer signal origin; MCED, multi-cancer early detection; PET-CT, positron emission tomography-computed tomography.

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