NHS-Galleri: Primary Results From a Randomised Controlled Trial to Assess the Clinical Utility of a Multi-Cancer Early Detection (MCED) Test in Population Screening

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PRESENTED BY: Charles Swanton, MBPhD

Key Takeaways

In the largest and first randomised controlled screening trial of an MCED test:

Clinical Utility

- Primary endpoint not met (stage III/IV reduction)
- Observed reduction in stage IV cancers and increase in stage I-II cancers–both prespecified secondary endpoints

Safety and Performance

- Demonstrated safe implementation and robust performance across 3 screening rounds in an NHS population
- Prevalent round performance was consistent with other prospective clinical studies[1,2]

Routes to Diagnosis

- 4-fold increase in screen-detected cancers
- Reduction in cancers detected through emergency presentation

MCED, multi-cancer early detection; NHS, National Health Service.

1. Schrag D, et al. *Lancet*. 2023;402(10409):1251-1260. 2. Nabavizadeh N, et al. Presentation at European Society for Medical Oncology Congress. October 17-21. 2025; Berlin Germany.

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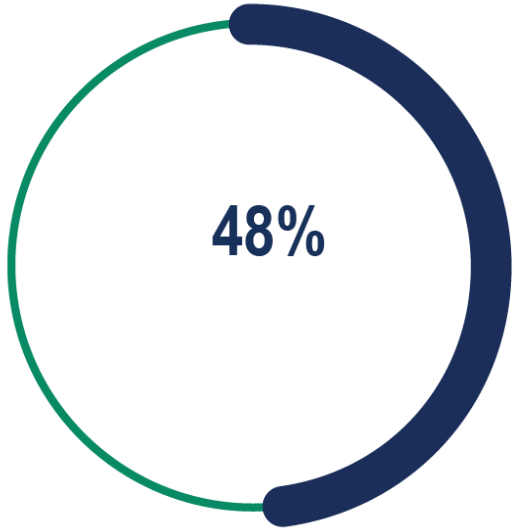
Most Cancer Diagnoses and Deaths Are From Types Without Guideline-Recommended Population Screening

Cancers **detected** through guideline-recommended **population screening**[a]

Cancer deaths **not** addressed by current screening implementation

Stage IV cancers represented 18% of all estimated diagnoses, but contribute to



of all estimated cancer-related deaths within 5-years in the US[4]

[a]Includes screening programmes for breast, cervical, and bowel in the UK and screening programmes for breast, cervical, colorectal, and lung in the US.

1. NHS England. Routes to Diagnosis, 2018. Accessed May 19, 2026. https://digital.nhs.uk/data-and-information/publications/statistical/routes-to-diagnosis/2018/results. 2. NORC at the University of Chicago: Percent of Cancers Detected by Screening in the US. Accessed May 19, 2026. https://cancerdetection.norc.org/. 3. American Cancer Society. Cancer Facts & Figures 2026. Accessed May 19, 2026. https://www.cancer.org/research/cancer-facts-statistics/all-cancer-facts-figures/2026-cancer-facts-figures.html. 4. Clarke CA, et al. *Cancer Epidemiol Biomarkers Prev*. 2020 May;29(5):895-902.

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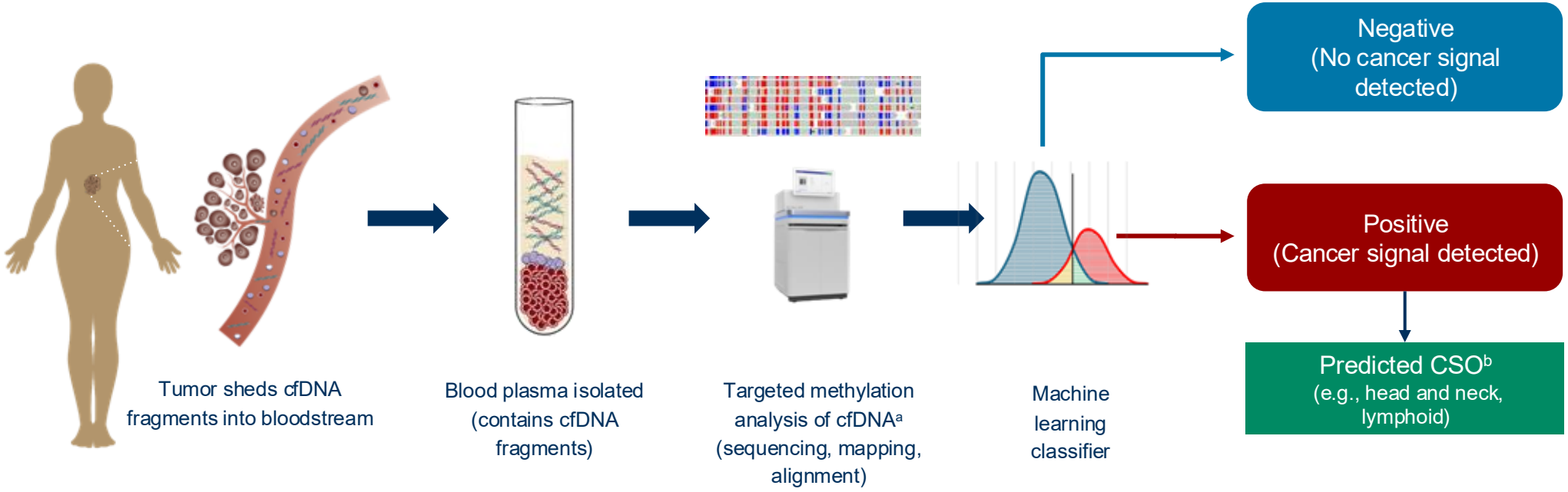
Blood-Based Targeted Methylation MCED Test

The MCED test detects a cancer signal from cell-free DNA (cfDNA) in blood and predicts cancer signal origin (CSO) to guide diagnostic evaluation



Clinically validated in case-control and population-scale intended-use studies.[1-4]
Clinical evidence program includes >380,000 participants across 9 studies in North America and the UK.

MCED, multi-cancer early detection. [a]Bisulfite treatment; targeted probes pull out fragments matching regions of interest. [b]For a detected signal, this MCED test version predicts 1-2 CSOs that can be either an anatomic site (eg, colorectal) or a cellular lineage (eg, lymphoid). Adapted from Liu MC, et al. 1. Liu MC, et al. *Ann Oncol.* 2020;31(6):745-759. 2. Klein EA, et al. *Ann Oncol.* 2021;32(9):1167-1177. 3. Schrag D, et al. *Lancet.* 2023;402(10409):1251-1260. 4. Nabavizadeh N, et al. Presentation at European Society for Medical Oncology Congress. October 17-21. 2025; Berlin, Germany.

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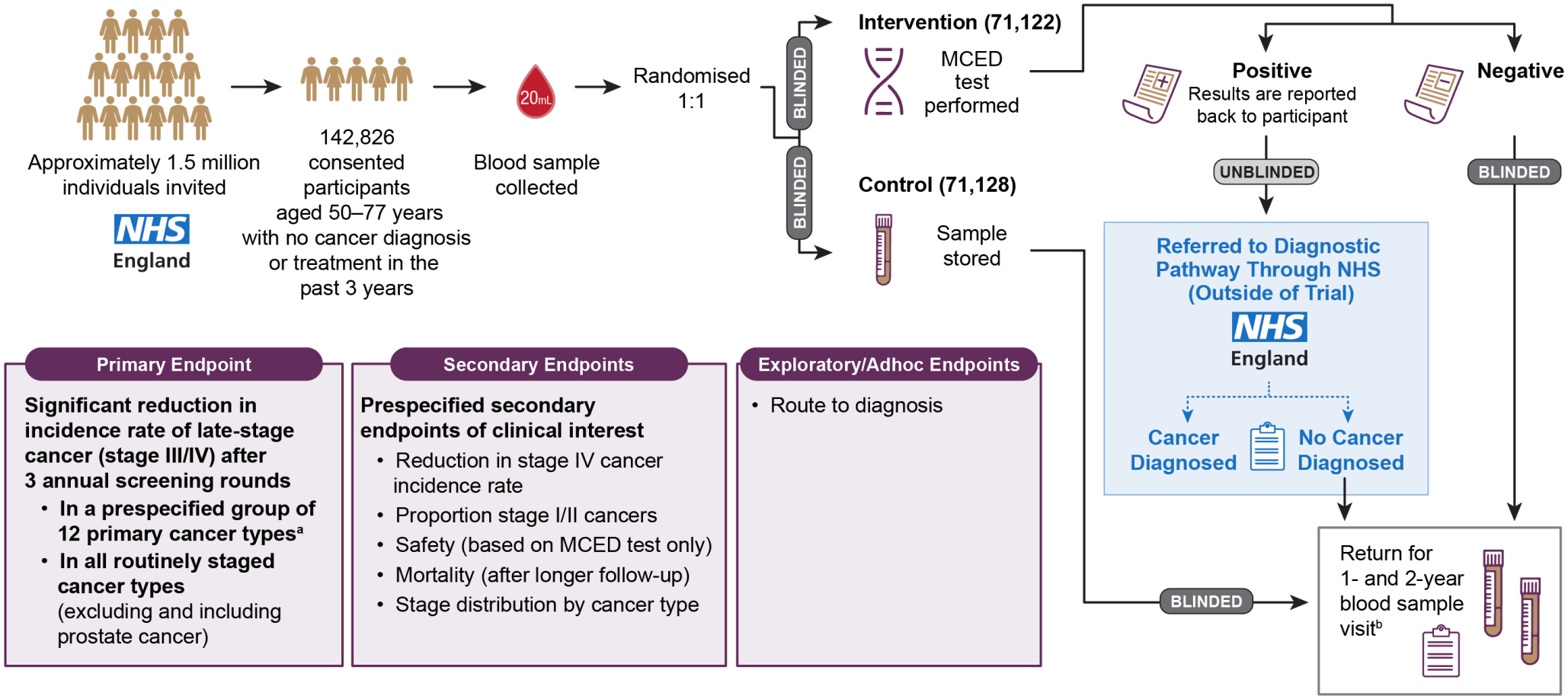
NHS-Galleri Is the Largest, First, and Only Randomised Controlled Clinical Utility Trial of an MCED Test to Date



MCED, multi-cancer early detection; NHS, National Health Service.
[a]Lung, head & neck, colorectal, pancreas, myeloma/plasma cell neoplasm, liver/bile duct, stomach, esophagus, anus, lymphoma, ovary, and bladder. [b]Participants who were diagnosed with cancer were not required to return for blood samples.
Sasieni P, et al. *Cancers (Basel)*. 2022;14(19):4818.

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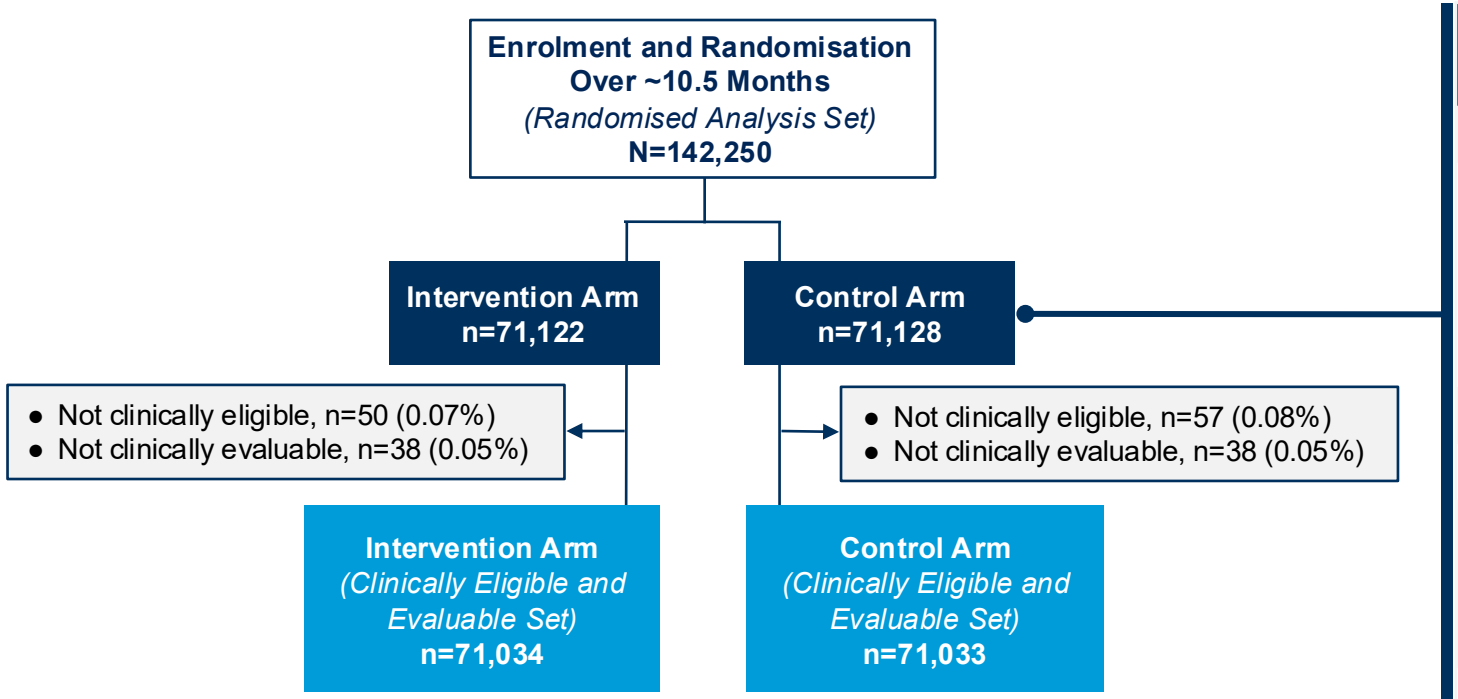
Trial Arms Were Well Balanced and Retained Majority of Participants Over 3 Screening Rounds



Participants retention was 91% in the second year and 88% in the third year of screening

Median follow-up of 17 months after last screen

Baseline Demographics and Characteristics	Intervention Arm (n=71,122)	Control Arm (n=71,128)
Median Age (IQR), years	66 (59, 71)	66 (59, 71)
Age Groups, years		
50-59	26.4%	26.6%
60-69	40.2%	40.5%
70+	33.4%	33.0%
Sex, Female	50.2%	50.2%
Race/Ethnicity, White	93.6%	93.6%
Index of Multiple Deprivation		
Most Deprived	22.6%	22.6%
Least Deprived	16.1%	16.0%
Education		
CSEs, O-Levels, or Lower	44.9%	45.2%
Bachelor's Degree or Higher	25.0%	25.1%
Smoking History		
Former Smoker	38.3%	38.2%
Current Smoker	6.7%	6.6%
Prior Cancer History	7.5%	7.5%

CSE, certificate of secondary education; IQR, interquartile range; O-levels, ordinary levels.

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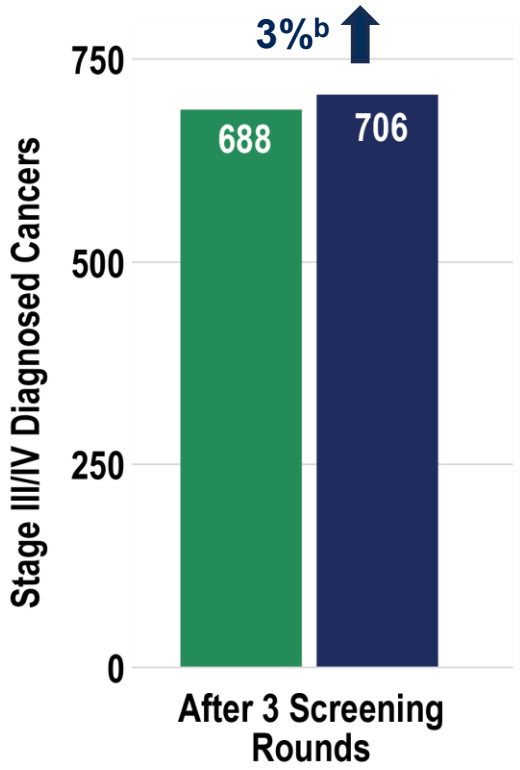
Primary Endpoint | 12 Prespecified Cancer Types[a]

No Significant Reduction in Stage III/IV Cancers Observed in the Intervention Arm With the Current Follow-Up Window



Incidence Rate Ratio[c] (Intervention/Control)

1.03
(95% CI, 0.92, 1.14)
p=0.6324

[a]12 prespecified cancer types were lung, head & neck, colorectal, pancreas, myeloma/plasma cell neoplasm, liver/bile duct, stomach, esophagus, anus, lymphoma, ovary, and bladder. [b]Percent difference was calculated with incidence rate ratios as part of the prespecified analysis, not raw cancer counts (graphed in bar charts for illustrative purposes).[c]Incidence rate ratio compares the frequency of cancer diagnoses between the intervention and control arm and accounts for different lengths of follow-up time.

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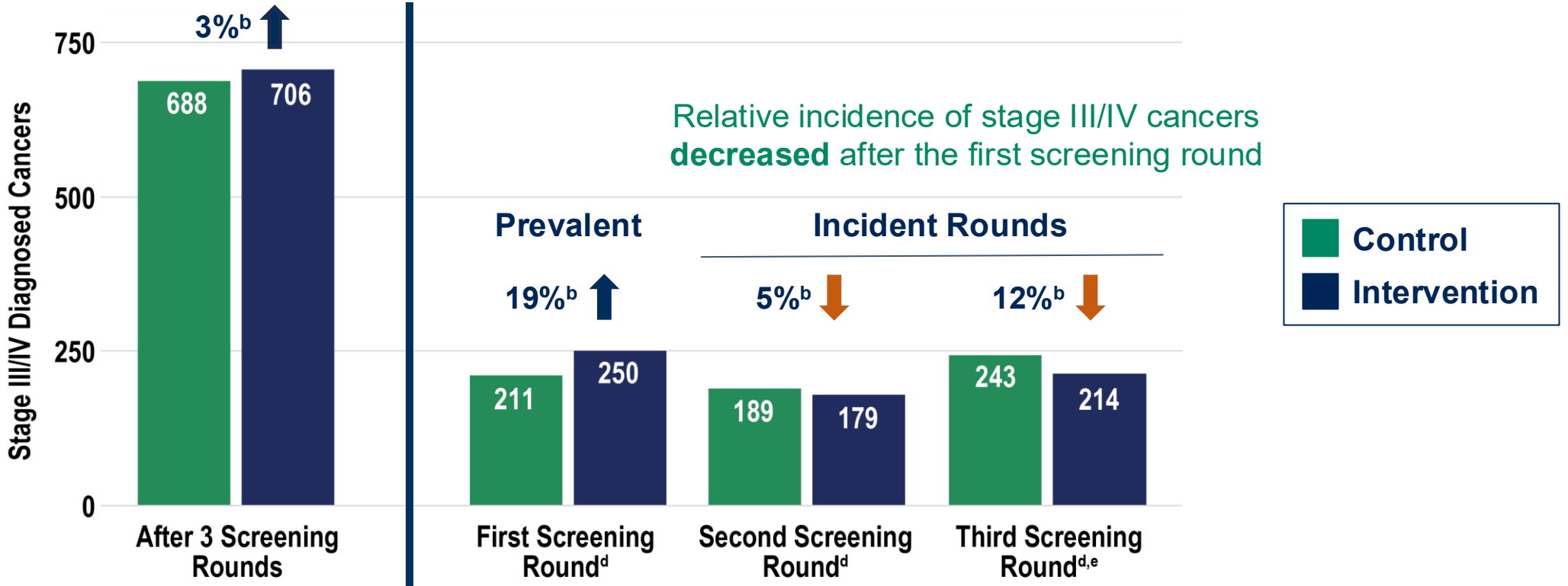

	After 3 Screening Rounds	First Screening Round[d]	Second Screening Round[d]	Third Screening Round[d,e]
Incidence Rate Ratio[c] (Intervention/Control)	**1.03 (95% CI, 0.92, 1.14) p=0.6324**	1.19 (0.98, 1.43)	0.95 (0.77, 1.17)	0.88 (0.73, 1.07)

[a]12 prespecified cancer types were lung, head & neck, colorectal, pancreas, myeloma/plasma cell neoplasm, liver/bile duct, stomach, esophagus, anus, lymphoma, ovary, and bladder. [b]Percent difference was calculated with incidence rate ratios as part of the prespecified analysis, not raw cancer counts (graphed in bar charts for illustrative purposes).[c]Incidence rate ratio compares the frequency of cancer diagnoses between the intervention and control arm and accounts for different lengths of follow-up time. [d]Not all participants attended every screening round; thus, some cancers were not assigned a screening round. [e]Follow-up time was variable in the third screening round and ranged from 12 to 22 months.

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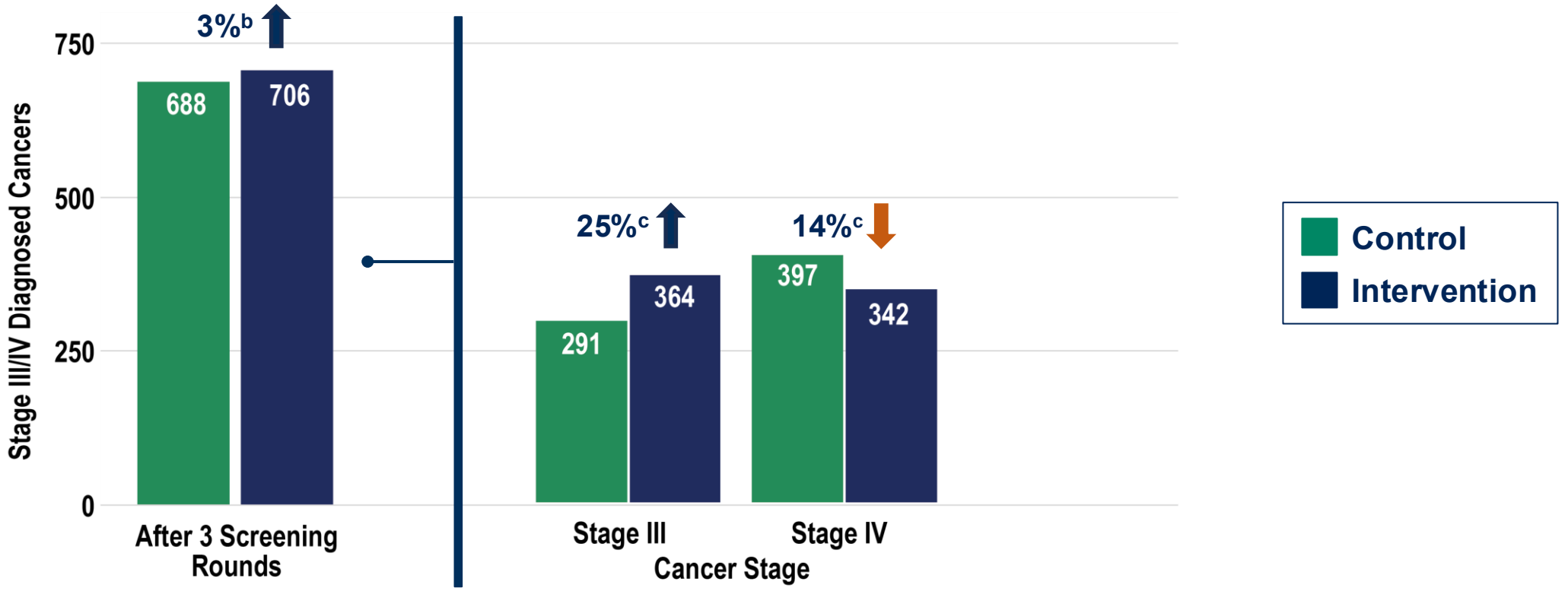
Descriptive Summary | 12 Prespecified Cancer Types[a]

No Significant Reduction in Stage III/IV Cancers Appears to Be Driven by Increase in Stage III Cancers Diagnosed



Incidence Rate Ratio[d] (Intervention/Control)

1.03 (95% CI, 0.92, 1.14) p=0.6324

[a]12 prespecified cancer types were lung, head & neck, colorectal, pancreas, myeloma/plasma cell neoplasm, liver/bile duct, stomach, esophagus, anus, lymphoma, ovary, and bladder. [b]Percent difference was calculated with incidence rate ratios as part of the prespecified analysis, not raw cancer counts (graphed in bar charts for illustrative purposes).[c]Percent difference was calculated with raw cancer counts for illustrative purposes, not as part of a stage-shift endpoint. [d]Incidence rate ratio compares the frequency of cancer diagnoses between the intervention and control arm and accounts for different lengths of follow-up time.

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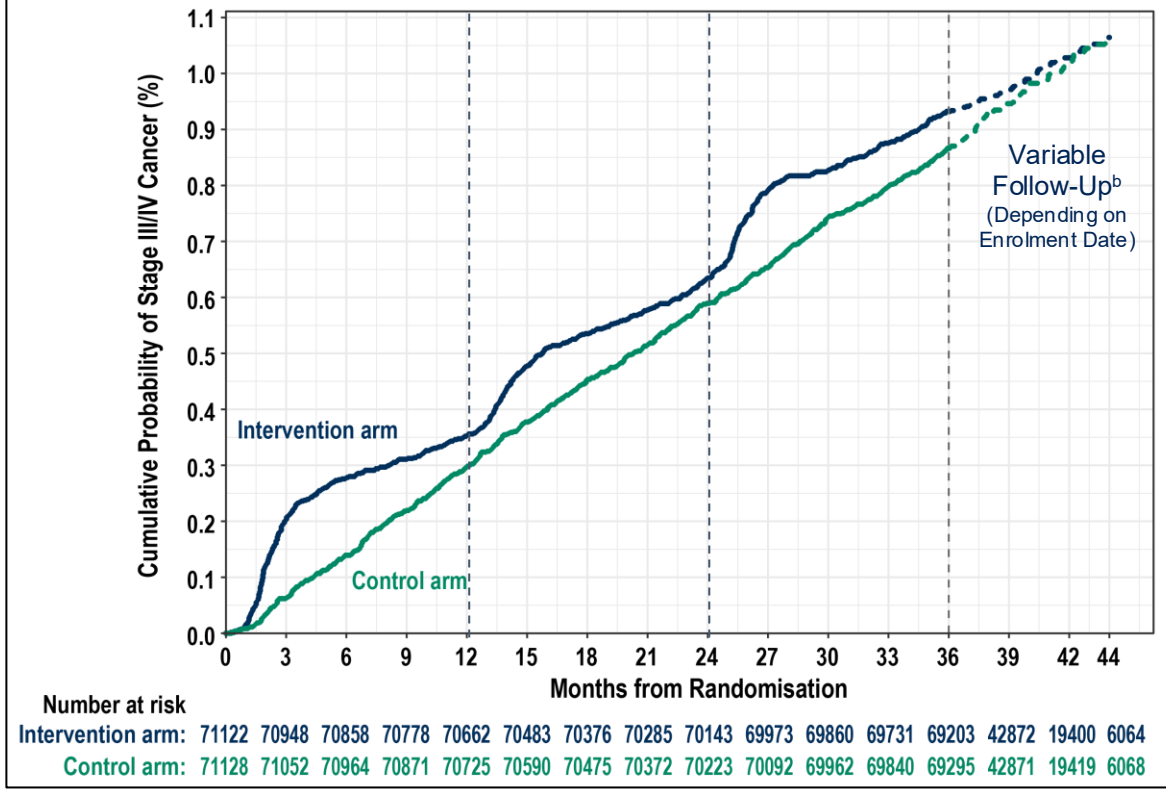
Primary Endpoint | 12 Prespecified Cancer Types[a]

No Significant Reduction in Stage III/IV Cancers Observed in the Intervention Arm With the Current Follow-Up Window

Cumulative Probability of Stage III/IV Cancer



Relative incidence of stage III/IV cancers **decreased** after the first screening round

Stage III/IV Cancers Diagnosed	Intervention vs Control	
	Incidence Rate Ratio	% Difference[c] (n vs n)[d]
After 3 Screening Rounds	**1.03 (0.92, 1.14) p=0.6324**	**↑ 3% 706 vs 688**
First Screening Round (Prevalent)	1.19 (0.98, 1.43)	↑ 19% 250 vs 211
Second Screening Round (Incident)	0.95 (0.77, 1.17)	↓ 5% 179 vs 189
Third Screening Round (Incident)[e]	0.88 (0.73, 1.07)	↓ 12% 214 vs 243

[a]12 prespecified cancer types were lung, head & neck, colorectal, pancreas, myeloma/plasma cell neoplasm, liver/bile duct, stomach, esophagus, anus, lymphoma, ovary, and bladder. [b]Administrative censoring. [c]Percent difference was calculated with incidence rate ratios as part of the prespecified analysis, not raw cancer counts (included for illustrativepurposes). [d]Not all participants attended every screening round; thus, some cancers were not assigned a screening round. [e]Follow-up time was variable in the third screening round and ranged from 12 to 22 months.

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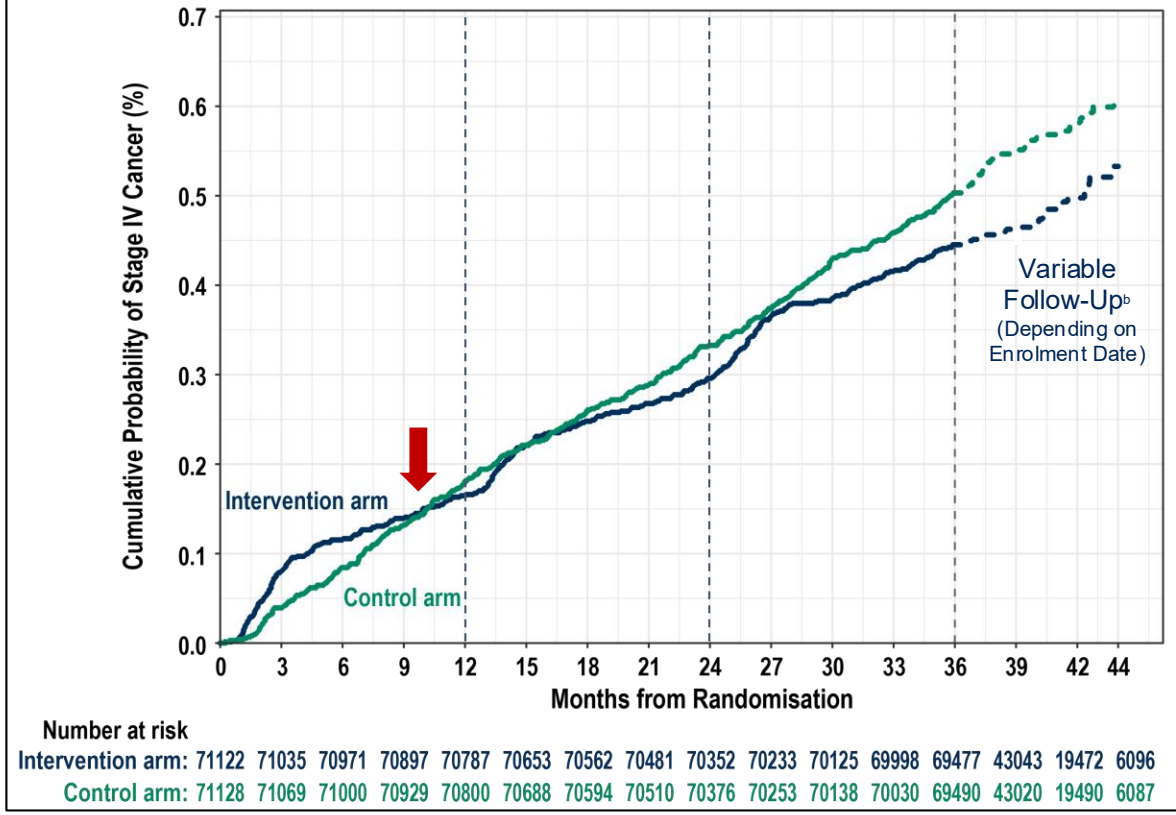
Secondary Endpoint | 12 Prespecified Cancer Types[a]

14% Reduction in Stage IV Cancers Observed in the Intervention Arm; ≥22% Reduction in Incident Rounds

Cumulative Probability of Stage IV Cancer



Relative incidence of stage IV cancers **decreased** each screening round

Stage IV Cancers Diagnosed	Intervention vs Control	
	Incidence Rate Ratio	% Difference[c] (n vs n)[d]
After 3 Screening Rounds	**0.86 (0.744, 0.998)**	**↓ 14% 342 vs 397**
First Screening Round (Prevalent)	0.91 (0.71, 1.18)	↓ 9% 117 vs 128
Second Screening Round (Incident)	0.78 (0.57, 1.06)	↓ 22% 78 vs 100
Third Screening Round (Incident)[e]	0.74 (0.57, 0.95)	↓ 26% 104 vs 142

[a]12 prespecified cancer types were lung, head & neck, colorectal, pancreas, myeloma/plasma cell neoplasm, liver/bile duct, stomach, esophagus, anus, lymphoma, ovary, and bladder. [b]Administrative censoring. [c]Percent difference was calculated with incidence rate ratios as part of the prespecified analysis, not raw cancer counts (included for illustrativepurposes). [d]Not all participants attended every screening round; thus, some cancers were not assigned a screening round. [e]Follow-up time was variable in the third screening round and ranged from 12 to 22 months.

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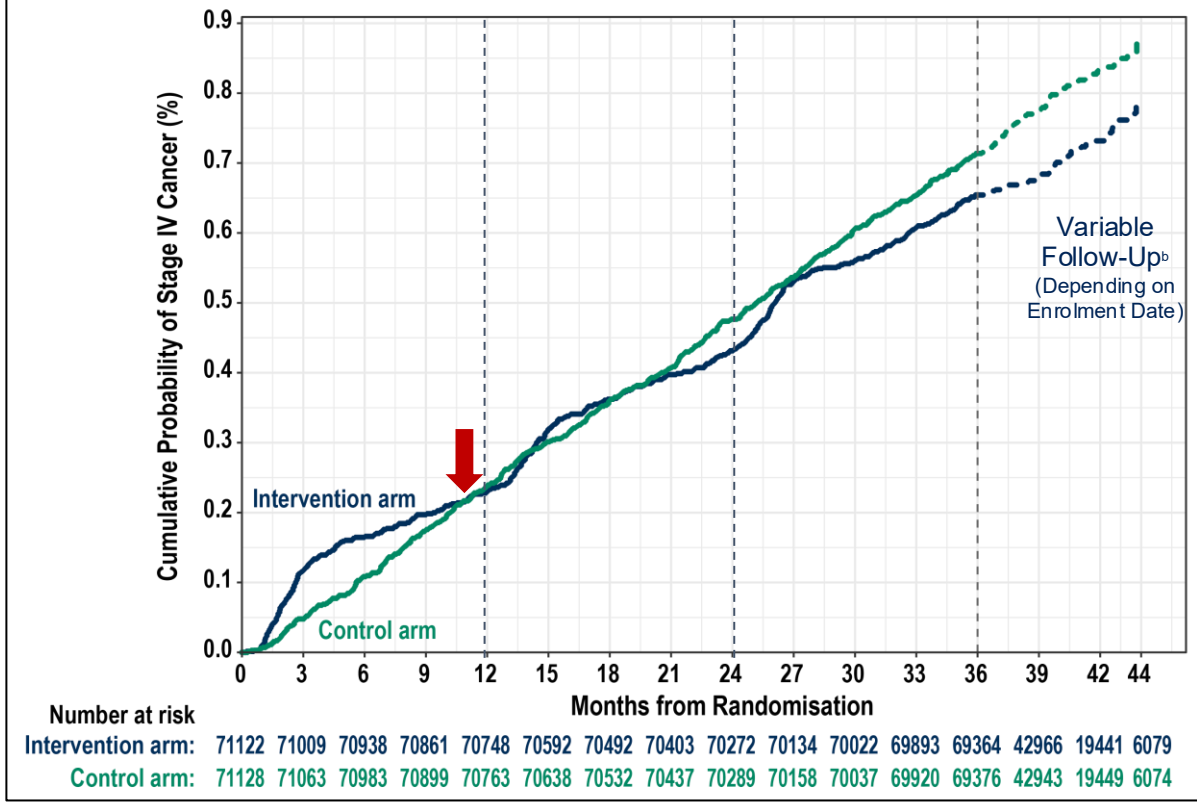
Secondary Endpoint | All Routinely Staged Cancer Types[a]

11% Reduction in Stage IV Cancers Observed Across All Cancers in the Intervention Arm; >20% Reduction in Incident Rounds

Cumulative Probability of Stage IV Cancer



Relative incidence of stage IV cancers **decreased** each screening round

Stage IV Cancers Diagnosed	Intervention vs Control	
	Incidence Rate Ratio	% Difference[c] (n vs n)[d]
After 3 Screening Rounds	**0.89 (0.79, 1.01)**	**↓ 11% 503 vs 563**
First Screening Round (Prevalent)	0.97 (0.78, 1.21)	↓ 3% 164 vs 169
Second Screening Round (Incident)	0.78 (0.61, 1.00)	↓ 22% 120 vs 154
Third Screening Round (Incident)[e]	0.80 (0.65, 0.99)	↓ 20% 158 vs 198

[a]Including prostate. [b]Administrative censoring. [c]Percent difference was calculated with incidence rate ratios as part of the prespecified analysis, not raw cancer counts (included for illustrative purposes). [d]Not all participants attended every screening round; thus, some cancers were not assigned a screening round. [e]Follow-up time was variable in the third screening round and ranged from 12 to 22 months.

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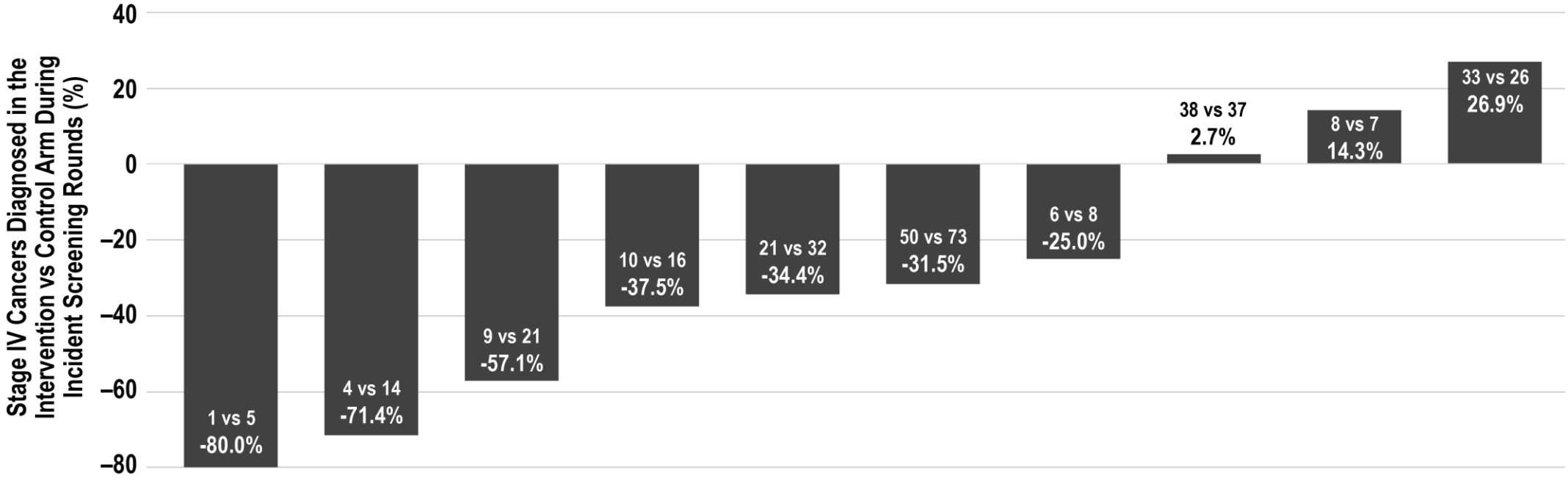
Descriptive Summary | 12 Prespecified Cancer Types[a]

Differences in Stage IV Diagnoses by Cancer Types



		Bladder	Liver/bile duct	Oesophagus	Head & neck	Colorectum	Lung	Stomach	Lymphoma	Ovary	Pancreas
England 5-year net survival estimates[b,1]	Stage IV	5.8%	2.6%	6.2%	38.4%	11.0%	4.5%	4.5%	65.7%	16.2%	2.1%
	Stage III	31.8%	13.5%	24.7%	54.5%	64.2%	16.7%	24.6%	72.6%	32.4%	8.7%
	Difference	+26.0%	+10.9%	+18.5%	+16.1%	+53.2%	+12.2%	+20.1%	+6.9%	+16.2%	+6.6%

[a]12 prespecified cancer types were lung, head & neck, colorectal, pancreas, myeloma/plasma cell neoplasm, liver/bile duct, stomach, esophagus, anus, lymphoma, ovary, and bladder. Anus and myeloma/plasma cell neoplasms were excluded from the graph due to having only 0 to 1 stage IV cancers in each arm.[b]For patients diagnosed in England 2018-2022 (all ages) by stage at diagnosis. [1]Cancer Survival in England, cancers diagnosed 2018 to 2022, followed up to 2023. 2026. Accessed May 19, 2026. https://digital.nhs.uk/data-and-information/publications/statistical/cancer-survival-in-england/.

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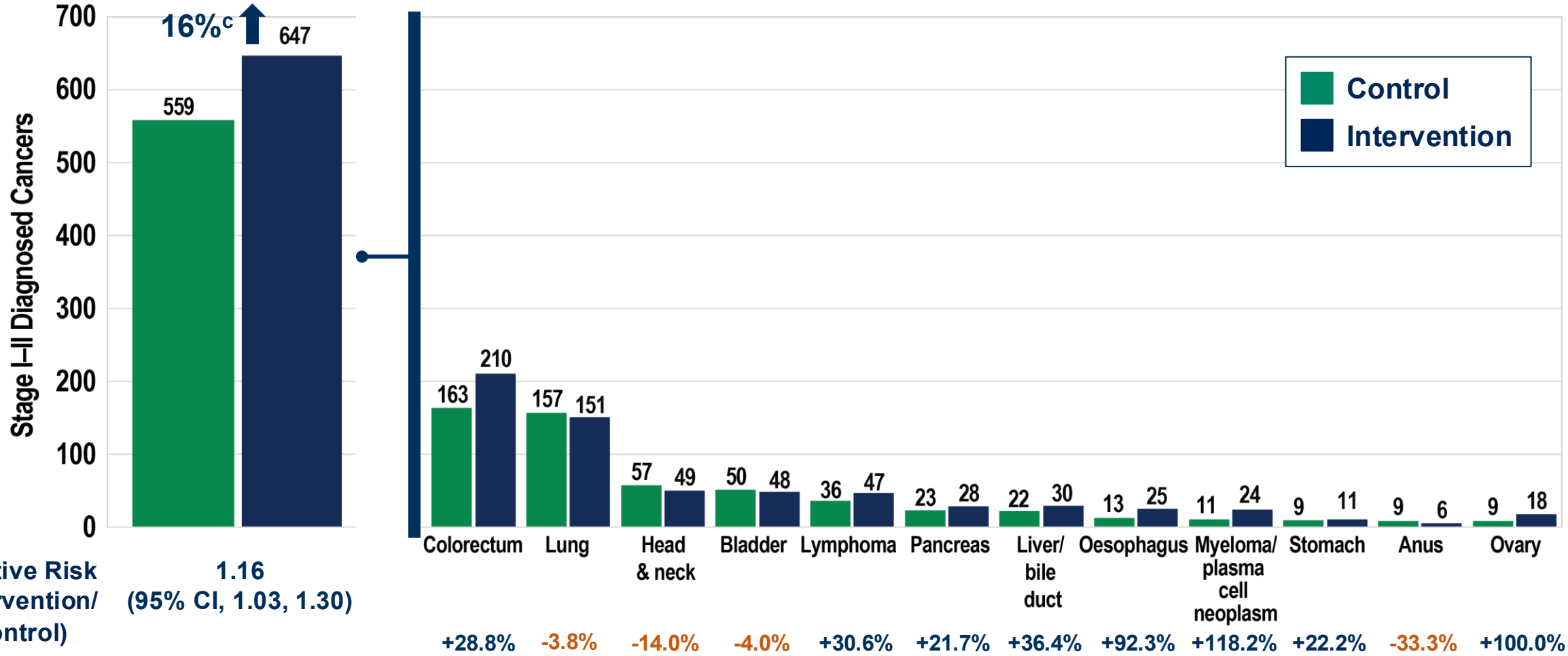
Descriptive Summary | 12 Prespecified Cancer Types[a]

Shift to Stage I-II Cancer[b] Detection With MCED Screening Added to SOC After 3 Screening Rounds



MCED, multi-cancer early detection; SOC, standard-of-care. [a]12 prespecified cancer types were lung, head & neck, colorectal, pancreas, myeloma/plasma cell neoplasm, liver/bile duct, stomach, esophagus, anus, lymphoma, ovary, and bladder. [b]Per highest stage. [c]Percent difference was calculated with relative risk as part of the prespecified analysis, not raw cancer counts (graphed in bar charts for illustrative purposes).

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Secondary Endpoint | Intervention Arm[a]

Robust MCED Test Performance in UK Population

Aggregate MCED Test Performance Over 3 Screening Rounds[b]

		Cancer Status			
		Cancer Diagnosis (n=3051)	No Cancer Diagnosis (n=194,095)	Total (N=197,146)	Performance Metric (95% CI)
MCED Test Result	Positive	937	864	1801	**PPV[c] 52.0%** (49.7-54.3%)
	Negative	2114	193,231	195,345	**NPV 98.92%** (98.87-98.96%)
Performance Metric (95% CI)		**Episode Sensitivity[d,e] 30.7%** (29.1-32.4%)	**Specificity 99.55%** (99.52-99.58%)		

CSO Accuracy 92.5% (90.7%-94.0%)

Episode Sensitivity[d,f] for 12 prespecified cancer types 54.7% (51.8%-57.5%)

MCED, multi-cancer early detection; NPV, negative predictive value; PPV, positive predictive value. [a]Intervention-arm test performance analysable set. [b]Calculated using all participants within the performance analysable set, defined as participants who were clinically eligible and evaluable and had evaluable MCED test results; third round follow-up time was 12 months. [c]PPV for the first (prevalent) screening round only was 58.0% (54.4%-61.6%). [d]12-month episode sensitivity was calculated as the number of participants with a positive MCED test result and a cancer diagnosis within the follow-up period for that round out of all participants with a cancer diagnosed within the follow-up period. [e]Episode sensitivity for all cancers during the first (prevalent) screening round only was 37.2% (34.4%-40.0%). [f]Episode sensitivity for the 12 prespecified cancers during the first (prevalent) screening round only was 63.4% (58.9%-67.7%).

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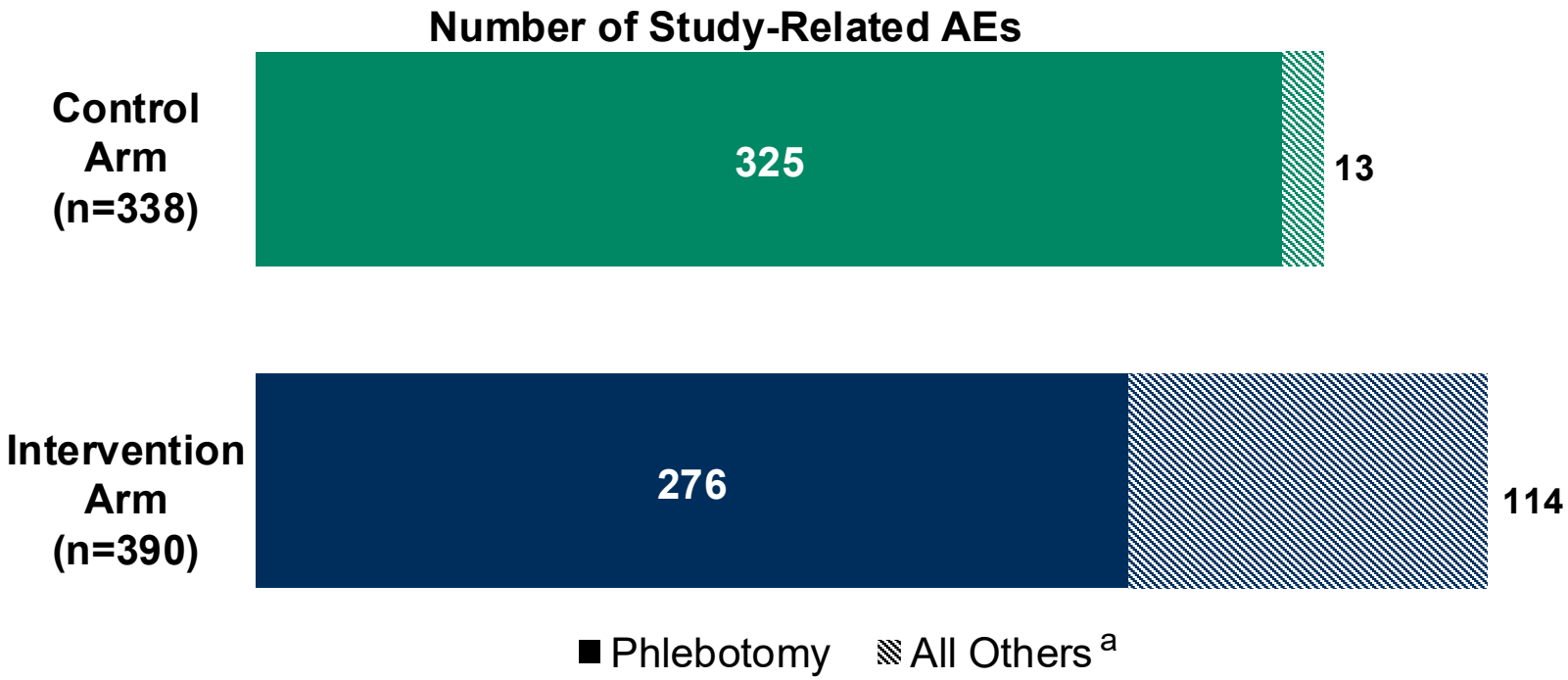
Secondary Endpoint | Randomised Analysis Set

The MCED Test Itself Was Safe When Implemented at Population Scale

0.45% (321/71,128) and **0.52% (371/71,122)** participants in the control and intervention arms, respectively, **experienced a study-related AE** collected from blood sample collection up to referral into NHS



No serious study-related AEs occurred from blood sample collection or return-of-test results

Non-phlebotomy related AEs were mostly:

- Anxiety (1/13 control; 88/114 intervention)
- Emotional distress (10/13 control; 9/114 intervention)

AE, adverse event; MCED, multi-cancer early detection.
[a]All others includes non-phlebotomy AEs, with anxiety and emotional distress being the most common.

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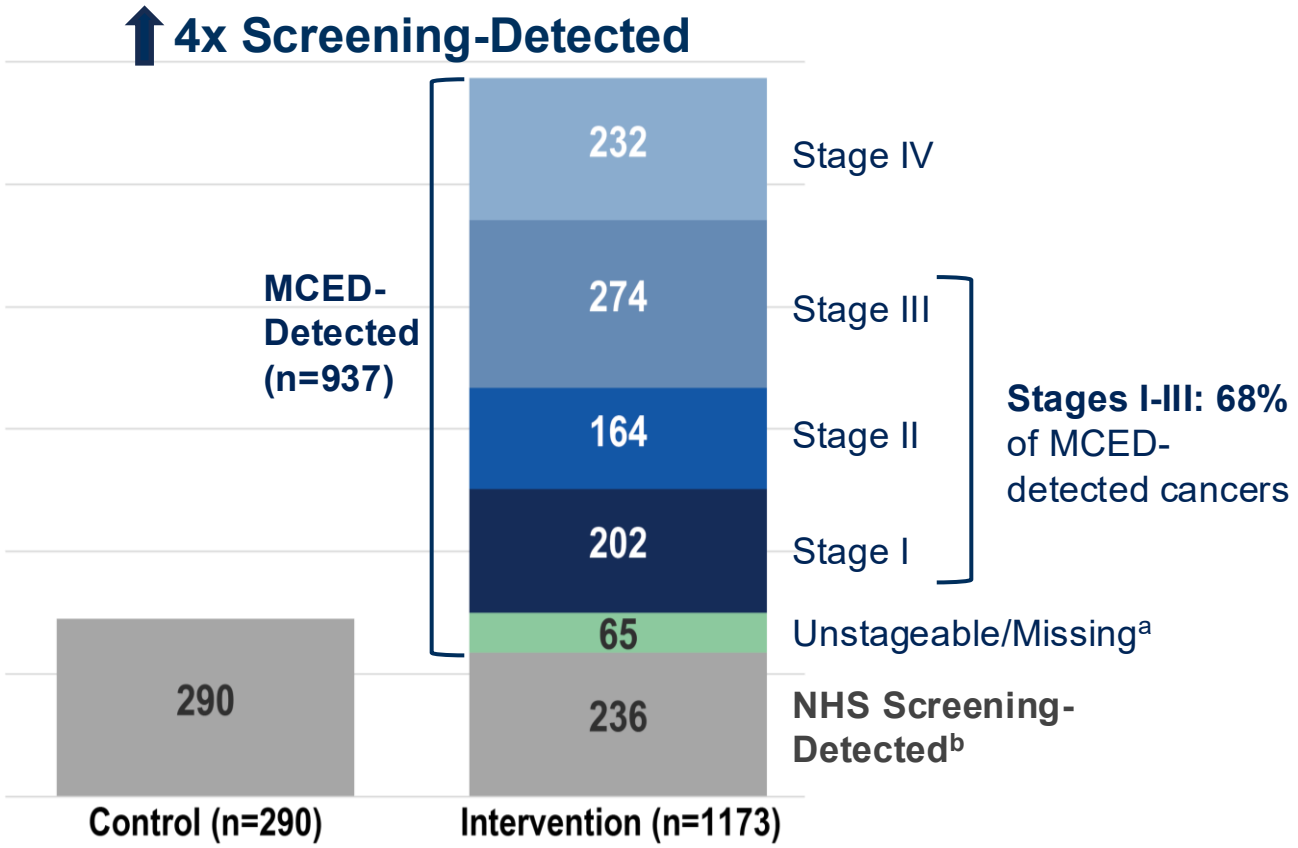
Exploratory | All Detected Cancers

MCED Quadrupled the Number of Screening-Detected Cancers and Reduced Clinically Detected Cancers and Emergency Presentations



- **21% reduction in clinically detected cancers[c]**
  Control vs Intervention:
  3110 vs 2464
- **25% reduction in emergency presentation diagnoses[d]**
  Control vs Intervention:
  286 vs 213

MCED, multi-cancer early detection. [a]Includes 10 unstageable cancers (no staging system exists) and 55 cancers with missing stage information. [b]Breast, colorectal, cervical, and lung (for high-risk individuals) cancer. [c]Clinical detection included cancers classified as being diagnosed in urgent cancer referral, emergency presentation, General Practitioner referral, and other (outpatient, inpatient elective, death certificate only, unknown, missing). [d]This estimate is a supportive sensitivity analysis after targeted review of 39 participants with an MCED-positive result and Emergency Presentation route to diagnosis. Of these, 12 had documented evidence against Emergency Presentation and were no longer classified as Emergency Presentation in this analysis; all randomised participants were included.

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Key Takeaways

In the largest and first randomised controlled screening trial of an MCED test:

Clinical Utility

- **Primary endpoint not met (stage III/IV reduction)**
- **In the prespecified secondary endpoints, observed a >20% reduction in stage IV cancers[a] in incident rounds and a 16% increase in cancers[a] detected at stage I-II**

Safety and Performance

- **Demonstrated safety, PPV of 52%, and specificity of 99.55%, consistent with other studies[1,2], in a large randomised controlled trial across 3 screening rounds in an NHS population**

Routes to Diagnosis

- **4-fold increase in screen-detected cancers**
- **25% reduction in cancers detected through emergency presentation**

MCED, multi-cancer early detection; NHS, National Health Service; PPV, positive predictive value. [a]Among 12 prespecified cancer types.

1. Schrag D, et al. *Lancet*. 2023;402(10409):1251-1260. 2. Nabavizadeh N, et al. Presentation at European Society for Medical Oncology Congress. October 17-21. 2025; Berlin, Germany.

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- Cancer Alliances
- National Cancer Registration and Analysis Service (NCRAS)
- Cancer Research UK Cancer Prevention Trials Unit (CPTU)

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