SeekIn 思勤

真理至上，以人为本

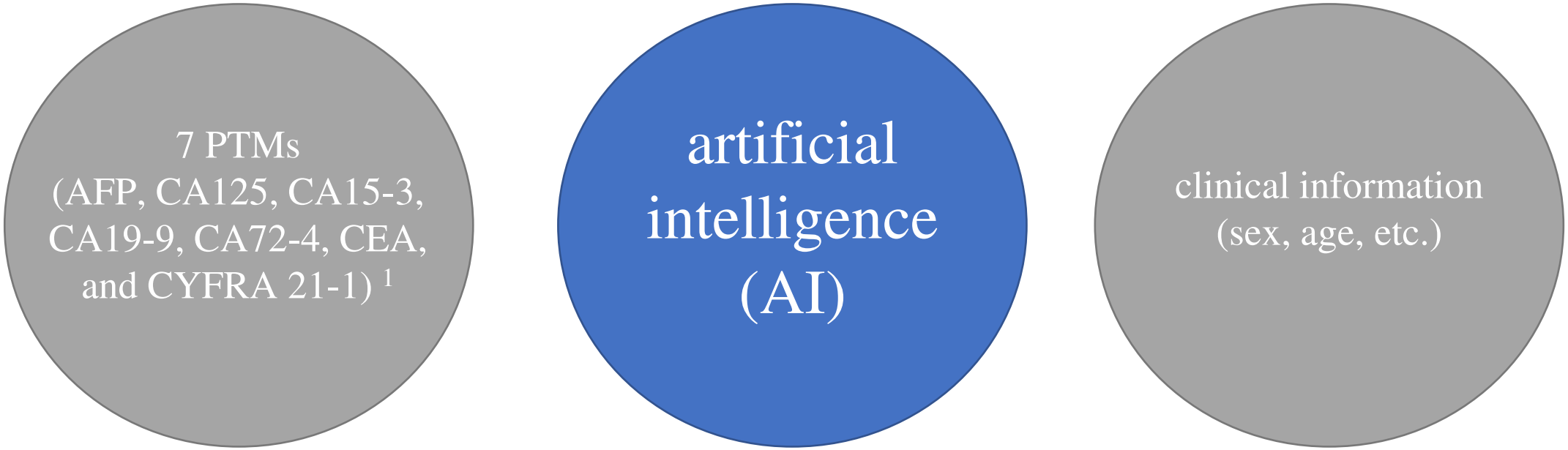
seek and you will find

Large-scale validation studies of a blood-based effective and affordable test for multi-cancer early detection

SeekIn

Oct 2024

AI-powered MCED Test - OncoSeek



PTM: Protein Tumor Markers

1. Ji X, Li J, Huang Y, et al. Identifying occult maternal malignancies from 1.93 million pregnant women undergoing noninvasive prenatal screening tests. Genetics in Medicine 2019; 21: 2293–302.

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The performance of OncoSeek was validated in seven independent cohorts (I)

	Training cohort	Independent validation cohort 1	Independent validation cohort 2*
Sample origin	SeekIn/China	SYSMH/China	JHUSM/USA
Sample type	Plasma	Serum	Plasma
Platform	Roche cobas e411	Roche cobas e601	Bio-Rad Bio-Plex 200
Sample size	Cancer (n = 591) Non-cancer (n = 1055)	Cancer (n = 363) Non-cancer (n = 5556)	Cancer (n = 1005) Non-cancer (n = 812)

SYSMH: Sun Yat-sen Memorial Hospital, Sun Yat-sen University
JHUSM: Johns Hopkins University School of Medicine.
*Cohen, et al. Science. 2018 Feb 23;359(6378):926-930.

Luan, Y., Zhong, GL., Li, SY., Wu, W., Liu, SQ., Zhu, DD., Feng, YM., Zhang, YX., Duan, CH., and Mao, M. A panel of seven protein tumour markers for effective and affordable multi-cancer early detection by artificial intelligence: a large-scale and multicentre case–control study, eClinicalMedicine 2023;61: 102041

The performance of OncoSeek was validated in seven independent cohorts (II)

	Independent validation cohort 3*	Independent validation cohort 4	Independent validation cohort 5
Sample origin	BGI/China	Oncocare/Brazil	HNCH/China
Sample type	Plasma	Plasma	Serum
Platform	GBI ELISA	Roche cobas e601	Roche cobas e601/e602
Sample size	Cancer (n = 34) Non-cancer (n = 416)	Cancer (n = 18) Non-cancer (n = 110)	Cancer (n = 869) Non-cancer (n = 555)
		Blinded/Prospective	Symptomatic

*Ji, X., Li, J., Huang, Y., Sung, P.-L., Yuan, Y., Liu, Q., Chen, Y., Ju, J., Zhou, Y., Huang, S., Chen, F., Han, Y., Yuan, W., Fan, C., Zhao, Q., Wu, H., Feng, S., Liu, W., Li, Z., … Mao, M. Identifying occult maternal malignancies from 1.93 million pregnant women undergoing noninvasive prenatal screening tests. Genet Med. 2019;21(10):2293-2302.

The performance of OncoSeek was validated in seven independent cohorts (III)

Independent validation cohort 6

Sample origin	PUSH/China
Sample type	Serum
Platform	Abbott I2000
Sample size	Cancer (n = 149) Non-cancer (n = 3589)

The data strongly proved the robustness of OncoSeek

	Training cohort (SeekIn/China)		Validation cohort 1 (SYSMH/China)		Validation cohort 2 (JHUSM/USA)	
	Cancer	Non-cancer	Cancer	Non-cancer	Cancer	Non-cancer
Predict cancer	344	105	141	332	527	90
Predict non-cancer	247	950	222	5224	478	722
Sensitivity (95% CI)	58·2% (54·1%, 62·2%)		38·8% (33·8%, 44·1%)		52·4% (49·3%, 55·6%)	
Specificity (95% CI)	90·0% (88·1%, 91·8%)		94·0% (93·4%, 94·6%)		88·9% (86·6%, 91·0%)	
PPV (95% CI)	76·6% (72·4%, 80·5%)		29·8% (25·7%, 34·2%)		85·4% (82·4%, 88·1%)	
NPV (95% CI)	79·4% (77·0%, 81·6%)		95·9% (95·4%, 96·4%)		60·2% (57·3%, 63·0%)	

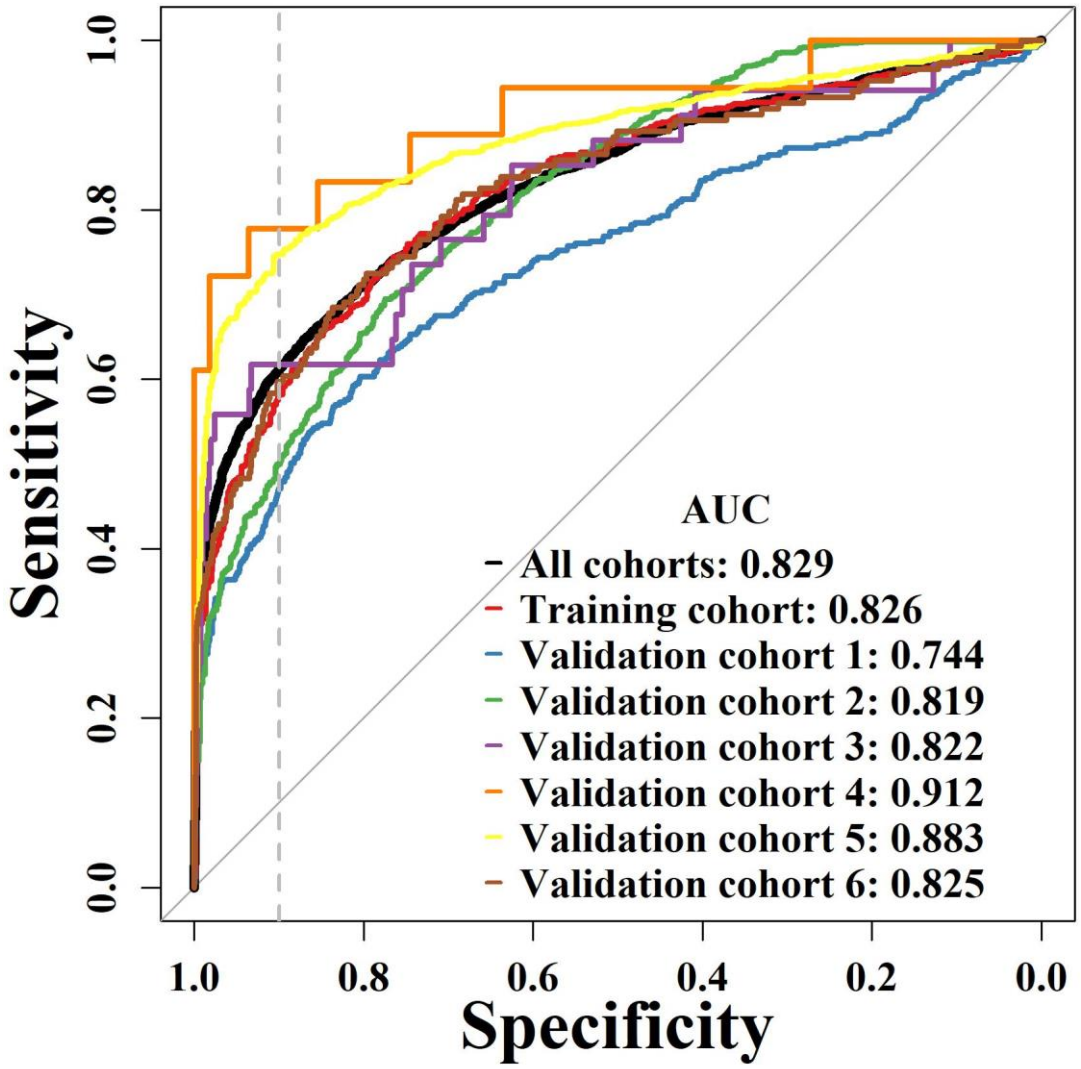
	Validation cohort 3 (BGI/China)		Validation cohort 4 (Oncocare/Brazil)		Validation cohort 5 (HNCH/China)		Validation cohort 6 (PUSH/China)	
	Cancer	Non-cancer	Cancer	Non-cancer	Cancer	Non-cancer	Cancer	Non-cancer
Predict cancer	19	21	13	7	635	52	89	359
Predict non-cancer	15	395	5	103	234	503	60	3230
Sensitivity (95% CI)	55·9% (37·9%, 72·8%)		72.2% (46.5%, 90.3%)		73·1% (70·0%, 76·0%)		59.7% (51.4%, 67.7%)	
Specificity (95% CI)	95·0% (92·4%, 96·8%)		93.6% (87.3%, 97.4%)		90·6% (87·9%, 92·9%)		90.0% (89.0%, 91·0%)	
PPV (95% CI)	47·5% (31·5%, 63·9%)		65.0% (40.8%, 84.6%)		92·4% (90·2%, 94·3%)		19.9% (16.3%, 23.9%)	
NPV (95% CI)	96·3% (94·0%, 97·9%)		95.4% (89.5%, 98.5%)		68·2% (64·8%, 71·6%)		98.2% (97.7%, 98.6%)	

SYSMH: Sun Yat-sen Memorial Hospital. JHUSM: Johns Hopkins University School of Medicine. HNCH: Henan Cancer Hospital. PUSH: Peking University Shenzhen Hospital.

PPV: positive predictive value. NPV: negative predictive value.

Please note that all samples from JHUSM and PUSH, and some samples from HNCH, do not include CA 72-4. For these samples, we used the mean value of healthy controls (4.38 U/ml) instead.

The data strongly proved the robustness of OncoSeek



Total 15,122 cases, including 3029 cancer patients and 12,093 non-cancer individuals

	Cancer	Non-cancer
Predict cancer	1768	966
Predict non-cancer	1261	11127
Sensitivity (95% CI)	58.4% (56.6%, 60.1%)	
Specificity (95% CI)	92.0% (91.5%, 92.5%)	
PPV (95% CI)	64.7% (62.8%, 66.5%)	
NPV (95% CI)	89.8% (89.3%, 90.3%)	

OncoSeek Workflow

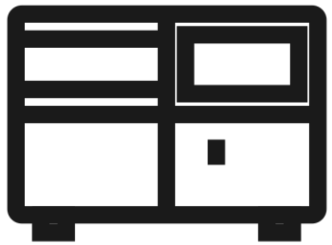
1. Sample collection

Collect a tube of blood

2. Transportation

Mail to central lab

3. PTM quantification



Quantify by ECLI

4. Data analysis

POC & TOO by AI

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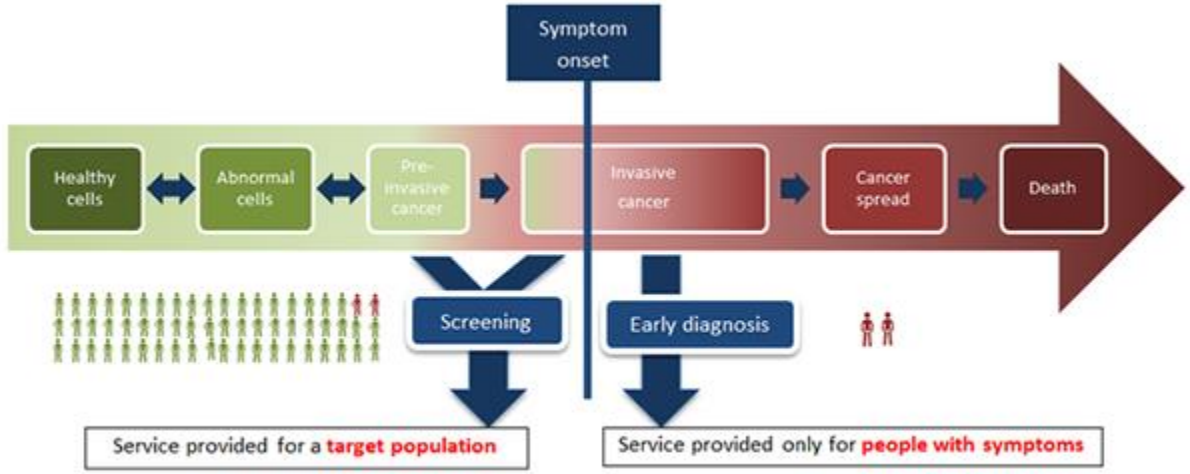
Robustness of OncoSeek

- Largest MCED clinical study to date: 15,122 cases (3,029 cancer and 12,093 non-cancer).
- Fourteen tumor types: bill duct, breast, cervical, colorectum, endometrial, head & neck, gallbladder, liver, lung, lymphoma, esophagus, ovary, pancreas, and stomach
- Seven cohorts/centers: SeekIn, SYSMH, JHUSM, BGI, Oncocare, HNCH, PUSH.
- Three countries: Brazil, China, USA.
- Four platforms: Roche Cobas; Abbott Architect, Bio-Rad (Luminex) Bio-Plex, GBI ELISA.
- Two Sample types: plasma and serum.
- OncoSeek demonstrates adequate performance for MCED across various tumor types, centers, populations, platforms, and sample types. It achieves a sensitivity of 58.4% and a specificity of 92.0% across all cases.

Three Applications



Screening

Screening applies tests to a population who do not have signs or symptoms of a cancer and who are at average risk for it. OncoSeek conducts risk screening for nine high prevalent cancers among individuals and identifies high-risk individuals. By closely monitoring them, cancer can be detected in a curable stage. (58% sensitivity/92% specificity)

Early diagnosis

Early diagnosis is a critical public health strategy in all settings due to the improved outcomes by treatment at as the earliest stage as possible. In the early stages, surgery and radiotherapy are often successful. OncoSeek is proven to detect cancer from people with symptoms and trace the TOO efficiently, helping patients reduce the time to diagnose and enable them take appropriate treatment as early as possible. (73% sensitivity/91% specificity)

Reducing false-positives

With the support of AI algorithms, OncoSeek has reduced false-positive rate nearly 7-fold for the general population undergoing annual physical checks, effectively addressing the issue of high false-positive rates associated with tumor marker panels. This ensures accurate and reliable testing results for individuals undergoing annual physical checks. (false positive rate 46% -> 7%)

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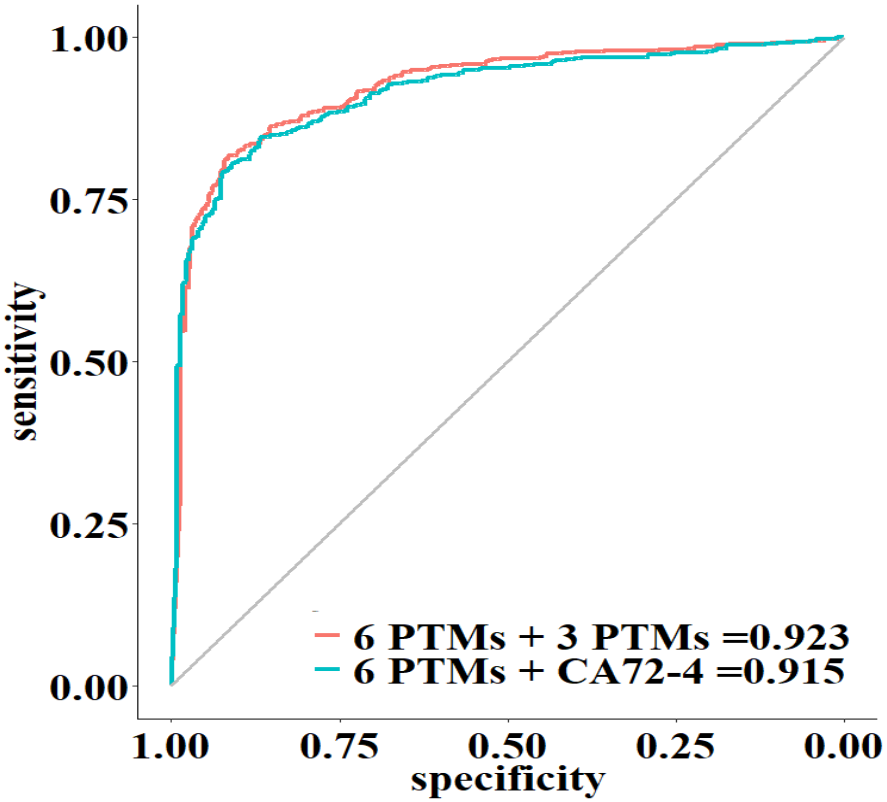
The performance of OncoSeek v2

In all the samples, Delong's test: p = 0.098



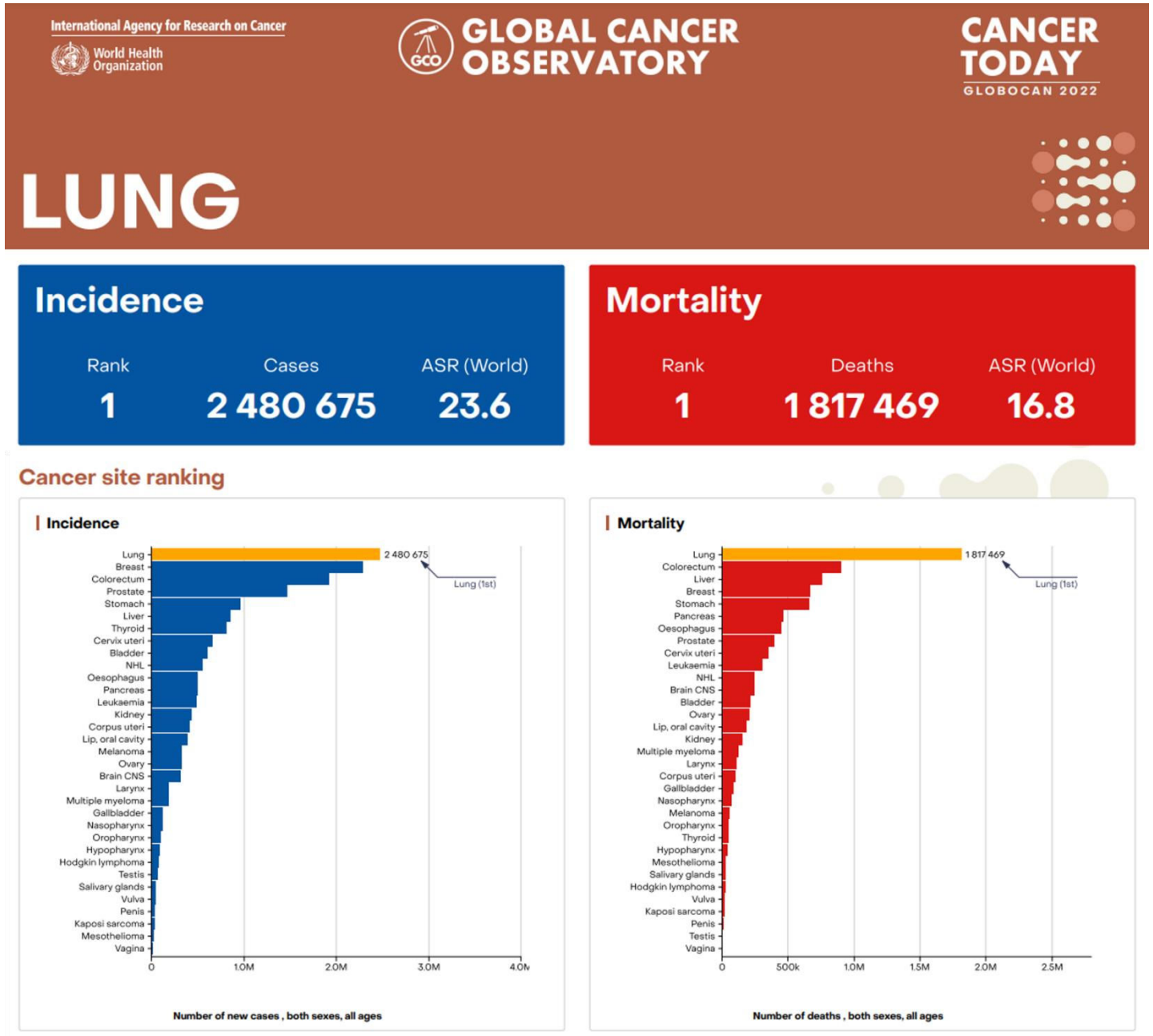
	Cancer	Non-cancer
Predict cancer	430	17
Predict non-cancer	155	338
Sensitivity (95% CI)	**73.5% (69.7%, 77.0%)**	
Specificity (95% CI)	**95.2% (92.4%, 97.2%)**	
PPV (95% CI)	96.2% (94.0%, 97.8%)	
NPV (95% CI)	68.6% (64.3%, 72.6%)	

An effective and affordable blood test for lung cancer early detection using four protein markers and artificial intelligence

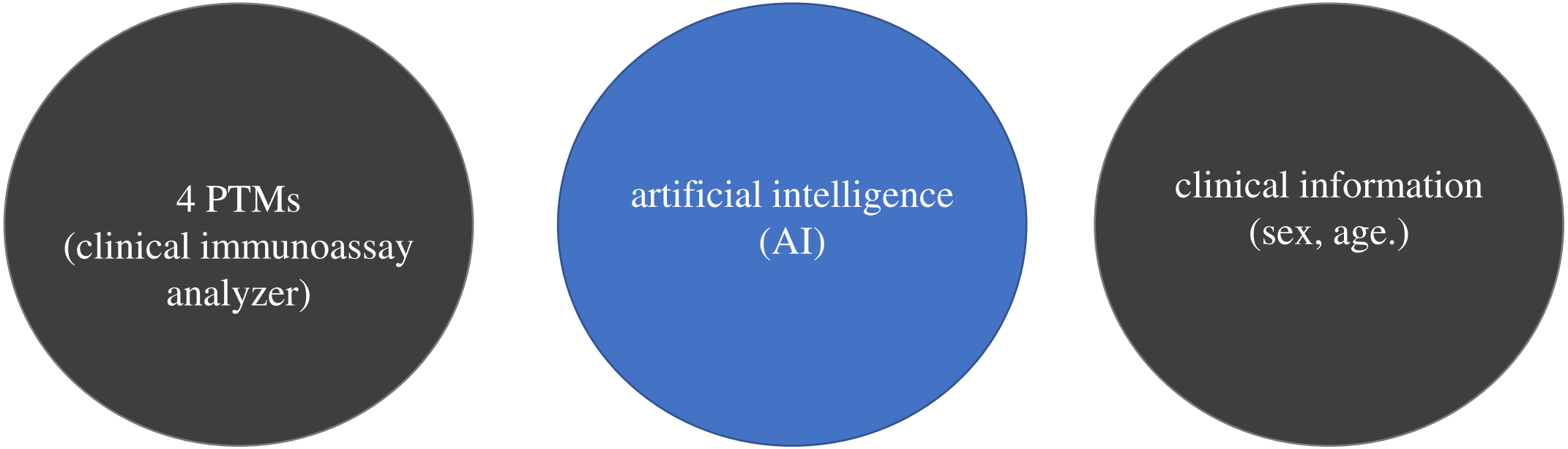
SeekIn

Oct 2024

Lung cancer is the most common and deadly malignancy worldwide



AI-powered lung cancer detection test - LungCanSeek



PTMs: Protein Tumor Markers

The performance of LungCanSeek test in the three cohorts and overall

	Training cohort		Validation cohort 1		Validation cohort 2		Total	
	Cancer	Non-cancer	Cancer	Non-cancer	Cancer	Non-cancer	Cancer	Non-cancer
Predicted cancer	288	33	81	17	545	20	914	70
Predicted non-cancer	95	299	39	161	47	189	181	649
Sensitivity (95% CI)	75.2% (70.6%, 79.4%)		67.5% (58.3%, 75.8%)		92.1% (89.6%, 94.1%)		83.5% (81.1%, 85.6%)	
Specificity (95% CI)	90.1% (86.3%, 93.1%)		90.4% (85.1%, 94.3%)		90.4% (85.6%, 94.1%)		90.3% (87.9%, 92.3%)	
PPV* (95% CI)	89.7% (85.9%, 92.8%)		82.7% (73.7%, 89.6%)		96.5% (94.6%, 97.8%)		92.9% (91.1%, 94.4%)	
NPV** (95% CI)	75.9% (71.4%, 80.0%)		80.5% (74.3%, 85.8%)		80.1% (74.4%, 85.0%)		78.2% (75.2%, 81.0%)	

*PPV, Positive predictive value.
**NPV, Negative predictive value

- LungCanSeek demonstrated an overall sensitivity of 83.5% at a specificity of 90.3%, resulting in 86.2% accuracy.

Performance of LungCanSeek, Early-CDT-Lung, FirstLook-Lung, and LDCT

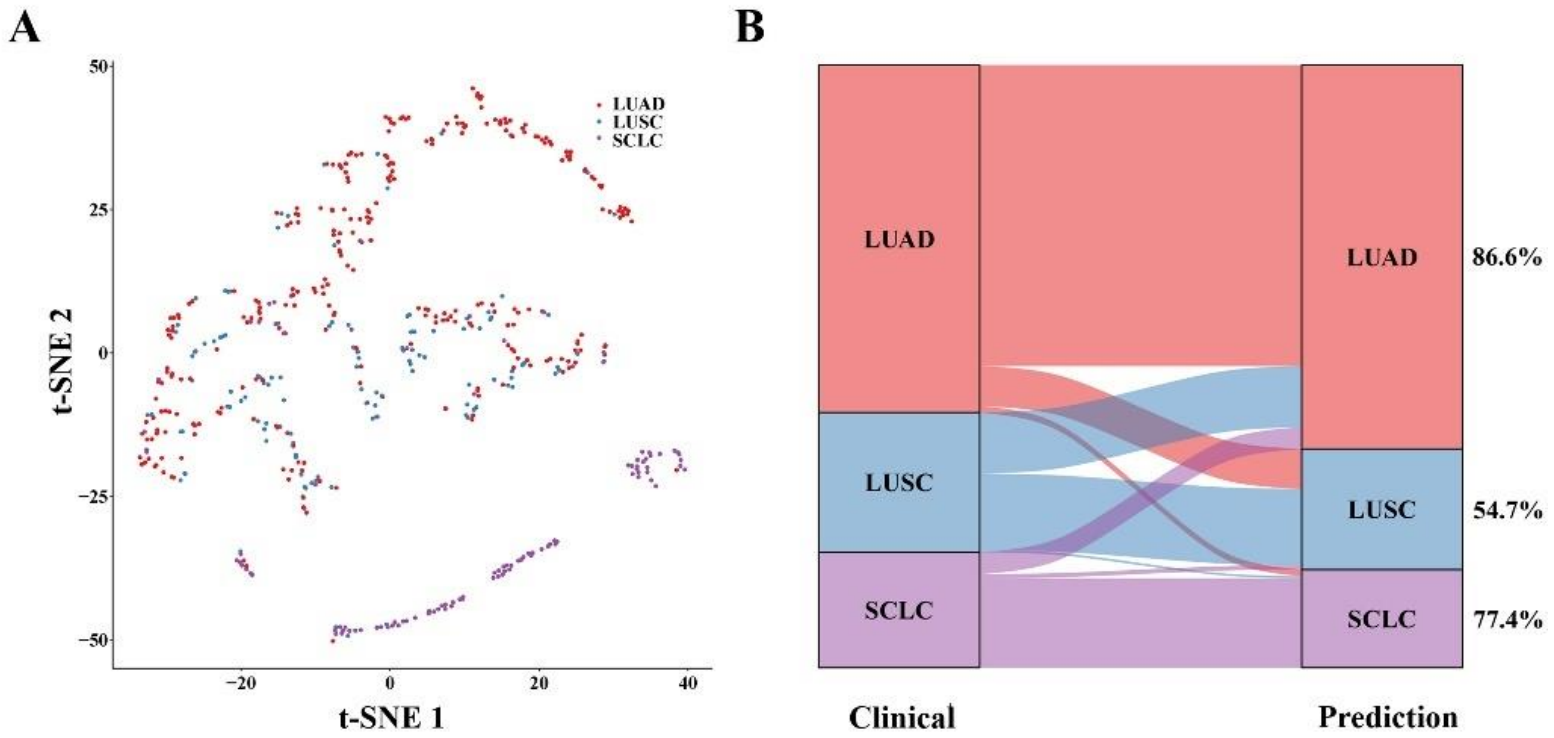
	LungCanSeek (SeekIn) (Lung cancer : Non-cancer = 1095 : 719)	Early-CDT-Lung[1] (OncImmune) (Lung cancer : Non-cancer = 235 : 266)	FirstLook-Lung[2] (DELFI) (Lung cancer : Non-cancer = 429 : 529)	LDCT (NLST Study[3]) (Lung cancer : Healthy = 642 : 25380)
Sensitivity	83.5%	41.0%	84.0%	93.1%
Specificity	90.3%	91.0%	50.9%	76.5%
Cost of per test	$80	$91[4]	~$300*	$277[5]

*According to Delfi Diagnostics executives, the cost of FirstLook-Lung is only one-third of the $949 price of GRAIL's Galleri test.

Ref:

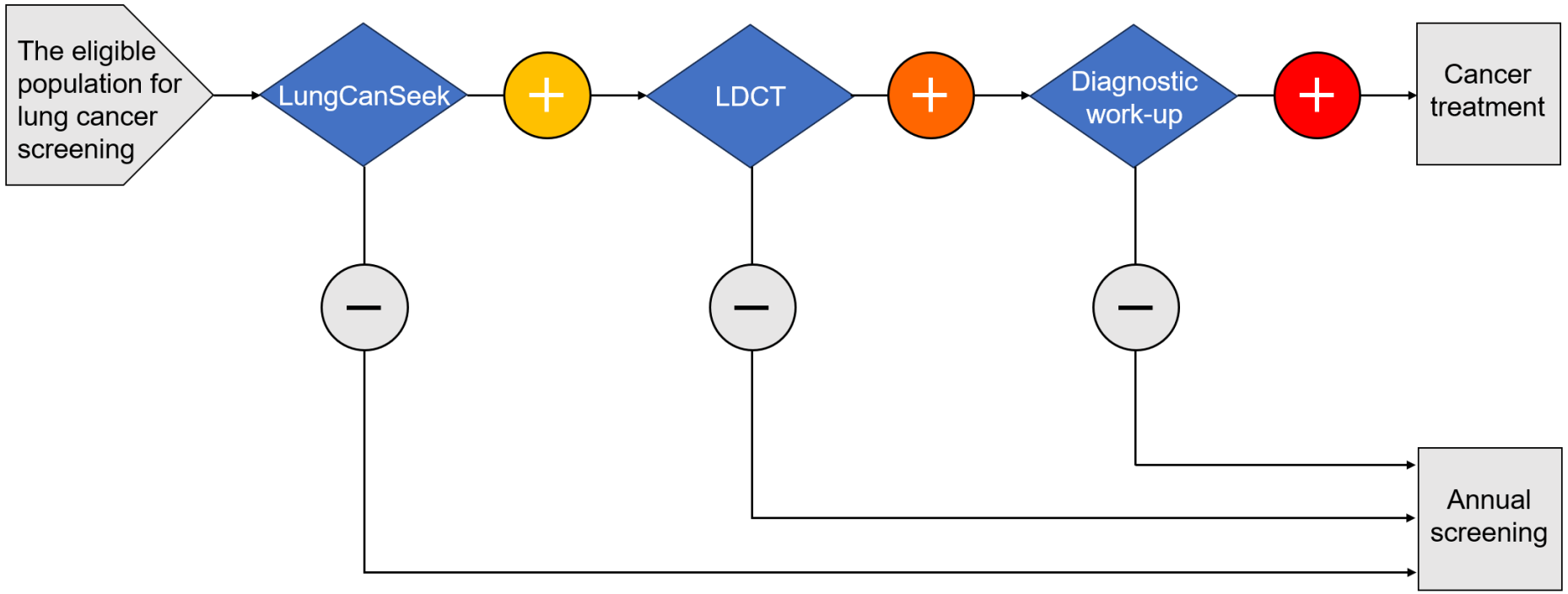
1. Chapman CJ, Healey GF, Murray A, et al. EarlyCDT®-Lung test: improved clinical utility through additional autoantibody assays. Tumor Biology. 2012;33(5):1319-1326. doi:10.1007/s13277-012-0379-2.
2. Mazzone PJ, Bach PB, Carey J, et al. Clinical validation of a cell-free DNA fragmentome assay for augmentation of lung cancer early detection. Cancer Discov. Jun 3, 2024. doi:10.1158/2159-8290.Cd-24-0519.
3. Pinsky PF, Gierada DS, Nath H, Kazerooni EA, Amorosa J. ROC curves for low-dose CT in the National Lung Screening Trial. J Med Screen. 2013;20(3):165-8.
4. Sutton AJ, Sagoo GS, Jackson L, et al. Cost-effectiveness of a new autoantibody test added to Computed Tomography (CT) compared to CT surveillance alone in the diagnosis of lung cancer amongst patients with indeterminate pulmonary nodules. PLoS One 2020;15(9):e0237492.
5. Halpern MT, Liu B, Lowy DR, Gupta S, Croswell JM, Doria-Rose VP. The Annual Cost of Cancer Screening in the United States. Ann Intern Med. Aug 6 2024;doi:10.7326/m24-0375.

The performance of lung cancer subtype classification

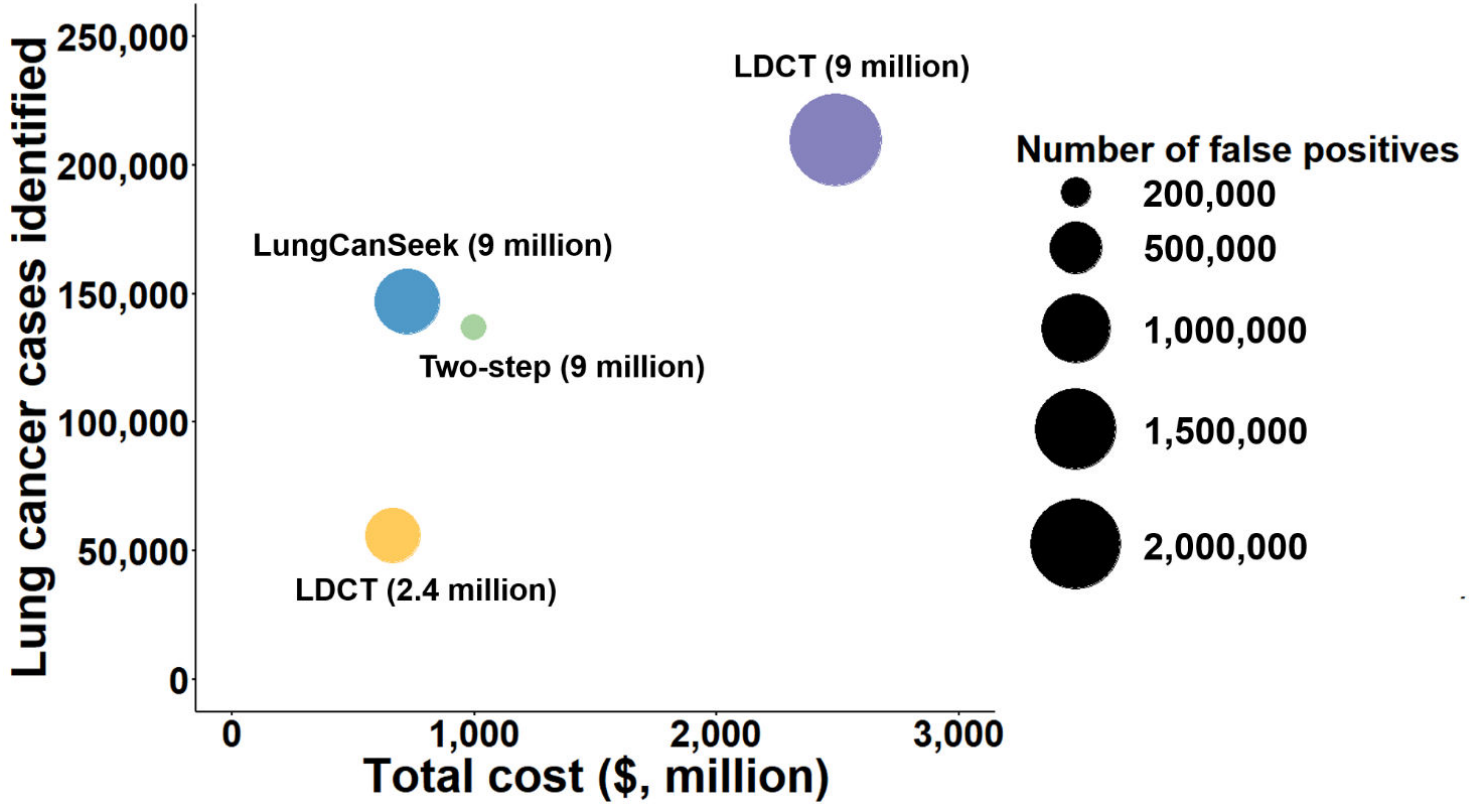


- Overall subtype classification accuracy was 77.4%, with specific accuracies of 74.8% for NSCLC (86.6% for LUAD and 54.7% for LUSC) and 77.4% for SCLC.

The screening pathway of Two-step (LungCanSeek+LDCT)



Comparison of cost among LungCanSeek, LDCT, and Two-step (LungCanSeek+LDCT)



A cost-effective two-step approach for multi-cancer early detection (MCED) in high-risk population

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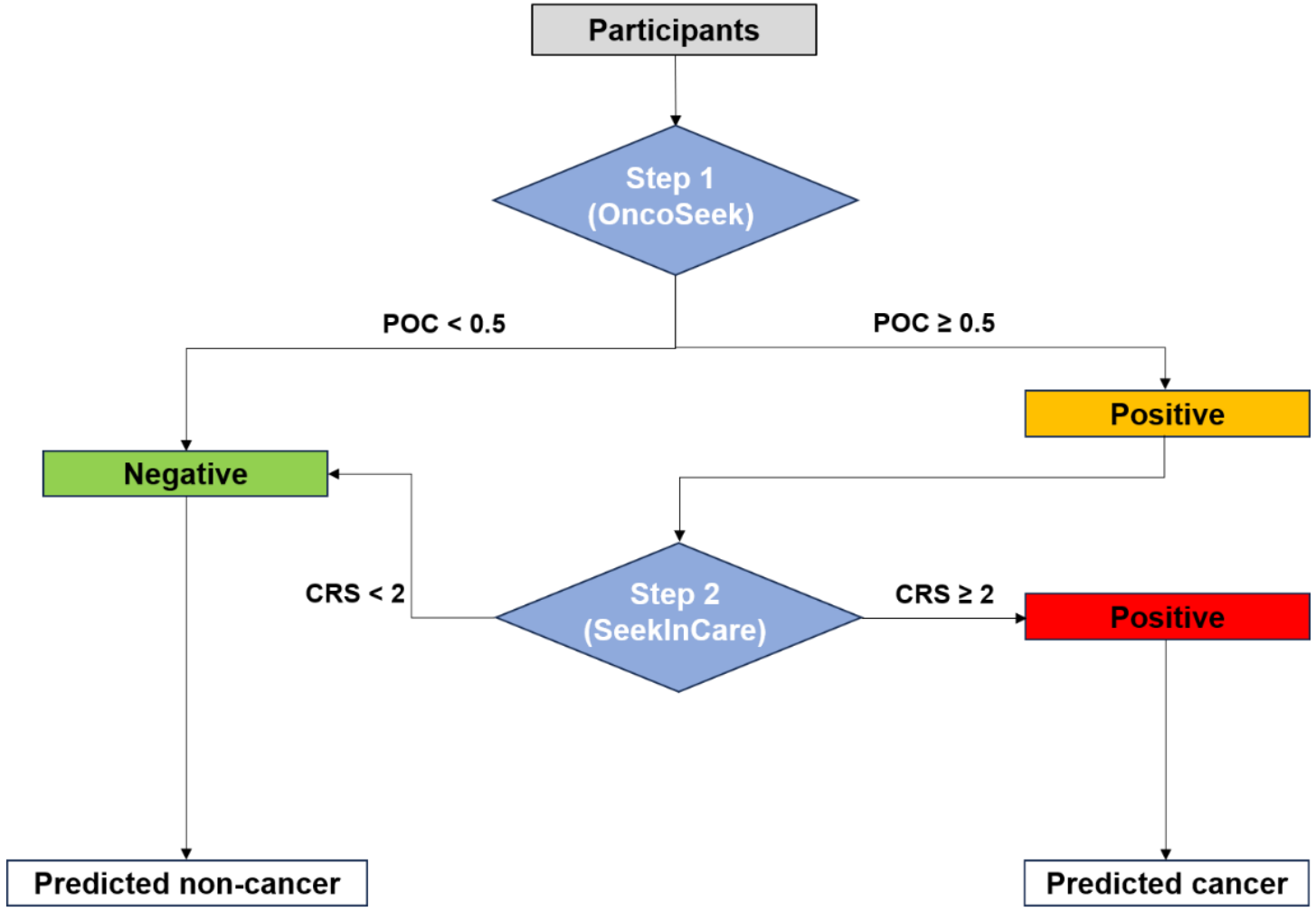
Oct 2024

Two-step MCED approach flowchart



In this two-step approach, the initial screening is conducted using OncoSeek, and SeekInCare is then used as the secondary test for those individuals who tested positive by OncoSeek.

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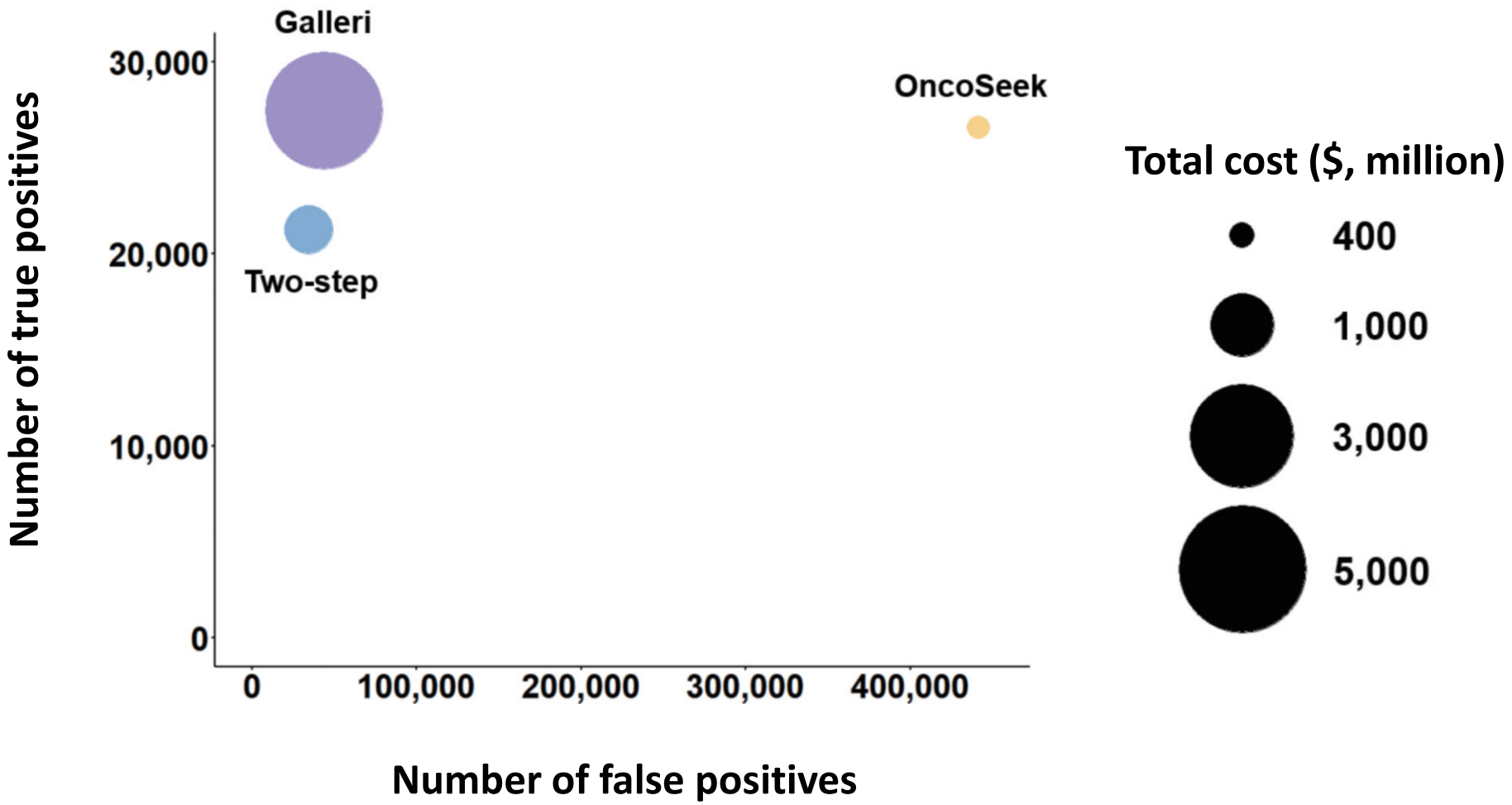
Cost-effectiveness comparison



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