Nereo Segnan MD, MS Epi

CPO Piemonte

Nuovi scenari per lo screening del CCR: i driver del cambiamento negli screening oncologici

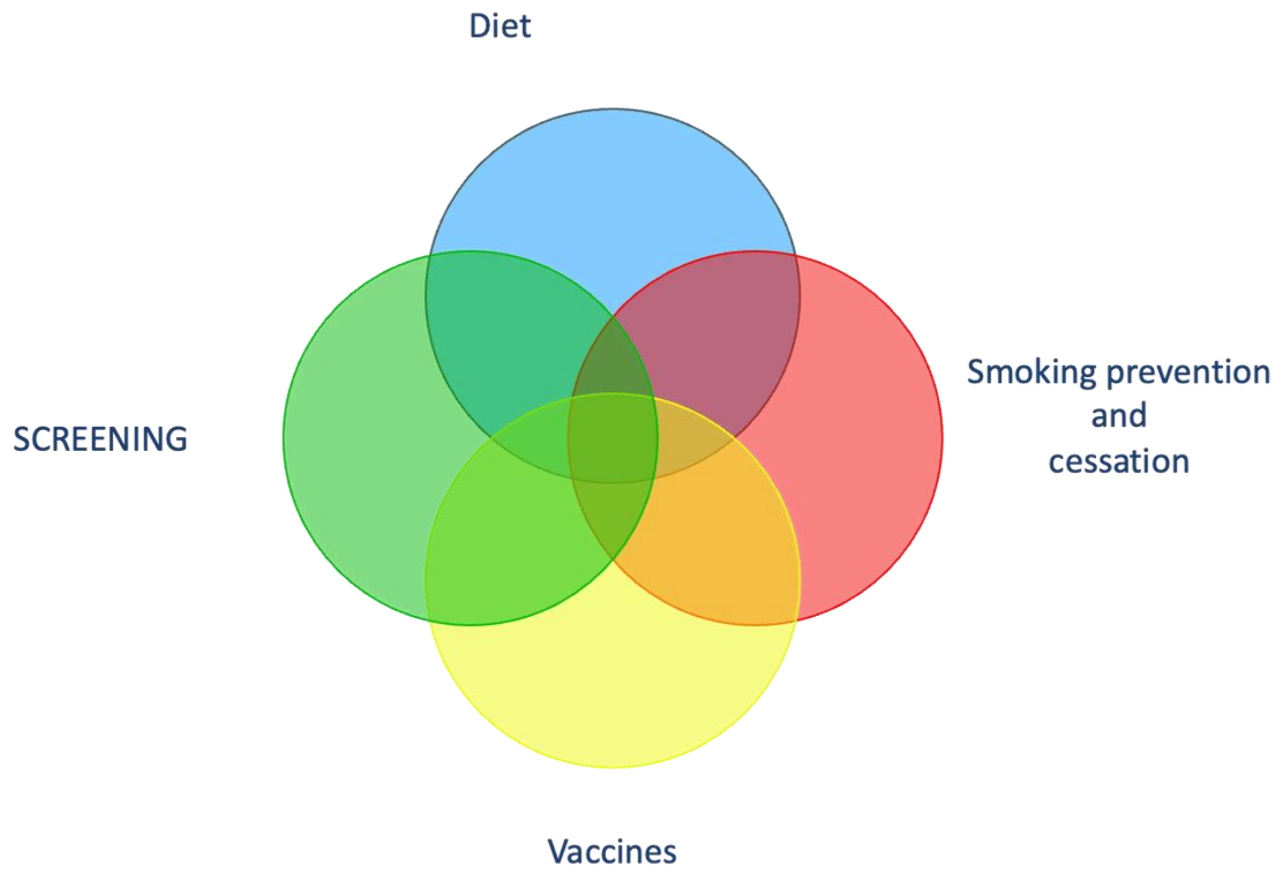
GISCOR

Cagliari

7 novembre 2025

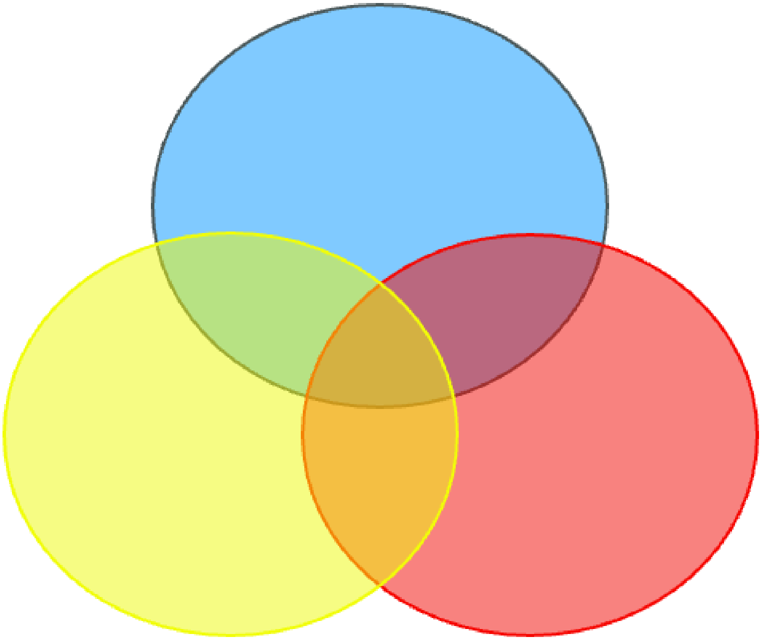
- **Nessun conflitto di interesse da dichiarare**

Primary and secondary prevention interventions target the same individual.



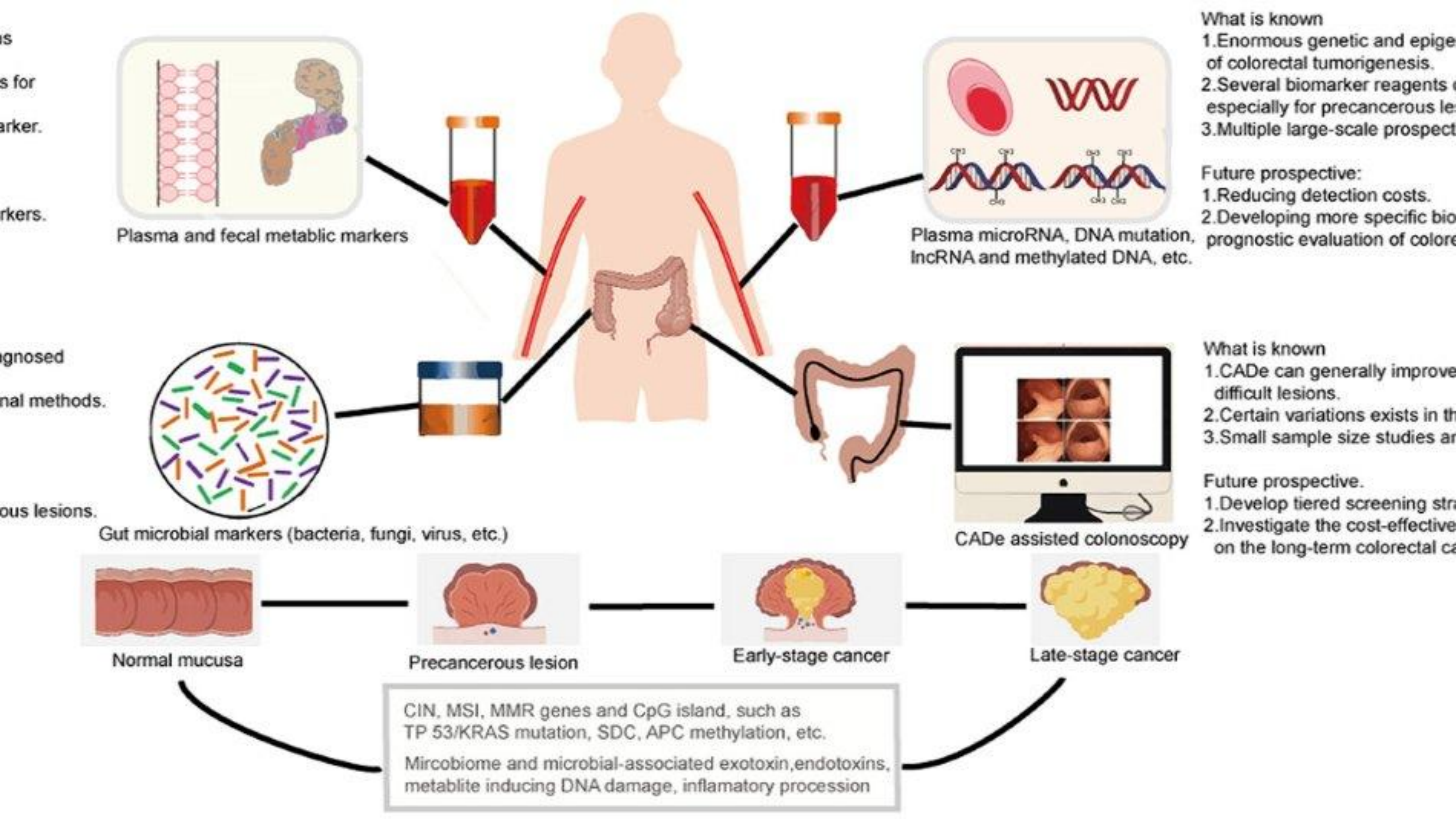
Only cancer?

The same risk factor may cause many chronic diseases which affect the same individual



Comorbidities

GISCOr come gruppo Italiano per lo screening del carcinoma colo-rettale dovrebbe seguire la evoluzione degli scenari di screening dei tumori a seguito dell'introduzione, ormai in atto, di nuove tecnologie (NT) per tutti le sedi di cancro potenzialmente prevenibili/curabili incluso il Cancro COLO-RETTALE.



Plasma and fecal metablic markers
Plasma microRNA, DNA mutation, lncRNA and methylated DNA, etc.
What is known
1.Enormous genetic and epige
of colorectal tumorigenesis.
2.Several biomarker reagents
especially for precancerous le
3.Multiple large-scale prospect
Future prospective:
1.Reducing detection costs.
2.Developing more specific bio
prognostic evaluation of colore
Gut microbial markers (bacteria, fungi, virus, etc.)
CADe assisted colonoscopy
What is known
1.CADe can generally improve
difficult lesions.
2.Certain variations exists in th
3.Small sample size studies ar
Future prospective.
1.Develop tiered screening stra
2.Investigate the cost-effective
on the long-term colorectal ca
Normal mucusa
Precancerous lesion
Early-stage cancer
Late-stage cancer
CIN, MSI, MMR genes and CpG island, such as
TP 53/KRAS mutation, SDC, APC methylation, etc.
Mircobiome and microbial-associated exotoxin,endotoxins,
metablite inducing DNA damage, inflamatory procession

Tamm *et al. BMC Medicine (2025) 23:503*
https://doi.org/10.1186/s12916-025-04339-w

RESEARCH Open Access

BMC Medicine

External validation of the COLOFIT colorectal cancer risk prediction model in the Oxford-FIT dataset: the importance of population characteristics and clinically relevant evaluation metrics

Andres Tamm[1,2*], Brian Shine[4], Tim James[4], Jaimie Withers[3,5], Hizni Salih[3,5], Theresa Noble[3,5], Kinga A. Varnai[3,5],
James E. East[3,6], Gary Abel[9], Willie Hamilton[9], Colin Rees[10,11], Eva J. A. Morris[2,7], Jim Davies[2,3,8] and Brian D. Nicholson[1]

Abstract

COLOFIT reduced

referrals by 8% overall without missing colorectal cancers compared to FIT ≥ 10 μg/g, but this varied from 23% reduction

to 2% increase depending on the period evaluated

International Journal of Colorectal Disease   (2025) 40:218 https://doi.org/10.1007/s00384-025-04949-z

REVIEW Effectiveness of artificial intelligence-assisted colonoscopy in detecting and diagnosing colorectal tumors: a systematic review and network meta-analysis

Shufa Tan1 · Pengfei Zeng2 · Shuang Liu1 · Yunyi Yang3 · Shikai Chen4 · Wei Zhang5 · Xiaoming Li6 · Dingbing Liu7 · Yuwei Li8 · Chen Xu8

- Conclusion ENDOANGEL model-assisted colonoscopy shows the best efficacy on both ADR and PDR, Endocuff-AI model-assisted colonoscopy shows the best performance on SSL, and compared with optical evaluation without CADx, real-time polyp assessment using CADx did not significantly increase the diagnostic sensitivity of neoplastic polyps during colonoscopy.

REVIEW ARTICLE | FOCUS
https://doi.org/10.1038/s41591-022-01746-x

nature medicine

Check for updates

The future of early cancer detection

Rebecca C. Fitzgerald[1], Antonis C. Antoniou[2], Ljiljana Fruk[3] and Nitzan Rosenfeld[4]

A proactive approach to detecting cancer at an early stage can make treatments more effective, with fewer side effects and improved long-term survival. However, as detection methods become increasingly sensitive, it can be difficult to distinguish inconsequential changes from lesions that will lead to life-threatening cancer. Progress relies on a detailed understanding of individualized risk, clear delineation of cancer development stages, a range of testing methods with optimal performance characteristics, and robust evaluation of the implications for individuals and society. In the future, advances in sensors, contrast agents, molecular methods, and artificial intelligence will help detect cancer-specific signals in real time. To reduce the burden of cancer on society, risk-based detection and prevention needs to be cost effective and widely accessible.

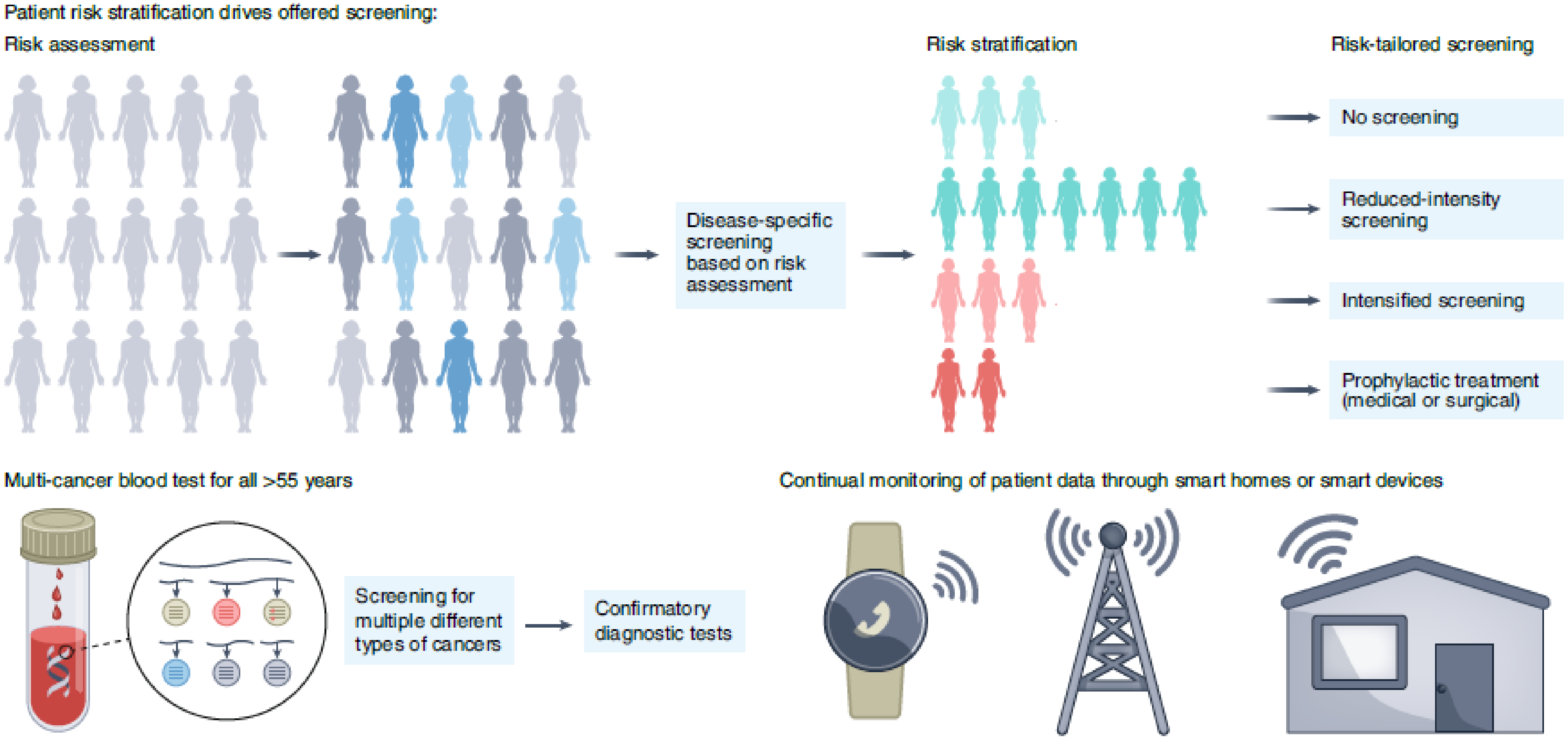


Fig. 4 | New paradigms for early cancer detection. Three potential scenarios are shown: a risk-stratified, holistic approach; a multicancer blood test; and smart devices for continuous monitoring. Top, a holistic approach would result in screening people for specific cancers on the basis of risk assessment. Further screening would stratify patients to levels of surveillance depending on their risk. Bottom left, a blood test capable of detecting multiple cancers would be used to screen the population over 55 years old. Companion diagnostic tests would confirm the results from the blood analysis. Bottom right, population data could be continually monitored through smart watches, phones or homes. Data would be transferred to data hubs for analysis.

Life Sciences 348 (2024) 122634

Contents lists available at ScienceDirect

Life Sciences

journal homepage: www.elsevier.com/locate/lifescie

Application of machine learning for high-throughput tumor marker screening

Xingxing Fu [a], Wanting Ma [a], Qi Zuo [a], Yanfei Qi [b,*], Shubiao Zhang [a,*], Yinan Zhao [a,*]

[a] Key Laboratory of Biotechnology and Bioresources Utilization of Ministry of Education, Dalian Minzu University, Dalian 116600, China
[b] Centenary Institute, The University of Sydney, Sydney, NSW 2050, Australia

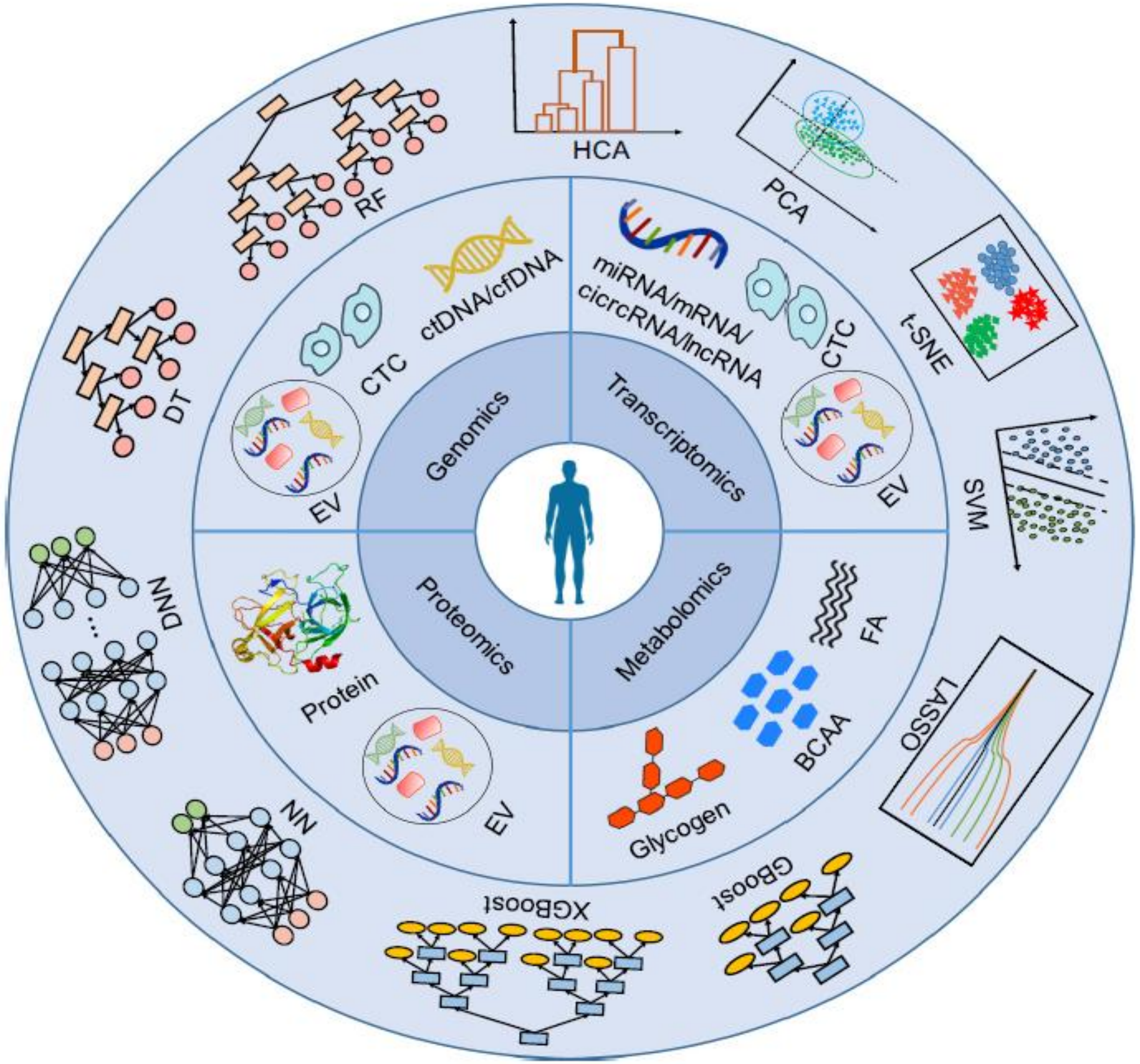


Fig. 1. Machine learning algorithms (outer ring) used for tumor marker (inner ring) screening of genomic, transcriptomic, proteomic, and metabolomic data. Common tumor markers are derived from circulating tumor cells (CTC), cell-free DNA (cfDNA), circulating tumor DNA (ctDNA), microRNA (miRNA), messenger RNA (mRNA), circular RNA (circRNA), long noncoding RNA (lncRNA), extracellular vesicle (EV), circulating tumor proteins, and metabolites (e.g., glycogen, branched-chain amino acids (BCAA), fatty acids (FA)). Commonly used algorithms in tumor marker screening are least absolute shrinkage and selection operator (LASSO), logistic regression (LR), decision tree (DT), random forest (RF), support vector machine (SVM), gradient boosting (GBoost), extreme gradient boosting (XGBoost), neural network (NN), deep neural network (DNN), hierarchical cluster analysis (HCA), principal component analysis (PCA), and t-distributed stochastic neighbor

Table 1
Machine learning algorithms used for genomic tumor marker screening.

Cancer type	Method	Biomarker	Function	Performance	Reference
colorectal cancer	LASSO-Cox, RF, clustering	ctDNA	early diagnosis, prognosis prediction	AUC 0.96	[22]
multi-cancer	RF, LR, XGBoost, CNN, GCNN	ctDNA	early detection, localization	sensitivity 72.4 % specificity 97.0 % accuracy 0.7	[26]
multi-cancer	PCA, XGBoost, RF, SVM, LR	ctDNA	diagnosis	AUC 0.96	[41]
urothelial carcinoma	RF, SVM and LASSO	cfDNA	detection, surveillance	sensitivity 86.5 % specificity 94.7 %	[37]
lung cancer	RF, generalized linear model, GBoost, DL, XGBoost	cfDNA	early detection	AUC >0.97	[42]
breast cancer	single-parametric linear model	cfDNA	prognosis prediction	AUC 0.80	[57]
pituitary neuroendocrine tumor	clustering, deconvolution	cfDNA	diagnosis, prognosis prediction	accuracy >93 %	[58]
lung cancer	multimodal model	cfDNA	detection, characterization	specificity 80 % AUC 0.98	[59]
sinonasal undifferentiated carcinoma	t-SNE, HCA, SVM, RF	DNA methylation	classification, diagnosis	specificity 0.982	[34]
triple-negative breast cancer	RF, SVM	DNA methylation	prognosis prediction	AUC 1.00	[43]
renal cell carcinoma	XGBoost	DNA methylation	detection of benign and malignant renal tumor subtypes	accuracy 0.96 AUC >0.98	[60]
leukemias	semi-supervised method	DNA methylation	diagnosis and prognosis	AUC 1.00	[61]
head and neck squamous cell cancers	RF, SVM NN, elastic net penalized LR	DNA methylation	predict the primary sites	accuracy 92 % sensitivity 88 % specificity 95 %	[62]

RF, random forest; SVM, support vector machine; LR, logistic regression; GBoost, gradient boosting; XGBoost, extreme gradient boosting; DL, deep learning; LASSO, least absolute shrinkage and selection operator; CNN, convolutional neural network; GCNN, graph convolutional neural network; t-SNE, t-distributed stochastic neighbor embedding; HCA, hierarchical cluster analysis; NN, neural network; PCA, principal component analysis; ctDNA, circulating tumor DNA; cfDNA, cell-free DNA; AUC, area under the receiver operating characteristic curve.

British Journal of Cancer www.nature.com/bjc

ARTICLE OPEN

Check for updates

Modelled mortality benefits of multi-cancer early detection screening in England

Peter Sasieni[1], Rebecca Smittenaar[2], Earl Hubbell[3], John Broggio[4], Richard D. Neal[5] and Charles Swanton[6,7]

RESULTS: Estimated late-stage and mortality reductions were robust to a range of assumptions. With the least favourable dwell (sojourn) time and cfDNA status hazard ratio assumptions, we estimated, among 100,000 screened individuals, 67 (17%) fewer cancer deaths per year corresponding to 2029 fewer deaths in those screened between ages 50–79 years.

CONCLUSION: Realising the potential benefits of MCED tests could substantially reduce late-stage cancer diagnoses and mortality.

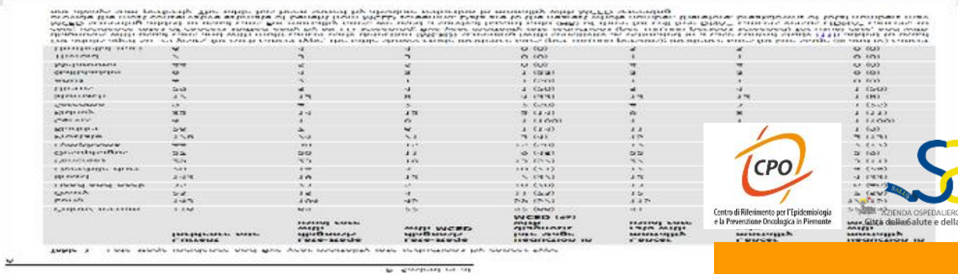


Table 3. Late-stage incidence and five-year mortality rate reductions by cancer type.

	Current incidence rate	Late-stage diagnosis with usual care	Late-stage diagnosis with MCED	Reduction in late-stage diagnosis with MCED (%)	Cancer mortality rate with usual care	Cancer mortality rate with MCED	Reduction in mortality with MCED (%)
Colon/ rectum	116	64	22	42 (66)	41	18	22 (54)
Lung	143	104	45	59 (57)	115	98	17 (15)
Ovary	23	15	4	11 (73)	12	5	7 (58)
Head and neck	35	23	5	18 (78)	13	7	6 (46)
Breast	143	19	12	7 (37)	12	8	4 (33)
Liver/bile duct	20	14	3	10 (71)	17	13	4 (24)
Pancreas	29	23	10	13 (57)	27	25	3 (11)
Oesophagus	27	20	11	9 (45)	22	20	2 (9)
Lymphoma	44	30	15	15 (50)	12	10	2 (17)
Prostate	178	74	71	3 (4)	15	14	2 (13)
Bladder	28	7	6	1 (14)	11	10	1 (9)
Cervix	4	1	0	1 (100)	1	1	1 (100)
Kidney	32	14	12	2 (14)	9	8	1 (11)
Sarcoma	9	4	2	2 (50)	4	3	1 (25)
Stomach	17	12	8	4 (33)	13	12	1 (8)
Uterus	29	5	4	1 (20)	5	4	1 (20)
Anus	4	2	1	1 (50)	1	1	0 (0)
Gallbladder	6	4	3	1 (25)	5	5	0 (0)
Melanoma	44	5	5	0 (0)	4	4	0 (0)
Thyroid	7	3	3	0 (0)	1	1	0 (0)
Urothelial tract	6	4	4	0 (0)	3	3	0 (0)

For adults aged 50–79 years, for each cancer type, the table shows: crude incidence rates (per 100,000 persons); incidence rates for late-stage (III and IV) cancer diagnoses with usual care, and with multi-cancer early detection (MCED) screening (with sensitivity as estimated in a case-control study [11]) added to usual care; incidence rates of cancers shifted early by MCED screening; five-year mortality rate reductions (per 100,000 persons screened) for usual care, and with MCED screening added to usual care. For mortality rates, we used a survival hazard ratio (HR) of three for cell-free DNA^{+} cancers versus cfDNA^{-} cancers, to provide the most conservative estimate of benefit from MCED screening. Data are to the nearest whole number; therefore, breakdowns of total numbers may not always sum perfectly. The table has been sorted by absolute reduction in mortality with MCED screening.

Diagnostic accuracy of currently available multi-cancer early detection

1. **Galleri®** (GRAIL, Menlo Park, CA, USA) sensitivity 20.8-66.3%, specificity 98.4-99.5% (three studies);
2. **CancerSEEK** (Exact Sciences, Madison, WI, USA) sensitivity 27.1-62.3%, specificity 98.9- 99.1% (two studies);
3. **SPOT-MAS™** (Gene Solutions, Ho Chi Minh City, Vietnam) sensitivity 72.4-100%, specificity 97.0-99.9% (two studies);
4. **Trucheck™** (Datar Cancer Genetics, Bayreuth, Germany) sensitivity 90.0%, specificity 96.4% (one study);
5. **Cancer Differentiation** Analysis (AnPac Bio, Shanghai, China) sensitivity 40.0%, specificity 97.6% (one study).

Wade R, Nevitt S, Liu Y, Harden M, Khouja C, Raine G, Churchill R, Dias S. Multi-cancer early detection tests for general population screening: a systematic literature review. Health Technol Assess. 2025 Jan;29(2):1-105. doi: 10.3310/DLMT1294. PMID: 39898371; PMCID: PMC11808444.

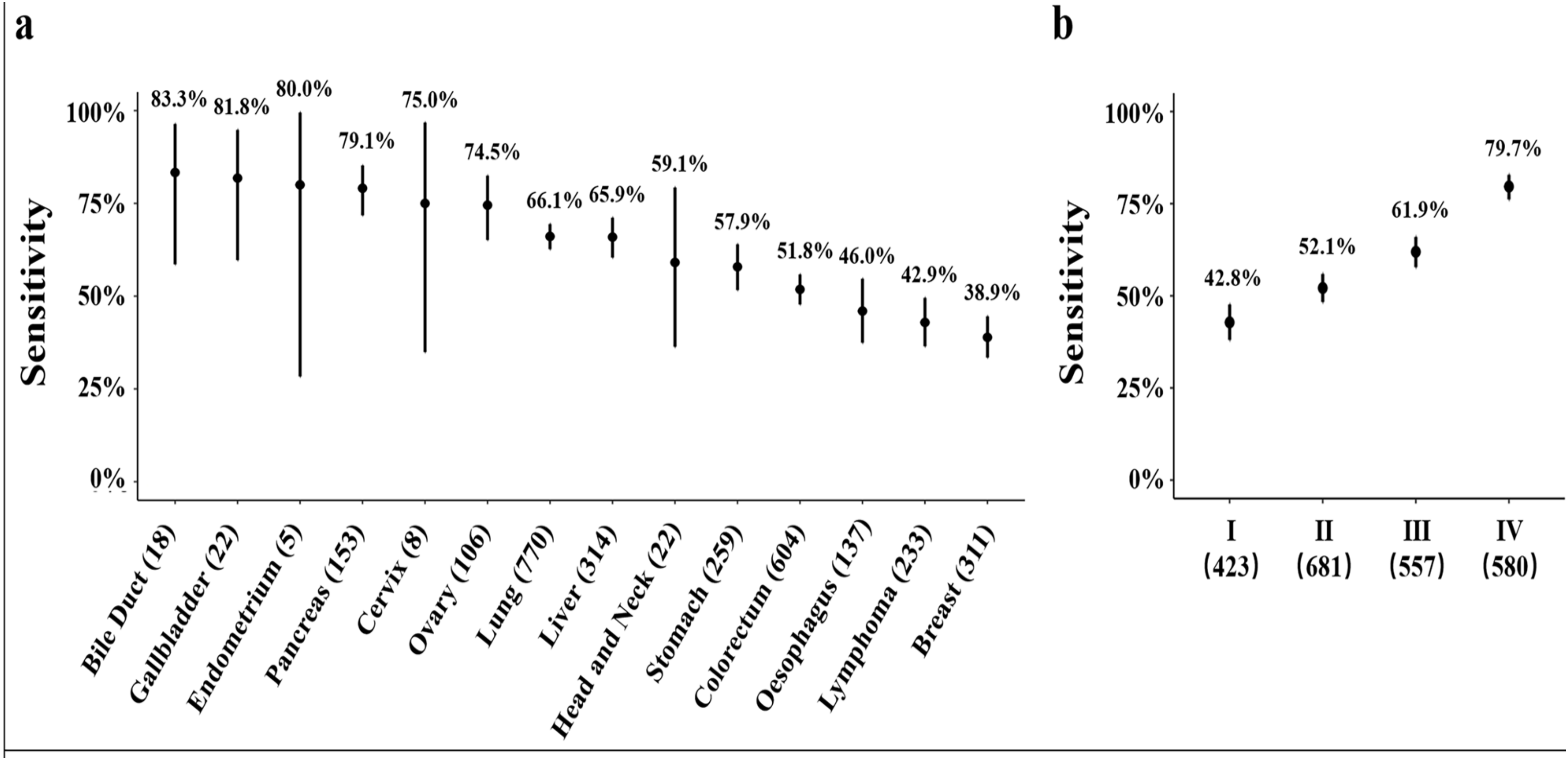
npj | precision oncology Article
Published in partnership with The Hormel Institute, University of Minnesota
https://doi.org/10.1038/s41698-025-01105-2

A large-scale, multi-centre validation study of an AI-empowered blood-based test for multi-cancer early detection

Yong Shen[1,8], Yong Xia[2,8], Yinyin Chang[3,8], Pingping Xing[3,8], Shiyong Li[4], WeiWu[4], Ruidan Zhu[1],
Guolin Zhong[4], Dandan Zhu[3], Raphael Brandão[5] , Qingxia Xu[1] , Ling Ji[2] & Mao Mao[6,7]
Cancer is a critical global health issue, especially in low- and middle-income countries (LMICs). In this

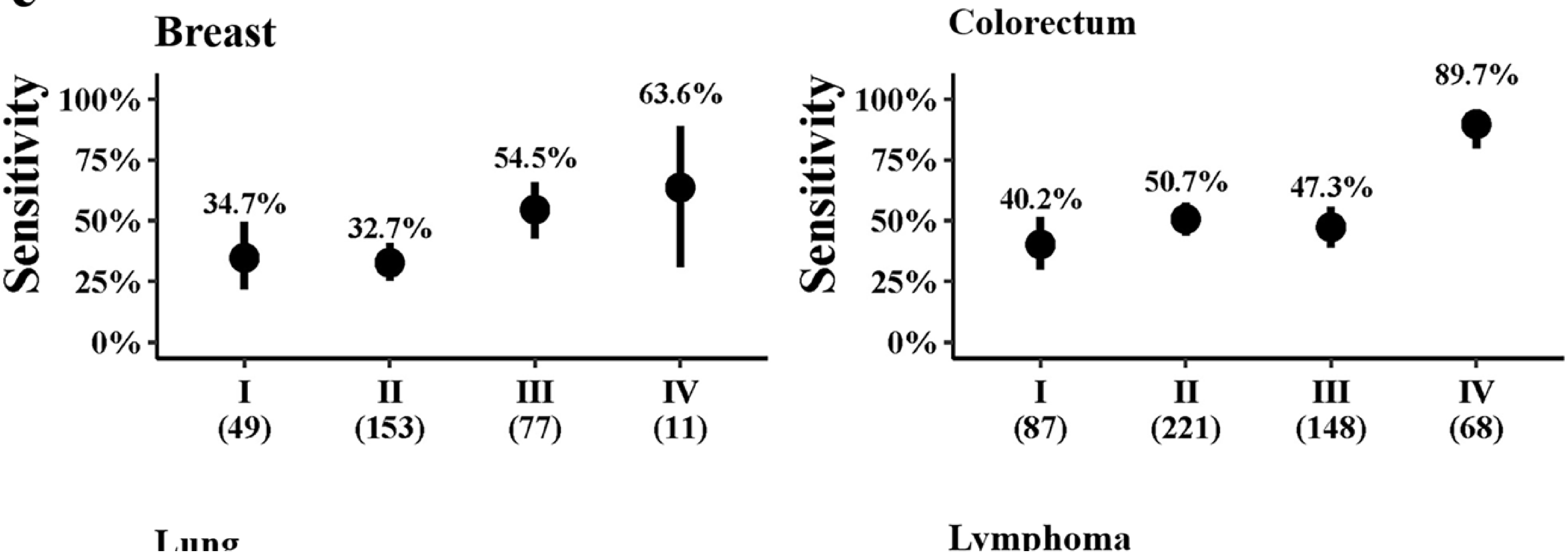
- OncoSeek
- Costo 25 Euro

ONCO SEEK



a
b
Sensitivity
100%
75%
50%
25%
0%
83.3%
81.8%
80.0%
79.1%
75.0%
74.5%
66.1%
65.9%
59.1%
57.9%
51.8%
46.0%
42.9%
38.9%
Bile Duct (18)
Gallbladder (22)
Endometrium (5)
Pancreas (153)
Cervix (8)
Ovary (106)
Lung (770)
Liver (314)
Head and Neck (22)
Stomach (259)
Colorectum (604)
Oesophagus (137)
Lymphoma (233)
Breast (311)
42.8%
52.1%
61.9%
79.7%
I (423)
II (681)
III (557)
IV (580)

c

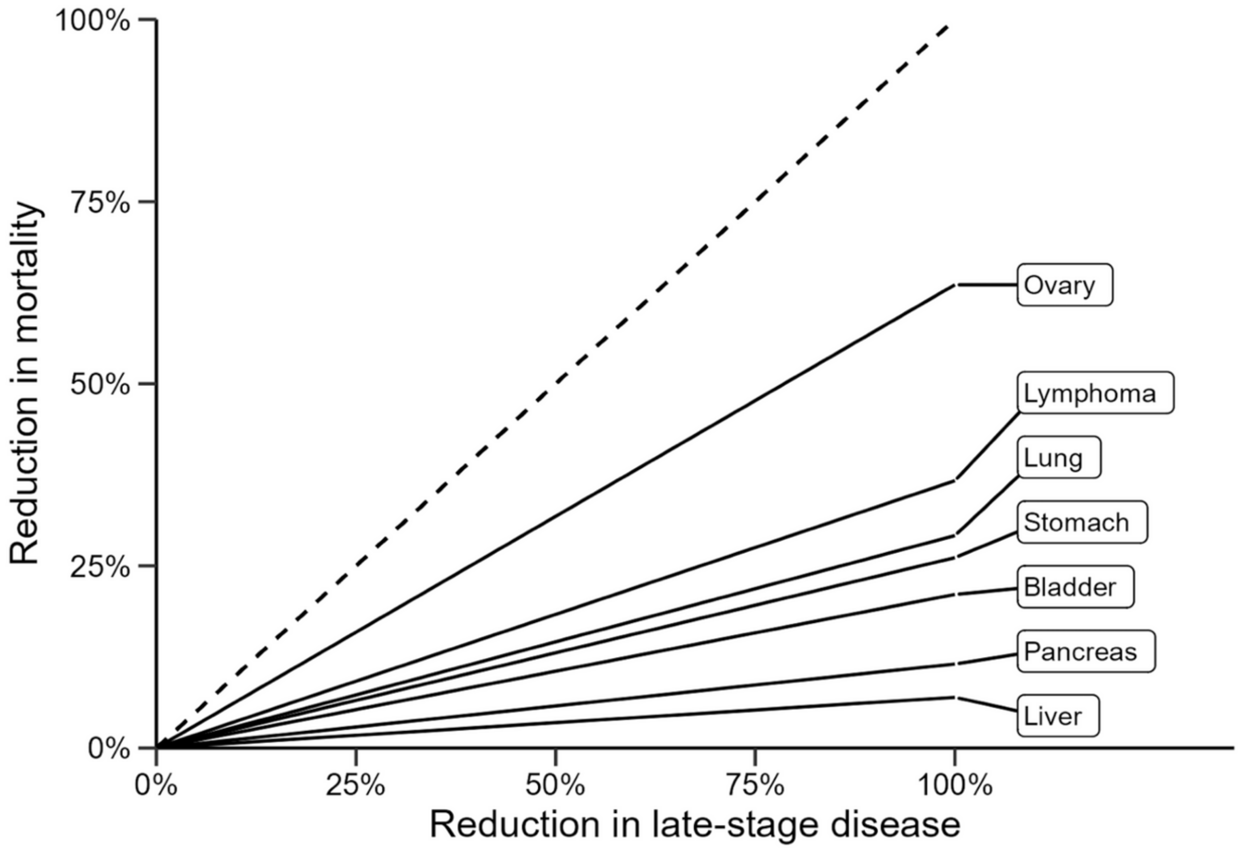

Breast
Colorectum
Sensitivity
100%
75%
50%
25%
0%
34.7%
32.7%
54.5%
63.6%
I
(49)
II
(153)
III
(77)
IV
(11)
40.2%
50.7%
47.3%
89.7%
I
(87)
II
(221)
III
(148)
IV
(68)
Lung
Lymphoma

- In MCED, any mortality benefit is likely to vary substantially across target cancers. Stage shift does not appear to be a reliable basis for inference about mortality reduction across cancers potentially detectable by MCED tests.

- Impact: Stage shift may be an appealing endpoint for evaluation of cancer screening tests but it appears to be an unreliable predictor of mortality benefit; further, the same stage shift can mean different things for different cancers." **Advanced cancer Incidence may a suitable endpoint**

Centro di Riferimento per l'Epidemiologia e la Prevenzione Oncologica in Piemonte

AZIENDA OSPEDALIERO-UNIVERSITARIA Città della Salute e della Scienza di Torino



Cancer Epidemiol Biomarkers Prev. 2022 July 01; 31(7): 1298–1304.?Stage Shift as an Endpoint in Cancer Screening Trials: Implications for Evaluating Multi-Cancer Early Detection Tests?
Lukas Owens, Roman Gulati, Ruth Etzion

"The figure shows that the same reduction in late-stage disease has a different implication for mortality depending on the characteristics of the cancer. For example, in ovarian cancer, ρ = 0.636, so a 20% reduction in late-stage disease is expected to result in a 13% mortality reduction, but for liver cancer, the value of the stage-shift multiplier is only 0.070, so a similar 20% reduction in late-stage disease would be expected to produce a 1% mortality reduction

- MCED and Detection of precursors lesions?

- Eighty % of the reduction of mortality (avoided death) for colorectal cancer is due to precursors lesions removal (adenomas) and 20% to stage shifting.

At the moment MCED may reduce cancer mortality not cancer incidence.

- Low sensitivity for early stages

- MCED and primary prevention: blood sample easier to take than to introduce behavioural changes or environmental prevention.

Possiamo aspettarci conseguenze rilevanti delle NT:

1. **sulla misura dell’impatto dello screening (metrica)**
2. **sulla stima del rischio individuale**
3. **sui protocolli e programmi di screening (interventi).**

Questi temi possono essere assunti come "driver" per l'aggiornamento e l'adattamento delle metodologie di screening dei tumori.

L'impatto dei "driver" sull'organizzazione, l'erogazione e la valutazione dello screening è cruciale per il futuro dello screening del cancro.

1. **Metrica** Un **unico indicatore** dovrebbe misurare l'impatto dello screening (metrica) sulla salute dell'individuo e della popolazione , in modo **da integrare la mortalità e le disabilità** che si verificano in due gruppi: individui sottoposti a screening rispetto a quelli non sottoposti a screening, in relazione alla storia di screening, per qualsiasi causa di morte e comorbilità.

La bilancia tra danni e benefici dello screening dei tumori è inadeguata poichè comprende indicatori eterogenei e non commensurabili tra di loro (falsi negativi , falsi positivi, casi intervallo, anni di vita salvati, sovratrattamento, trattamenti meno invasivi, ansia, rassicurazione ....).

Indicatori come i possono misurare i danni e i DALY’s (Disability Adjusted Life Years) o i QALY’s (Quality Adjusted Life Years) benefici dello screening, combinando gli anni di vita persi per morte prematura e gli anni vissuti con disabilità (DALY’S) e gli anni di vita vissuti corretti per qualità della vita (QUALY’).

La stima di DALY/QUALY incorpora anche l'effetto dell'intervento di prevenzione primaria, se presente, nei due gruppi e delle comorbidità presenti.

Coorti di popolazione possono consentire di confrontare le persone sottoposte a screening e non sottoposte a screening rispetto al rischio e alle stime di DALY/QUALY, utilizzando la densità di incidenza e la densità di incidenza cumulativa come parametri per misurare gli eventi nel processo di screening e l'intensità dello screening.

stratificazione del rischio per ……………………

- **Sede specifica : incidenza per tipo/sede**
- **Tutti le sedi: Incidenza tutti I tumori**
- **Morte: mortalità per tutte le cause**
- **Morte per cancro: mortalità per sede specifica**
- **Morte prematurah: anni di vita perduti**
- **Disabilità/qualità della vita : Disability Adjusted Life Years (DALY’s)/Quality Adjusted Life Years (QALY’s)**

2. Il **rischio individuale di cancro** dovrebbe governare il protocollo di screening, in termini di eligibilità, tipo di test e intensità dello screening.
Sono disponibili molti punteggi di rischio da cui derivare la soglia per l'eligibilità allo screening e le priorità di intervento. Un punteggio di rischio dovrebbe calcolare quanto una persona stia modificando il rischio di cancro attraverso le sue scelte di vita ed esposizioni ambientali esposizioni ambientali.

A seconda del rischio individuale, che incorpora variazioni dovute alla prevenzione primaria, lo screening personalizzato potrebbe essere proposto come test multitumorale o site specific, in relazione al livello di evidenza disponibile (DALY.s) di efficacia.

3. L'effetto dei "driver" sull'intervento (organizzazione, l'erogazione e la valutazione dello screening) è fondamentale per l'aggiornamento/modifica delle linee guida e la loro implementazione nei programmi di screening.

aggiornamento/modifica delle linee guida, e implementazione nei programmi di screening.

Biomarker per singole neoplasie e MCED validati

algoritmi diagnostici validati (deep learning, CAD....)

Affiancamento test già in uso (cotesting, triage) o test alternativo

Percorsi di Assessment adeguamento clinico

Adozione punteggi di rischio e protocolli di screening per differenti gruppi di rischio

Aggiornamento punteggi di rischio

Adeguamento sistemi operativi e flussi di screening

Sistemi informativi a supporto

Indicatore unificato (DALY’s/QALY’s)impatto screening

Punteggio di rischio

L'adozione di un unico indicatore comparabile come parametro per la valutazione dell’impatto dello screening e l'adozione di un punteggio di rischio di cancro sono grandemente necessarie. Ciò richiederebbe:

- l'interoperabilità e l'integrazione di molte banche dati provenienti dalle fonti disponibili a livello individuale;

- comunicazione interattiva con i pazienti e all'interno dei professionisti, evitando la duplicazione della raccolta dei dati;

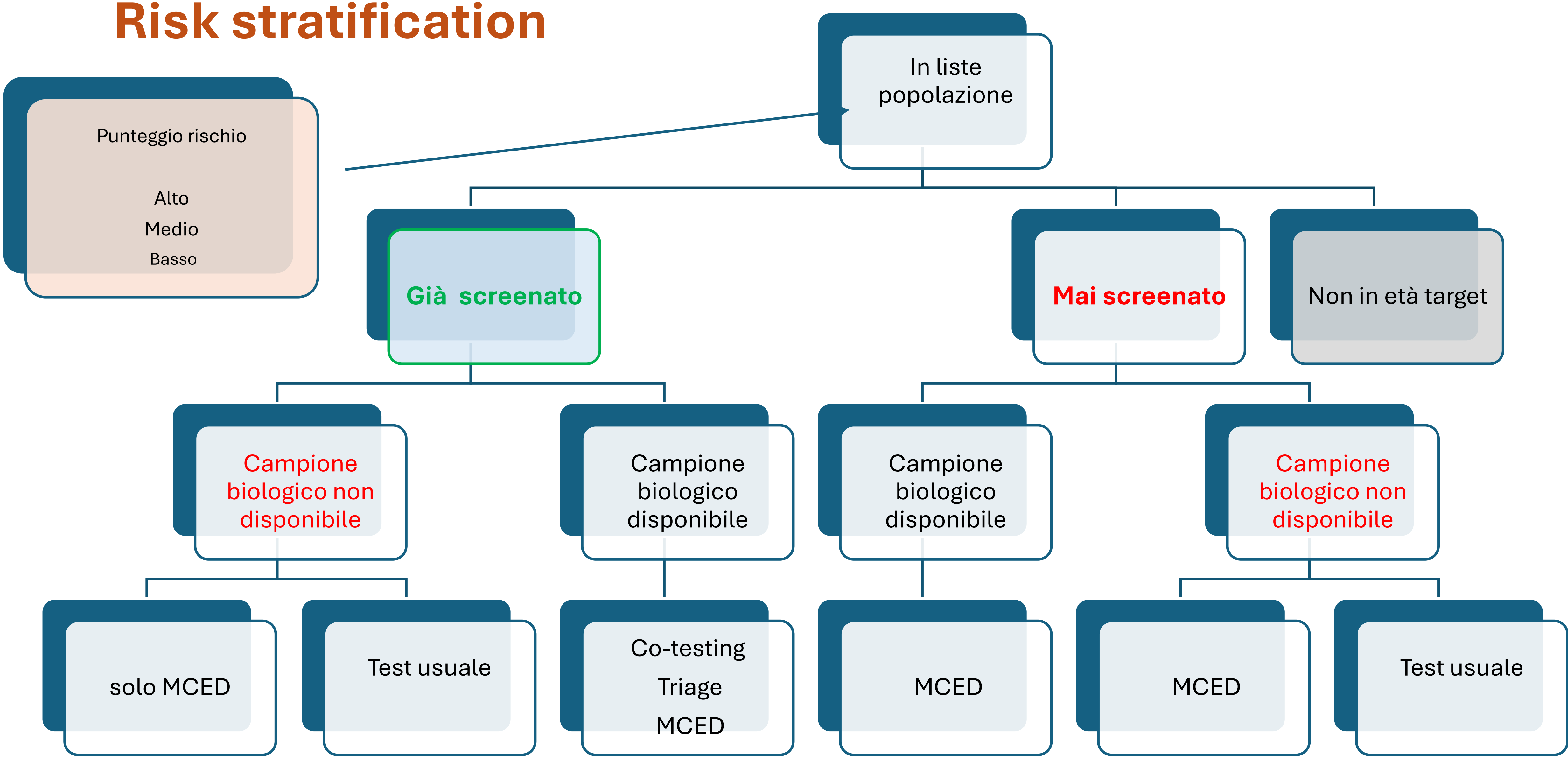
- elaborazione e aggiornamento periodico di stime di disabilità, e/o proxy robusti (ricovero, assistenza sanitaria domiciliare,.....) in assenza di stime specifiche

A livello individuale, l'uso dei dati più recenti disponibili per e dalla gestione dei pazienti dovrebbe consentire di aggiornare i registri e lo stato degli screening e consentire di ricalcolare il punteggio di rischio e la previsione della disabilità.

Allo stesso tempo, gli stessi dati dovrebbero alimentare i database della popolazione nella valutazione del monitoraggio e dello screening, imitando un disegno sequenziale dello studio.

- **L'intelligenza artificiale sta già sfruttando il suo potenziale in molti campi, dalla valutazione del rischio alla diagnosi del cancro, dall'organizzazione dello screening al trattamento, utilizzando le banche dati esistenti e gli strumenti di deep learning e sviluppando nuovi algoritmi per la diagnosi e il trattamento.**

Scenari screening e Risk stratification



MCED e FIT/CT/SF : screening primario, co-testing, triage?

- Proseguiamo come adesso, estendiamo la copertura da esami?
- Offriamo MCED a non aderenti? MCED e FIT
- Utilizziamo campioni esistenti.
- Triage in FIT + con MCED

Come governare il cambiamento: Progetti pilota

Grazie per l’attenzione

TABLE 4 Test performance and accuracy of the tests

	Test (manufacturer)								
	Galleri			CancerSEEK		SPOT-MAS		Trucheck	CDA
Study	CCGA sub-study 3[32]	PATH-FINDER[31]	SYMPLI-FY[40]	Cohen 2018[34]	DETECT-A[6]	Nguyen 2023[46]	K-DETEK[8]	RESO-LUTE[9]	Xie 2022[10] (PPCS)
Design	Case-control[a]	Cohort	Cohort	Case-control[a]	Cohort	Case-Control[a]	Cohort	Cohort	Cohort
Number analysed[b]	4077	6369	5461	1817	9911	713	2792	6884	1957
Total cancers (*n*)	2823	120	368	1005	96	239	6	10	10
TP (*n*)	1453	25	244	626	26	173[c]	6	9	4
FP (*n*)	6	33	79	7	108	14[c]	4	250	47
FN (*n*)	1370	95	124	379	70	66[c]	0[d]	1	6
TN (*n*)	1248	6216	5014	805	9707	460[c]	2782	6624	1900
Accuracy of the test, % (95% CI)									
Sensitivity	51.5 (49.6 to 53.3)	20.8 (14.0 to 29.2)[c]	66.3 (61.2 to 71.1)	62.3 (59.3 to 65.3)	27.1 (18.5 to 37.1)	72.4 (66.3 to 78.0)[c]	100[d] (54.1 to 100)[c]	90.0 (55.5 to 99.7)[c]	40.0 (12.2 to 73.8)[c]
Specificity	99.5 (99.0 to 99.8)	99.5 (99.3 to 99.6)	98.4 (98.1 to 98.8)	99.1 (98.5 to 99.8)	98.9 (98.7 to 99.1)	97.0 (95.1 to 98.4)[c]	99.9 (99.6 to 100)[c]	96.4 (95.9 to 96.8)[c]	97.6 (96.8 to 98.2)[c]
PPV	NA	43.1 (31.2 to 55.9)	75.5 (70.5 to 80.1)	NA	19.4 (13.1 to 27.1)	NA	60.0 (26.2 to 87.8)[c]	3.5 (1.6 to 6.5)[c]	7.8 (2.2 to 18.9)[c]
NPV	NA	98.5 (98.2 to 98.8)	97.6 (97.1 to 98.0)	NA	99.3 (99.1 to 99.4)	NA	100[d] (99.9 to 100)[c]	100 (99.9 to 100)[c]	99.7 (99.3 to 99.9)[c]
First CSO correct	88.7 (87.0 to 90.2)	84.0 (65.3 to 93.6)	85.2 (79.8 to 89.3)	67.7 (64.0 to 71.3)[c]	Not reported	Median 0.70 (range 0.55–0.78)[e]	83.3 (43.6 to 97)[c]	Not reported	Not reported

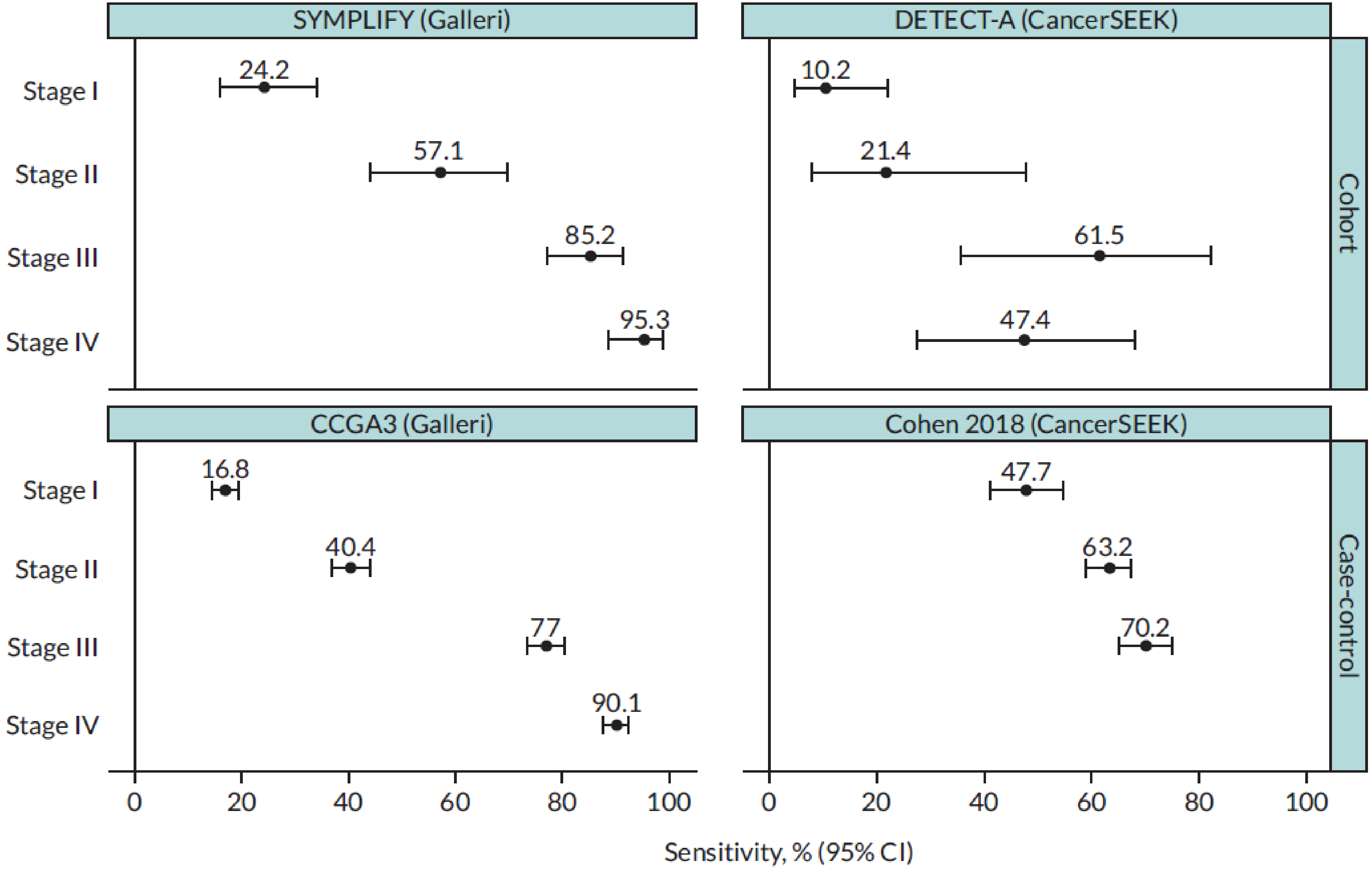


FIGURE 3 Performance (sensitivity) of MCED tests by cancer stage. Note: Cancer stage reported for solid tumours only, not for haematological malignancies.

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Multi-cancer early detection tests for general population screening: a systematic literature review

Ros Wade, Sarah Nevitt, Yiwen Liu, Melissa Harden, Claire Khouja, Gary Raine, Rachel Churchill and Sofia Dias

Artificial Intelligence

Campo della Computer Science che mira a creare macchine intelligenti che replicano o migliorano l'intelligenza umana:

- Machine learning

Un settore dell' AI che rende le macchine capaci di imparare dai dati esistenti per prendere decisioni o fare previsioni

- Deep learning

Una tecnica di Machine Learning in cui algoritmi di reti neurali sono usati per processare i dati e prendere decisioni basate su di essi

- Generative AI

Crea nuovi contenuti scritti, visuali , audio basati sui dati o richieste esistenti

Disability Adjusted Life Years (DALYs)

DALY = YLL + YLD

where:
YLL = years of life lost due to premature mortality
YLD = years lived with disability.

The global burden of cancer attributable to risk factors, 2010–19: a systematic analysis for the Global Burden of Disease Study 2019

GBD 2019 Cancer Risk Factors Collaborators*

Summary
Background Understanding the magnitude of cancer burden attributable to potentially modifiable risk factors is crucial for development of effective prevention and mitigation strategies. We analysed results from the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2019 to inform cancer control planning efforts globally.

Lancet 2022; 400: 563–91
See Comment page 540
*Collaborators are listed at th

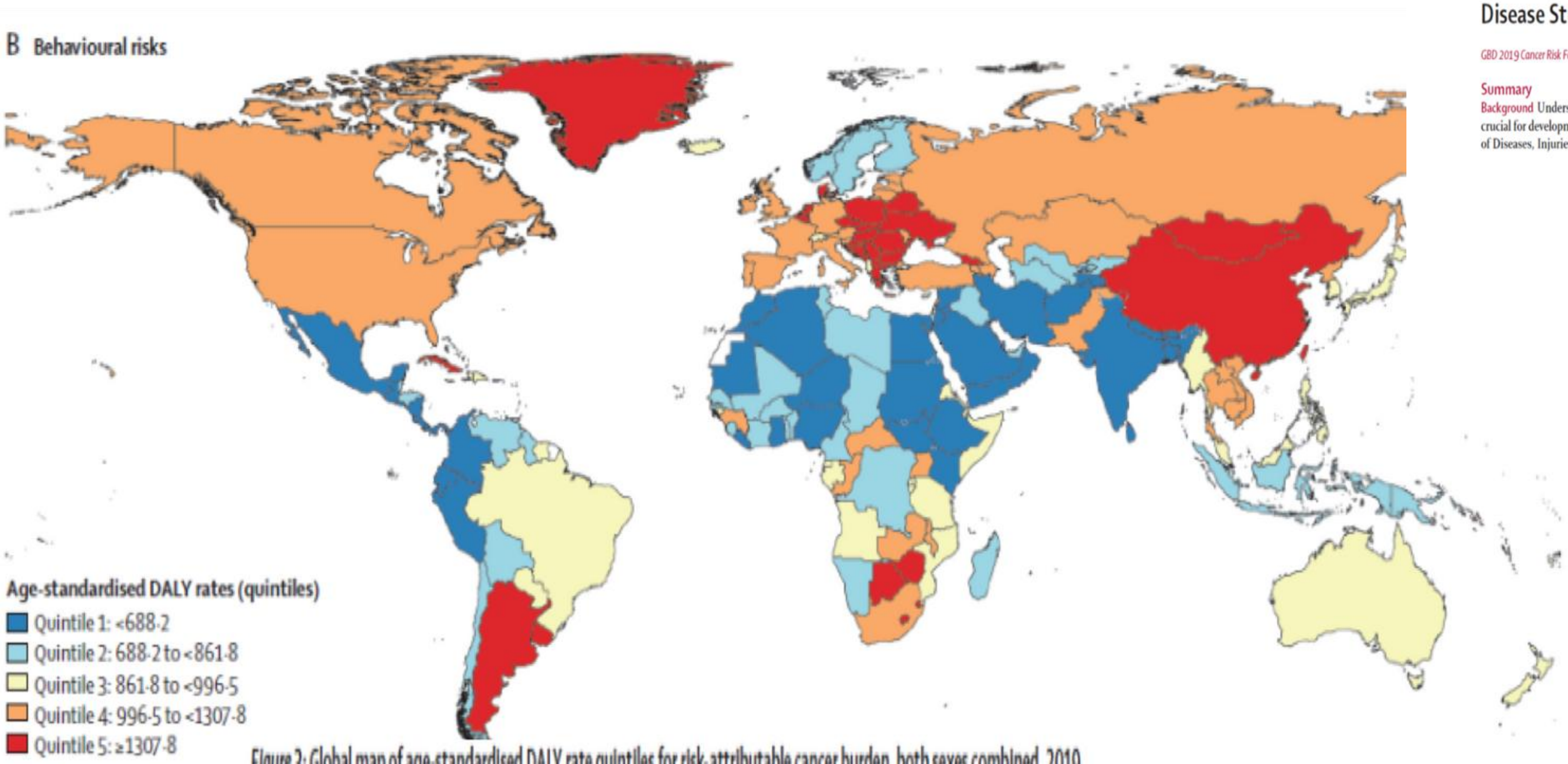

Figure 3: Global map of age-standardised DALY rate quintiles for risk-attributable cancer burden, both sexes combined, 2019
(A) Environmental and occupational risks. (B) Behavioural risks. (C) Metabolic risks. Each map represents estimates at the national level. Quintiles are based on age-standardised DALY rates per 100 000 person-years. See appendix (pp 165–68, 234–39) for further details of risk-attributable cancer deaths and DALYs for each country and territory. DALYs=disability-adjusted life-years.

Figure 3: Global map of age-standardised DALY rate quintiles for risk-attributable cancer burden, both sexes combined, 2019
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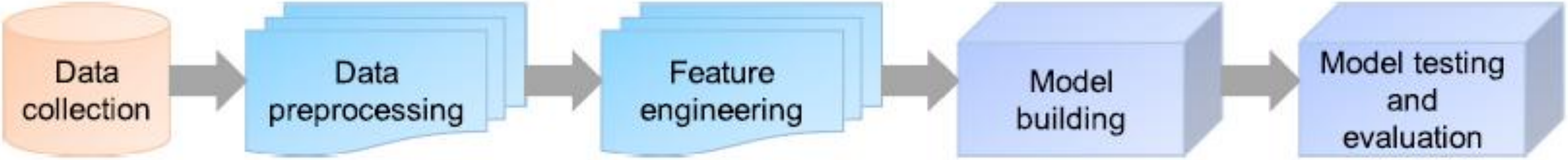

Fig. 2. General machine learning processes.

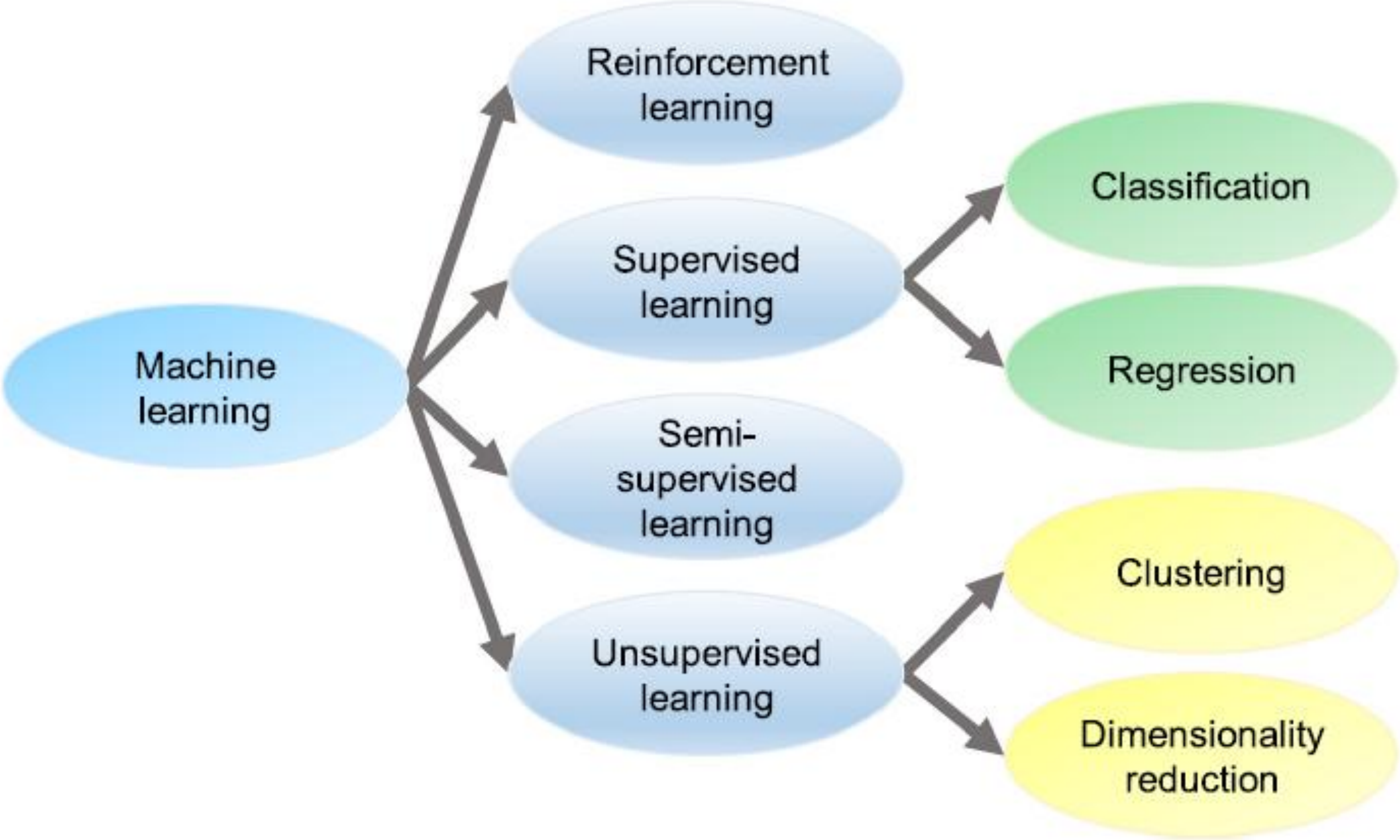

Fig. 3. Types of machine learning methods.

Tamm *et al. BMC Medicine (2025) 23:503*
https://doi.org/10.1186/s12916-025-04339-w

RESEARCH Open Access

BMC Medicine

External validation of the COLOFIT colorectal cancer risk prediction model in the Oxford-FIT dataset: the importance of population characteristics and clinically relevant evaluation metrics

Andres Tamm[1,2*], Brian Shine[4], Tim James[4], Jaimie Withers[3,5], Hizni Salih[3,5], Theresa Noble[3,5], Kinga A. Varnai[3,5],
James E. East[3,6], Gary Abel[9], Willie Hamilton[9], Colin Rees[10,11], Eva J. A. Morris[2,7], Jim Davies[2,3,8] and
Brian D. Nicholson[1]

Abstract

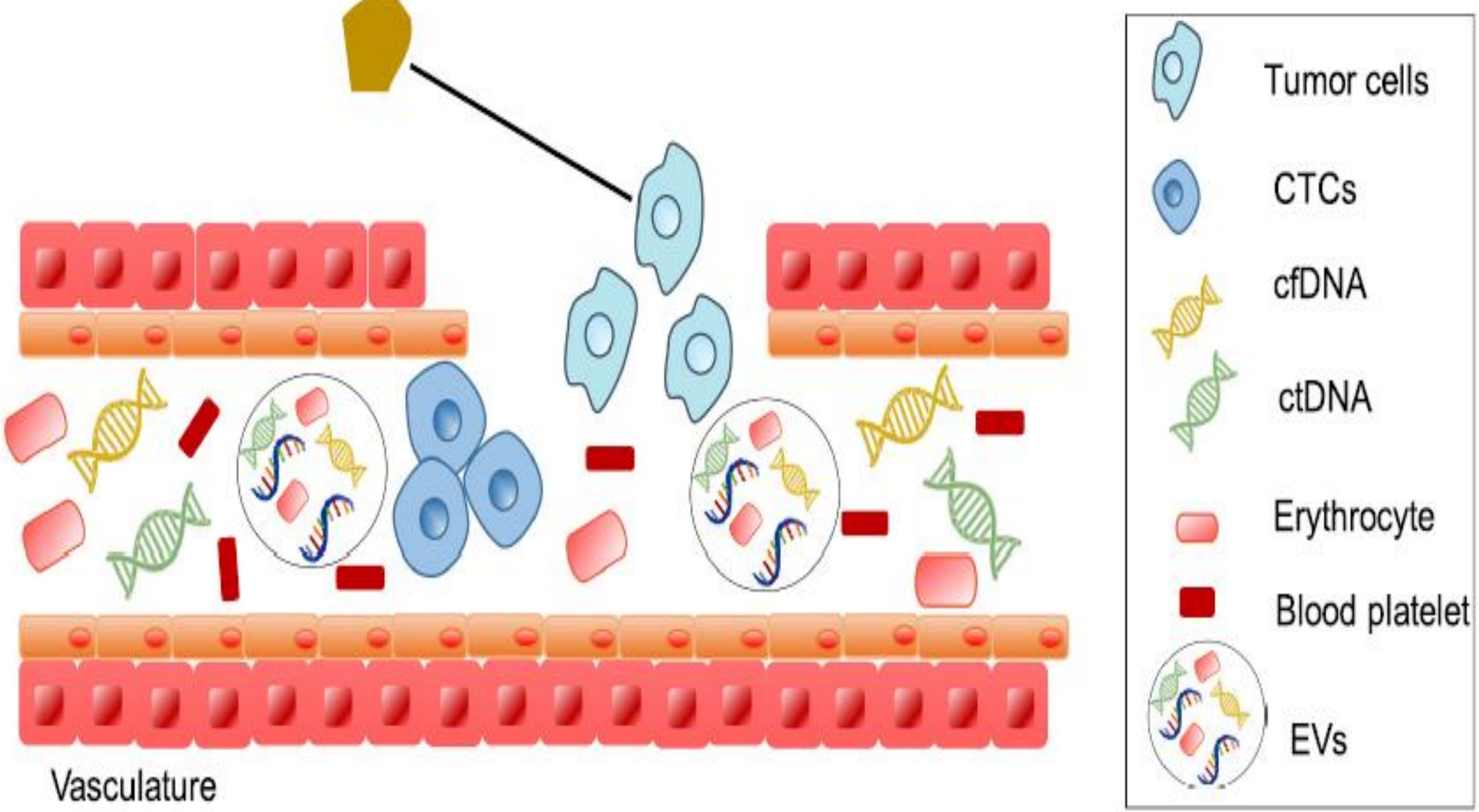

Fig. 4. Illustration of how circulating tumor DNA (ctDNA) enters the bloodstream. CtDNA is a cell-free DNA (cfDNA) fragment produced by tumor cells durin necrosis or apoptosis and released into the bloodstream. CtDNA can also be derived from circulating tumor cells (CTCs) or extracellular vesicles (EVs) secreted b tumor cells.

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Universal cancer screening: revolutionary, rational, and realizable

David A. Ahlquist[1]

npj Precision Oncology (2018)2:23

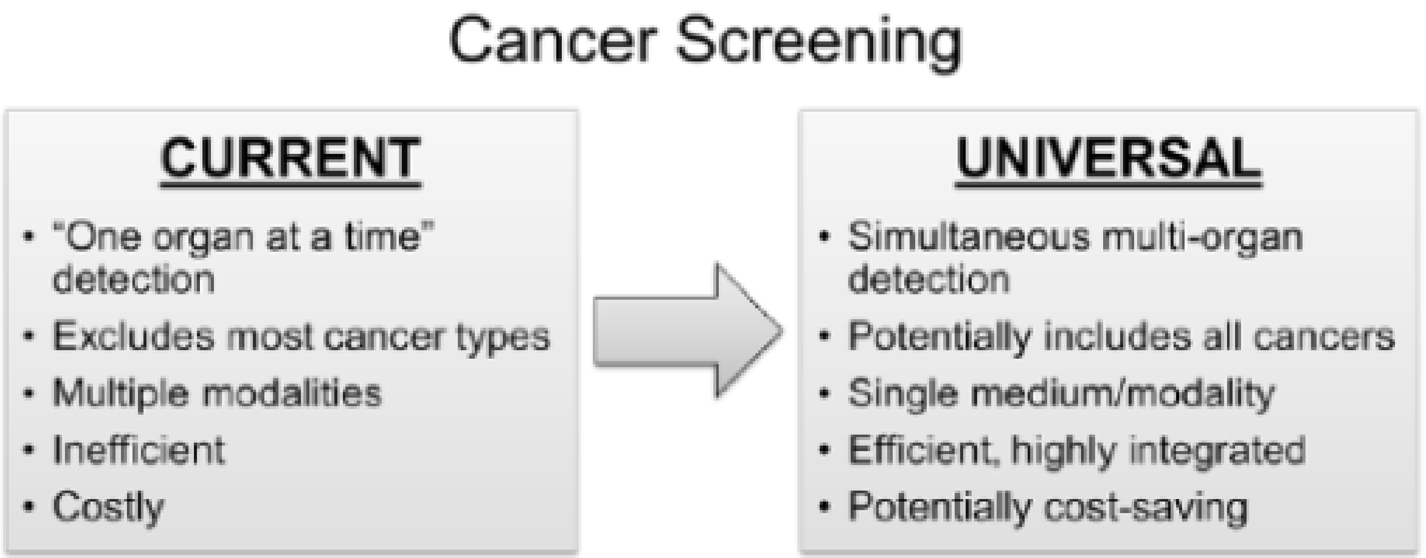

Fig. 1 Current single-organ and future universal cancer screening approaches: a conceptual comparison of features

TABLE 4 Test performance and accuracy of the tests

Study	Test (manufacturer)								
	Galleri			CancerSEEK		SPOT-MAS		Trucheck	CDA
	CCGA sub-study 3[32]	PATHFINDER[31]	SYMPLIFY[40]	Cohen 2018[34]	DETECT-A[6]	Nguyen 2023[46]	K-DETEK[8]	RESOLUTE[9]	Xie 2022[10] (PPCS)
Design	Case-control[a]	Cohort	Cohort	Case-control[a]	Cohort	Case-Control[a]	Cohort	Cohort	Cohort
Number analysed[b]	4077	6369	5461	1817	9911	713	2792	6884	1957
Total cancers (*n*)	2823	120	368	1005	96	239	6	10	10
TP (*n*)	1453	25	244	626	26	173[c]	6	9	4
FP (*n*)	6	33	79	7	108	14[c]	4	250	47
FN (*n*)	1370	95	124	379	70	66[c]	0[d]	1	6
TN (*n*)	1248	6216	5014	805	9707	460[c]	2782	6624	1900
Accuracy of the test, % (95% CI)									
Sensitivity	51.5 (49.6 to 53.3)	20.8 (14.0 to 29.2)[c]	66.3 (61.2 to 71.1)	62.3 (59.3 to 65.3)	27.1 (18.5 to 37.1)	72.4 (66.3 to 78.0)[c]	100[d] (54.1 to 100)[c]	90.0 (55.5 to 99.7)[c]	40.0 (12.2 to 73.8)[c]
Specificity	99.5 (99.0 to 99.8)	99.5 (99.3 to 99.6)	98.4 (98.1 to 98.8)	99.1 (98.5 to 99.8)	98.9 (98.7 to 99.1)	97.0 (95.1 to 98.4)[c]	99.9 (99.6 to 100)[c]	96.4 (95.9 to 96.8)[c]	97.6 (96.8 to 98.2)[c]
PPV	NA	43.1 (31.2 to 55.9)	75.5 (70.5 to 80.1)	NA	19.4 (13.1 to 27.1)	NA	60.0 (26.2 to 87.8)[c]	3.5 (1.6 to 6.5)[c]	7.8 (2.2 to 18.9)[c]
NPV	NA	98.5 (98.2 to 98.8)	97.6 (97.1 to 98.0)	NA	99.3 (99.1 to 99.4)	NA	100[d] (99.9 to 100)[c]	100 (99.9 to 100)[c]	99.7 (99.3 to 99.9)[c]
First CSO correct	88.7 (87.0 to 90.2)	84.0 (65.3 to 93.6)	85.2 (79.8 to 89.3)	67.7 (64.0 to 71.3)[c]	Not reported	Median 0.70 (range 0.55–0.78)[e]	83.3 (43.6 to 97)[c]	Not reported	Not reported
First or second CSO correct	Not reported	88.0 (70.0 to 95.8)	90.7 (86.0 to 93.9)	85.6 (82.7 to 88.2)	Not reported	Not reported	Not reported	Not reported	Not reported

CI, confidence interval; NA, not applicable; PPCS, Prospective Population-based Cohort Study.
a PPV and NPV statistics are not applicable for case-control studies including people known to have cancer.
b Number analysed is those who received the MCED test, with follow-up information and/or diagnostic resolution.
c Values calculated from other reported data.
d Only people with a positive signal on the SPOT-MAS test were followed up, so all negative signals are assumed to be TN and therefore sensitivity and NPV are calculated to be 100% due to this study design.
e Median and range of first CSO accuracy were reported in the Nguyen 2023 study;[46] no further data were reported to allow calculation of the percentage and 95% CI of first CSO accuracy.

Table 4 presents the results of the refined MCED test (Galleri). Only 120 cancers were detected in 6369 analysed participants (a cancer detection rate of 1.9%), reflecting the asymptomatic population recruited to this study. Sensitivity was low (20.8%, 95% CI 14.0% to 29.2%), although the first CSO was correct in 84.0% of cancers detected (95% CI 65.3% to 93.6%) increasing to 88.0% (95% CI 70.0% to 95.8%) for first or second CSO. The PPV was 43.1% (95% CI 99.3% to 99.6%). Specificity was high (99.5%, 95% CI 99.3% to 99.6%) and the NPV was also high (98.5%, 95% CI 98.2% to 98.8%), although a short follow-up and lack of reference standard testing on participants with a negative MCED test limit the interpretation of these results.

REVIEW ARTICLE | FOCUS
https://doi.org/10.1038/s41591-022-01746-x

nature medicine

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The future of early cancer detection

Rebecca C. Fitzgerald[1]✉, Antonis C. Antoniou[2], Ljiljana Fruk[3] and Nitzan Rosenfeld[4]

A proactive approach to detecting cancer at an early stage can make treatments more effective, with fewer side effects and improved long-term survival. However, as detection methods become increasingly sensitive, it can be difficult to distinguish inconsequential changes from lesions that will lead to life-threatening cancer. Progress relies on a detailed understanding of individualized risk, clear delineation of cancer development stages, a range of testing methods with optimal performance characteristics, and robust evaluation of the implications for individuals and society. In the future, advances in sensors, contrast agents, molecular methods, and artificial intelligence will help detect cancer-specific signals in real time. To reduce the burden of cancer on society, risk-based detection and prevention needs to be cost effective and widely accessible.

CANCER RESEARCH | POPULATION AND PREVENTION SCIENCE

A Systematic Review and Multilevel Regression Analysis Reveals the Comorbidity Prevalence in Cancer

Cilla E.J. Vrinzen[1,2], Linn Delfgou[1], Niek Stadhouders[1], Rosella P.M.G. Hermens[1], Matthias A.W. Merkx[1,2], Haiko J. Bloemendal[3], and Patrick P.T. Jeurissen[1]

«The weighted average comorbidity prevalence was 33.4%, and comorbidities were the most common in lung cancer (46.7%) and colorectal cancer (40.0%), followed by prostate cancer (28.5%), melanoma cancer (28.3%), and breast cancer (22.4%). The most common types of comorbidities were hypertension (29.7%), pulmonary diseases (15.9%), and diabetes (13.5%)"

Cancer Res 2023;83:1147–57

The comorbidities change the screening outcomes and benefits

Risk of ?
Stratified for

- Specific cancer
- Selected cancers
- Any cancer
- Death
- Cancer death
- Premature death
- Disability/ reduced quality of life

Klein EA, Richards D, Cohn A, et al. Clinical validation of a targeted methylation-based multi-cancer early detection test using an independent validation set. Ann Oncol. **2021;32(9):1167-1177.**

Specificity for cancer signal detection was 99.5% [95% confidence interval (CI): 99.0% to 99.8%].
Overall sensitivity for cancer signal detection was 51.5% (49.6% to 53.3%); sensitivity increased with stage [stage I: 16.8% (14.5% to 19.5%), stage II: 40.4% (36.8% to 44.1%), stage III: 77.0% (73.4% to 80.3%), stage IV: 90.1% (87.5% to 92.2%)].
Stage I-III sensitivity was 67.6% (64.4% to 70.6%) in 12 pre-specified cancers that account for approximately two-thirds of annual USA cancer deaths and was 40.7% (38.7% to 42.9%) in all cancers. Cancer signals were detected across >50 cancer types. Overall accuracy of CSO prediction in true positives was 88.7% (87.0% to 90.2%).

OXFORD

JNCI: Journal Of The National Cancer Institute, 2023, 115(3), 250–257

https://doi.org/10.1093/jnci/djac218

Advance Access Publication Date: 2 December 2022

Commentary

Study design considerations for trials to evaluate multicancer early detection assays for clinical utility

Lori M. Minasian, MD,[1*] Paul Pinsky, PhD,[1] Hormuzd A. Katki, PhD,[2] Tony Dickherber, PhD,[3] Paul K. J. Han, MD,[4] Lyndsay Harris, MD,[5] Christos Patriotis, PhD,[1] Sudhir Srivastava, PhD,[1] Carol J. Weil, JD,[1] Philip C. Prorok, PhD,[1] Philip E. Castle, PhD, MPH[1]

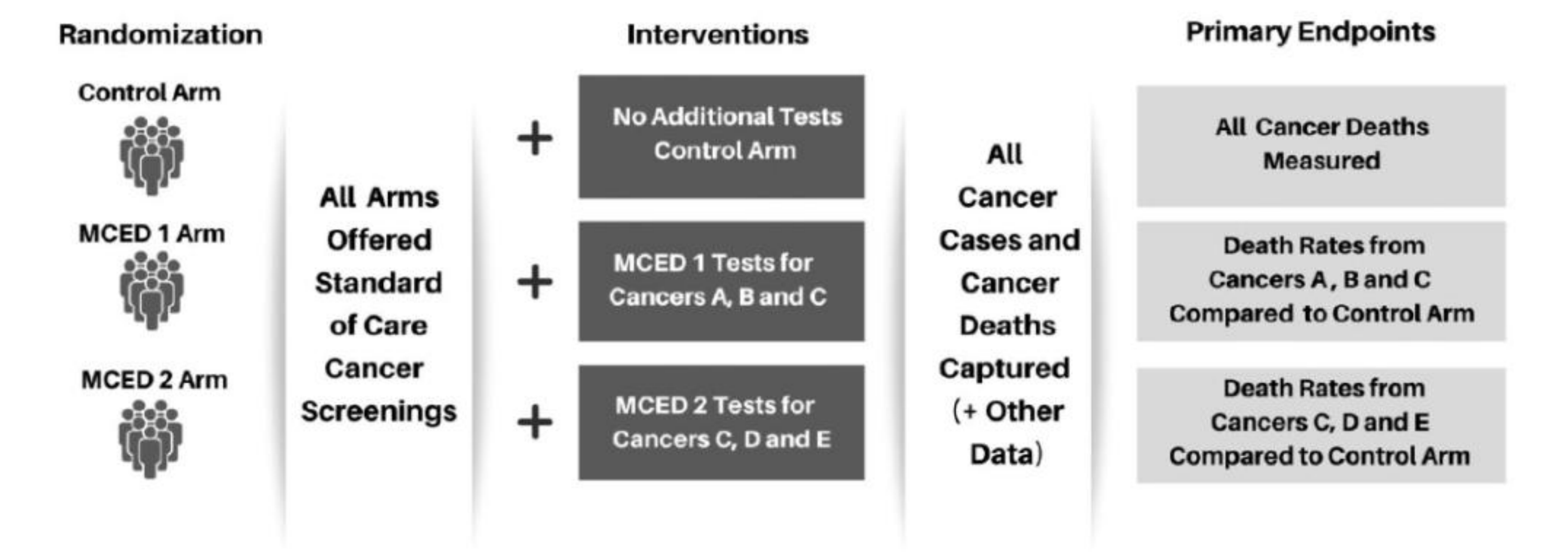

Figure 1. Platform study design schema. MCED = multicancer early detection

Multi-cancer early detection tests for general population screening: a systematic literature review

Ros Wade ,1 Sarah Nevitt ,1 Yiwen Liu ,1 Melissa Harden ,1 Claire Khouja ,1 Gary Raine ,1 Rachel Churchill 1 and Sofia Dias 1*
1Centre for Reviews and Dissemination, University of York, York, UK
***Corresponding author sofia.dias@york.ac.uk Jan 2025**

Results: Over 8000 records were identified. Thirty-six studies met the inclusion criteria: 1 ongoing randomised controlled trial, 13 completed cohort studies, 17 completed case-control studies and 5 ongoing cohort or case-control studies. Individual tests claimed to detect from 3 to over 50 different types of cancer. Diagnostic accuracy of currently available multi-cancer early detection tests varied substantially:

- **Galleri® (GRAIL, Menlo Park, CA, USA) sensitivity 20.8–66.3%, specificity 98.4–99.5% (three studies);**
- **CancerSEEK (Exact Sciences, Madison, WI, USA) sensitivity 27.1–62.3%, specificity 98.9– 99.1% (two studies);**
- **SPOT-MAS™ (Gene Solutions, Ho Chi Minh City, Vietnam) sensitivity 72.4–100%, specificity 97.0–99.9% (two studies);**
- **Trucheck™ (Datar Cancer Genetics, Bayreuth, Germany) sensitivity 90.0%, specificity 96.4% (one study);**
- **Cancer Differentiation Analysis (AnPac Bio, Shanghai, China) sensitivity 40.0%, specificity 97.6% (one study).**
- **AICS® (AminoIndex Cancer Screening; Ajinomoto, Tokyo, Japan) screens for individual cancers separately, so no overall test performance statistics are available.**

- **Where reported, sensitivity was lower for detecting earlier-stage cancers (stages I–II) compared with later-stage cancers (stages III–IV). Studies of sevenother multi-cancer early detection tests at an unclear stage of development were also summarised.**

- Process indicators (coverage by invitation, testing, positivity, detection rates, predictive values, process time intervals), intermediate outcomes (stage distributions, ……) are necessary for monitoring and quality improving of cancer screening.

They have to be comparable in different areas and time periods

- Incidence and/or mortality reduction is a necessary but not sufficient condition for adopting cancer screening. The harms to benefits balance should be favourable to screening

The balance of harms and benefits is difficult to assess and to compare across different cancer screenings .

At individual level values and expectations are different, at population level cancer screening may differ over different populations. The screening programs may adopt different tests, cut off, intervals and diagnostic assessment.

The determinants of the harms/benefits balance may vary as size and compositions

How to quantify and to measure the harms/benefits balance?

DALY’s is a composite indicator, taking into account death and disability (specular to survival and quality of life)

DALY’s estimates can be used as a common and unique measure to compare harms of screening (and prevention), clinical assessment and treatment (and by default absence of harms i.e. benefits) in population groups:

- **organized screening (group 1)**
- **opportunistic screening (group 2)**
- **unscreened persons (group 3)**

Until now the harms/benefits balance measures involved only the Harms/Benefits balance in organized screening settings and not opportunistic screening or unscreened persons

The global burden of cancer attributable to risk factors, 2010–19: a systematic analysis for the Global Burden of Disease Study 2019

*GBD 2019 Cancer Risk Factors Collaborators**

Summary

Background Understanding the magnitude of cancer burden attributable to potentially modifiable risk factors is crucial for development of effective prevention and mitigation strategies. We analysed results from the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2019 to inform cancer control planning efforts globally.

Lancet 2022; 400: 563–91

See Comment page 540

*Collaborators are listed at tl

The estimated number of DALYs for screened and unscreened persons can be compared for the cancer screening(s) of interest.

The DALY's depending or associated with screening harms are included in the point estimates, comprising also DALY's eventually due to **lead time** and **over-diagnosis.**