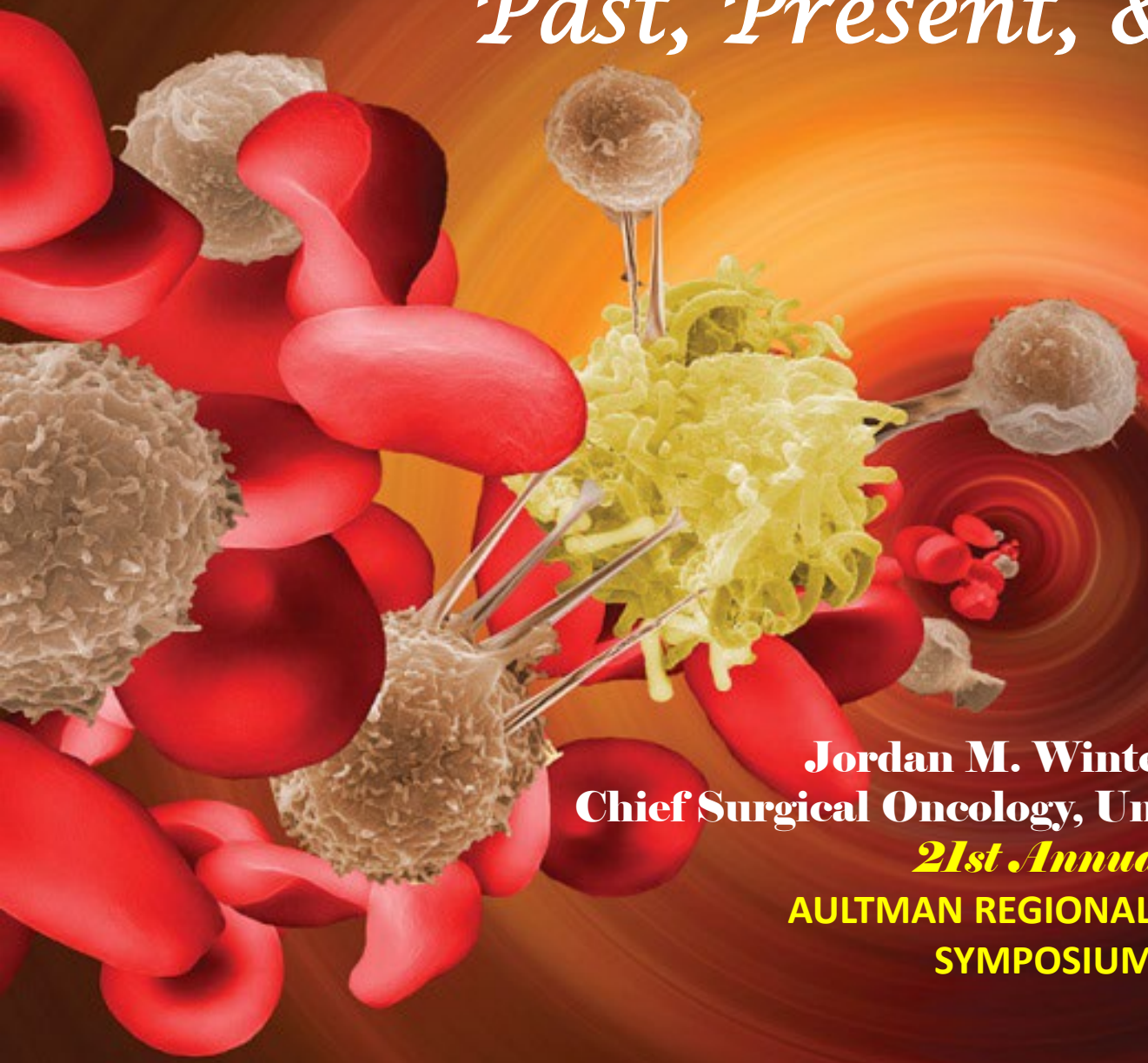
Early Cancer Detection: Past, Present, & Future

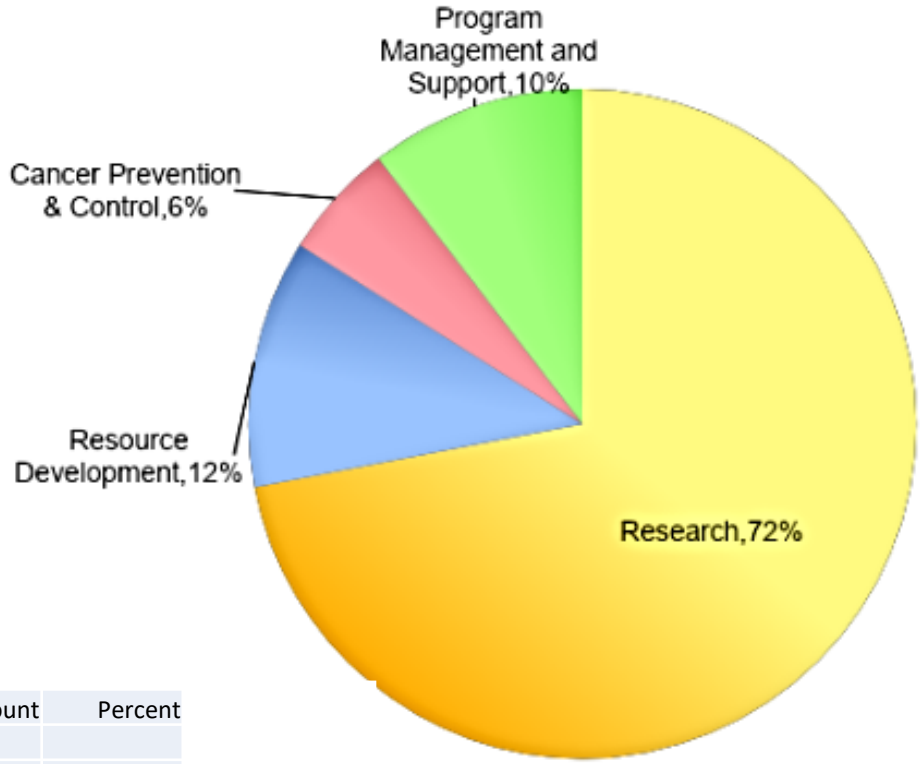


Jordan M. Winter, MD
Chief Surgical Oncology, University Hospitals

21st Annual

AULTMAN REGIONAL CANCER SYMPOSIUM

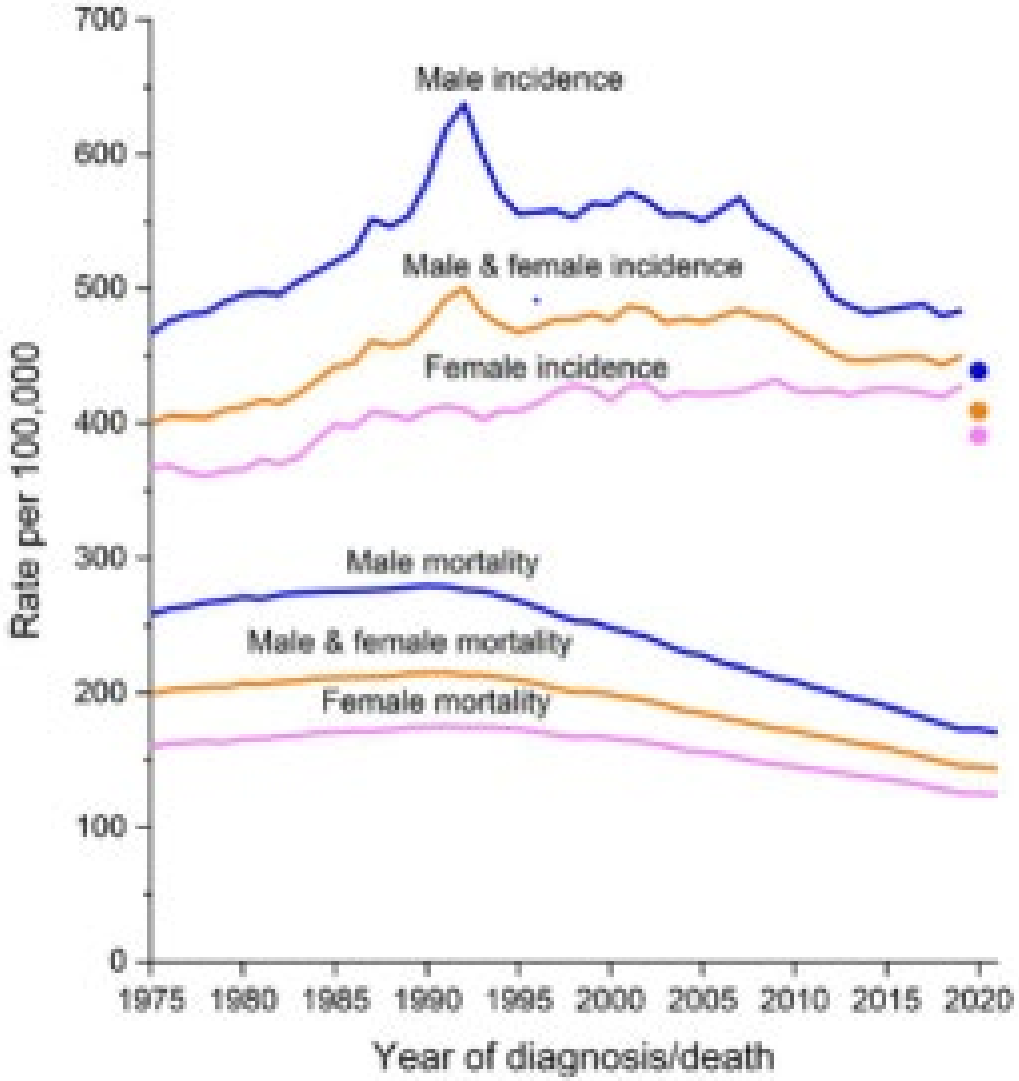
NCI Budget, 2023



Budget Activity	Amount	Percent
Research		
Childhood Cancer Data Initiative (CCDI)**	$46,482,004	0.6%
Cancer Causation	$1,524,477,358	21.2%
Detection and Diagnosis Research	**$683,735,556**	**9.5%**
Treatment Research	$1,763,275,996	24.5%
Cancer Biology	1,153,696,700	16.1%
Total Research	5,171,667,615	72.0%
Resource Development:		
Cancer Centers	606,650,926	8.4%
Research Manpower Development	225,489,043	3.1%
Buildings and Facilities	30,000,000	0.4%
Total Resource Development	862,139,969	12.0%
Cancer Prevention and Control	**402,180,432**	**5.6%**
Program Management and Support	751,456,503	10.5%
*Total NCI	$7,187,444,519	100%

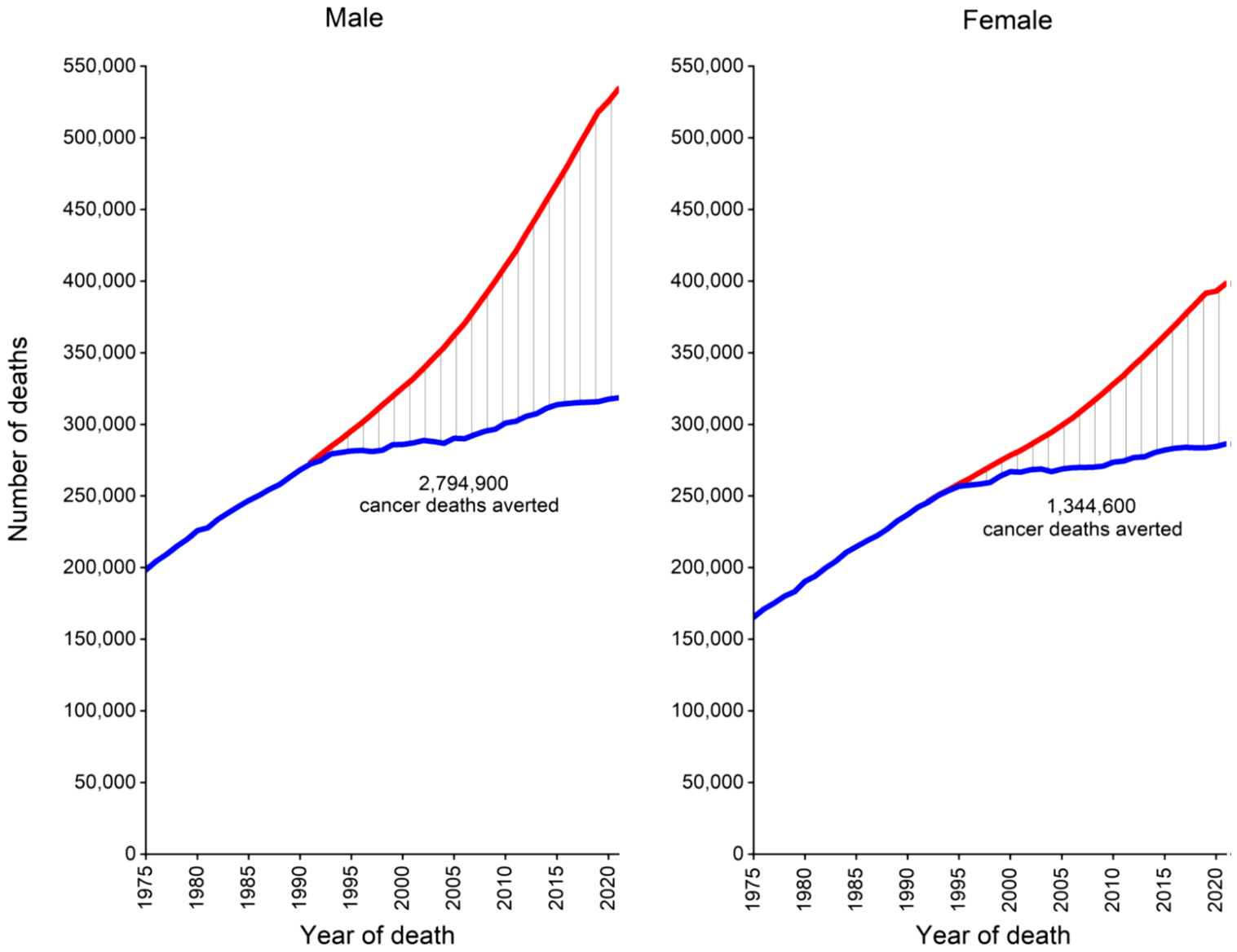
20,000 Foot View

Trends



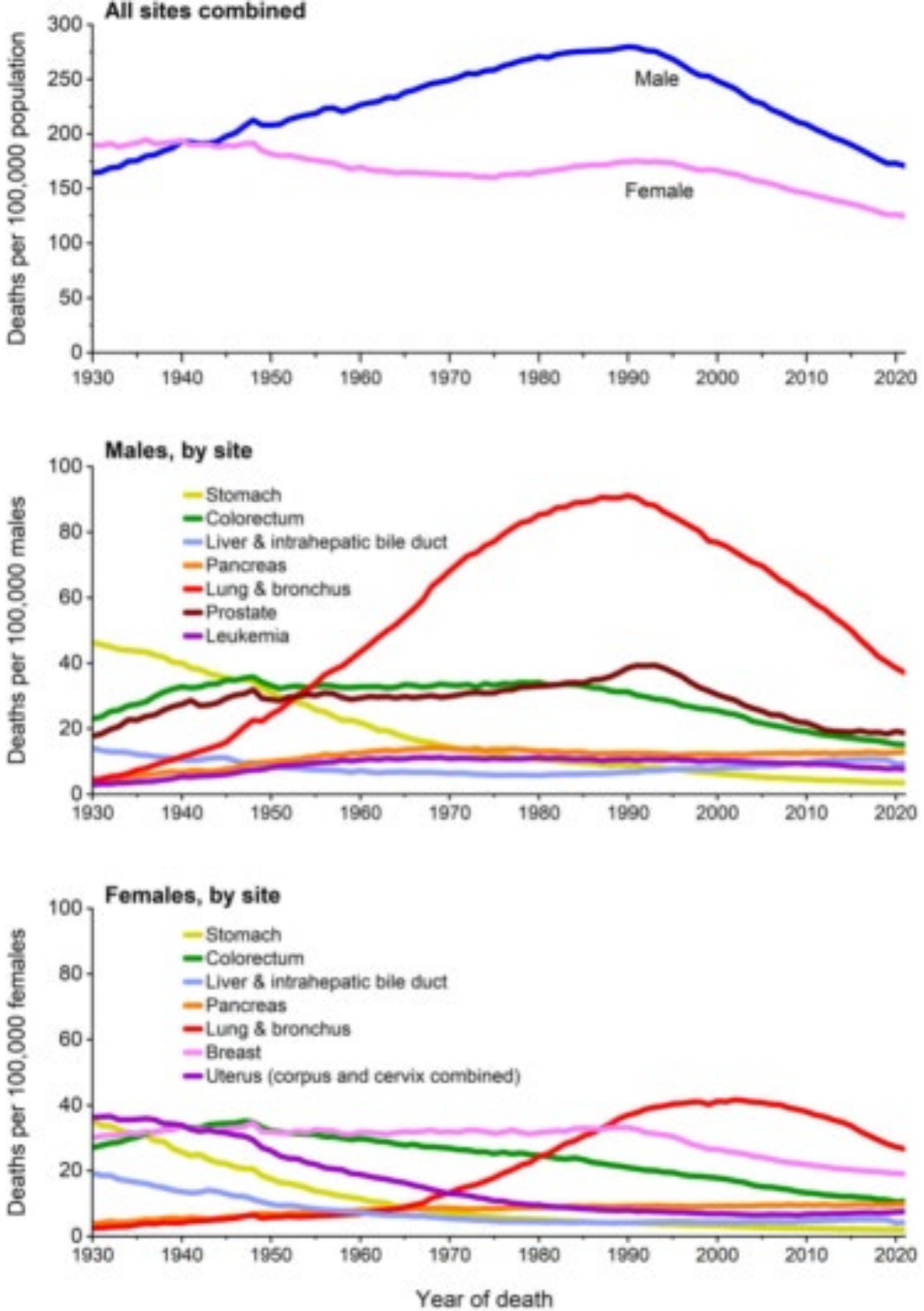
CA Cancer J Clin 2024

Cancer deaths averted



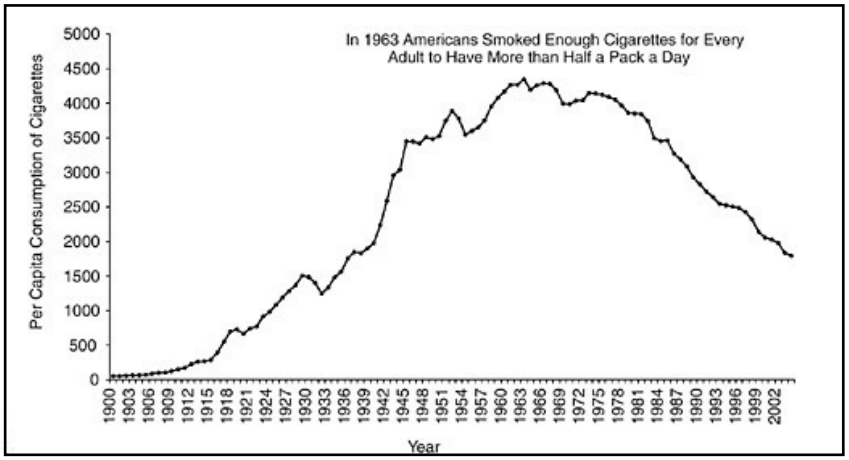
CA Cancer J Clin 2024

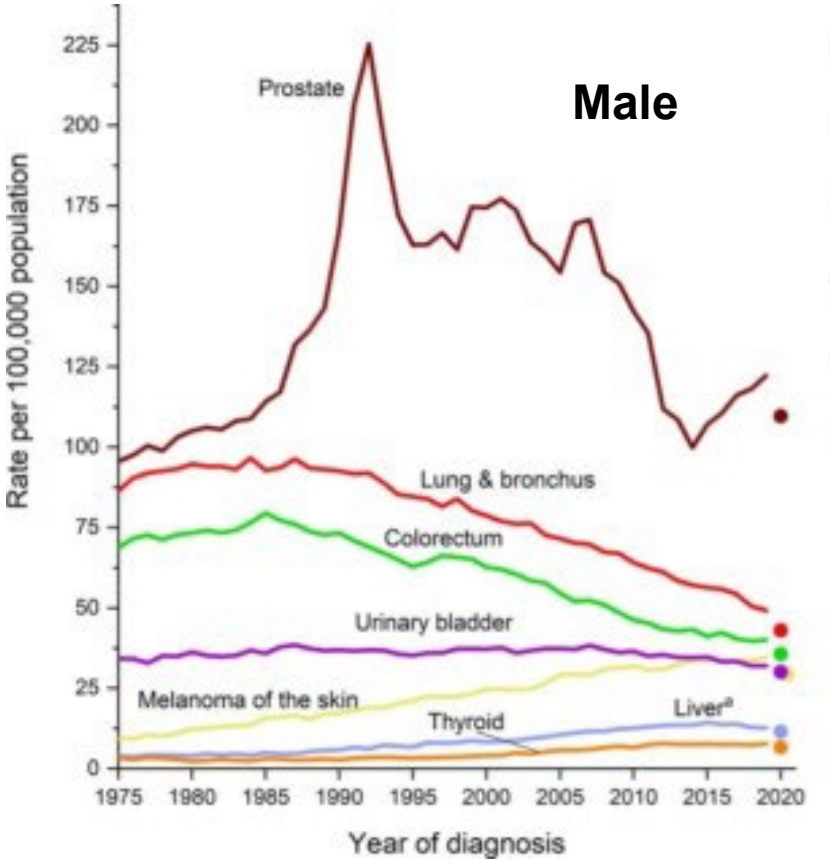
Trends: mortality

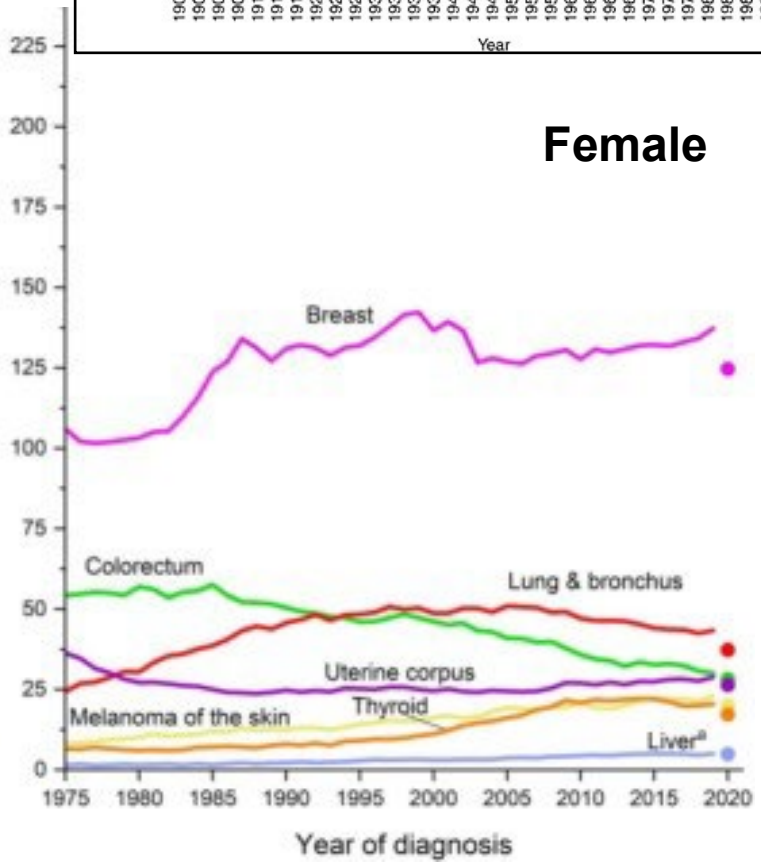


CA Cancer J Clin 2024

Trends: incidence







CA Cancer J Clin 2024

https://nap.nationalacademies.org/read/11795/chapter/4#42

New Cases

#	Cancer	New Cases/Yr
1	Breast	313,510
2	Prostate	299,010
3	Lung	234,580
4	Colorectal	152,810
5	Melanoma	100,640
6	Bladder	83,190
8	Kidney	81,610
7	NHL	80,620
9	Uterine	67,680
10	Pancreas	66,440
11	Leukemia	62,770
12	Oral	58,450

#	Cancer	New Cases/Yr
13	Thyroid	44,020
14	Liver	41,630
15	Myeloma	35,780
16	Stomach	26,890
17	Brain	25,400
18	Esophagus	22,370
19	Ovary	19,680
20	Cervix	13,820
21	Soft tissue	13,590
22	Larynx	12,650
23	Bile duct cancer	12,350

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Deaths

#	Cancer	Deaths/Yr
1	Lung	125,070
2	Colorectal	53,010
3	Pancreas	51,750
4	Breast	42,780
5	Prostate	35,250
6	Liver	29,840
7	Leukemia	23,670
8	NHL	20,140
9	Brain	18,760
10	Bladder	16,840
11	Esophagus	16,130
12	Kidney	14,390

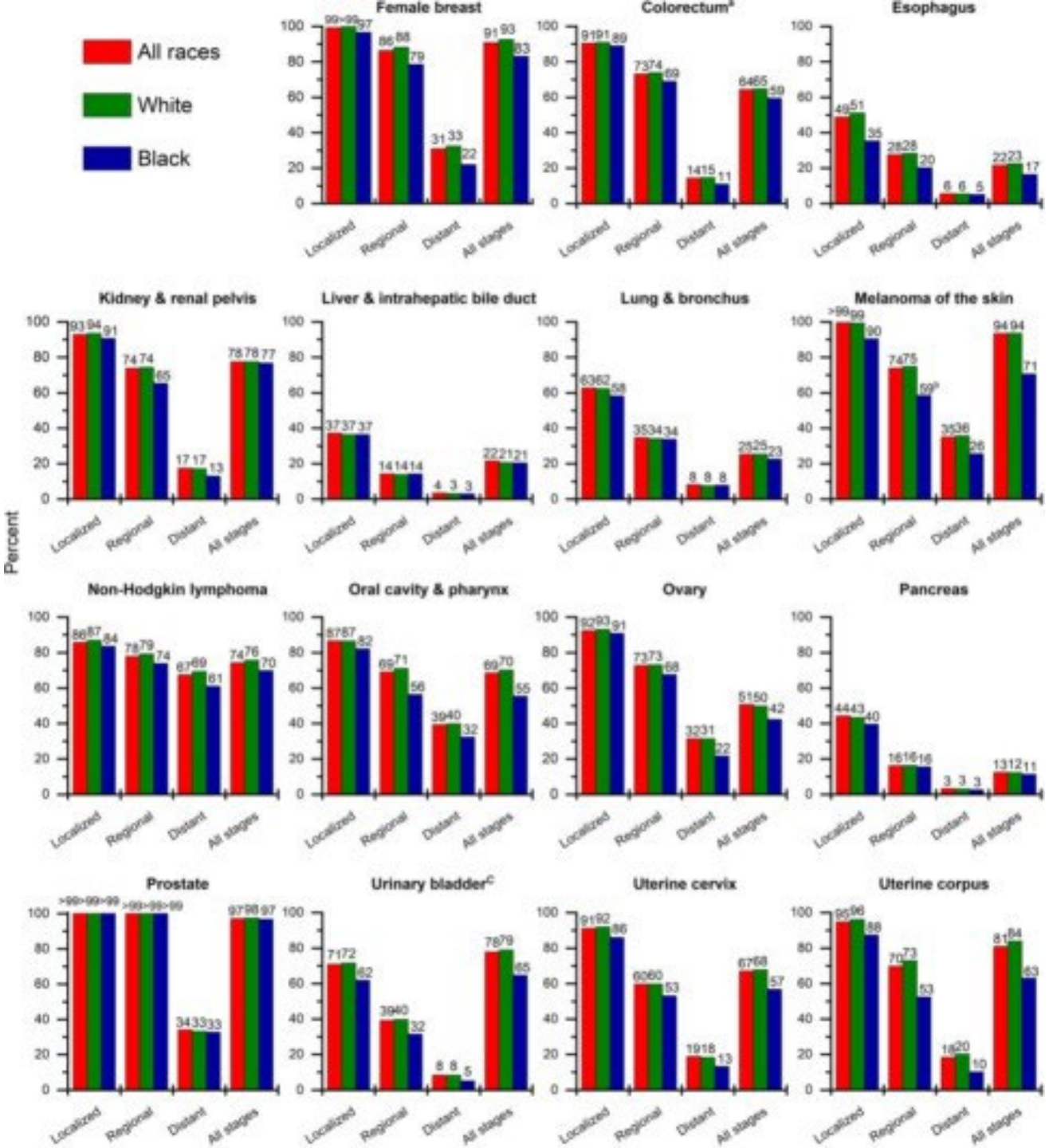
#	Cancer	Deaths/Yr
13	Uterine	13,250
14	Ovary	12,740
15	Myeloma	12,540
16	Oral	12,230
17	Stomach	10,880
18	Melanoma	8,290
19	Soft tissue	5,200
20	Bile duct	4,530
21	Cervix	4,360
22	Thyroid	2,170

CA Cancer J Clin 2024

#	Cancer	Death rate
1	Pancreas	77.71%
2	Brain	76.54%
3	Esophagus	74.77%
4	Liver	71.29%
5	Ovary	67.33%
6	Lung	53.31%
7	Stomach	42.00%
8	Leukemia	39.78%
9	Soft tissue	38.36%
10	Bile duct cancer	36.91%
11	Myeloma	35.24%
12	Colorectal	34.34%

#	Cancer	Death rate
13	Uterine	19.68%
14	Kidney	18.20%
15	Breast	14.54%
16	Prostate	12.04%
17	Melanoma	8.19%

5 year survival



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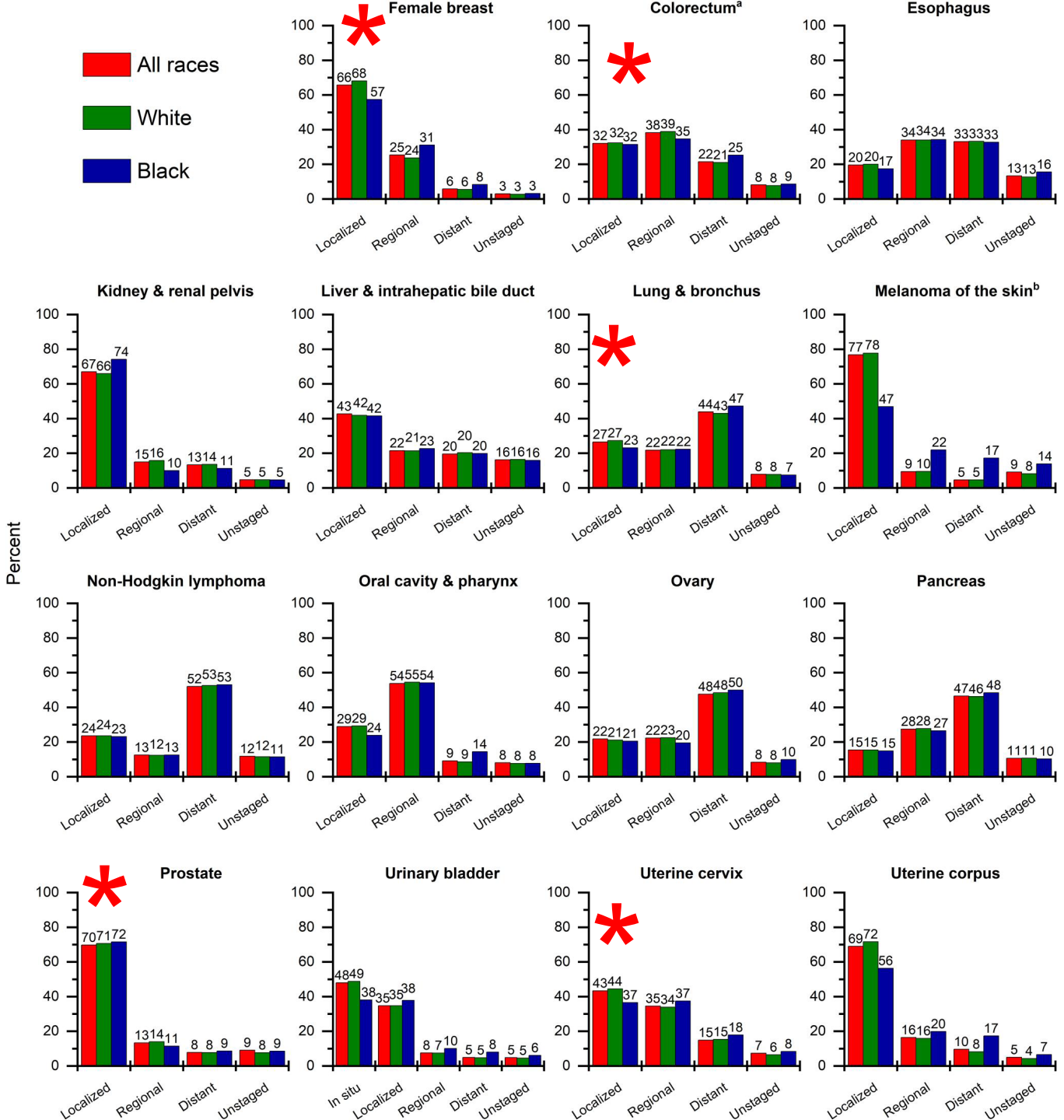
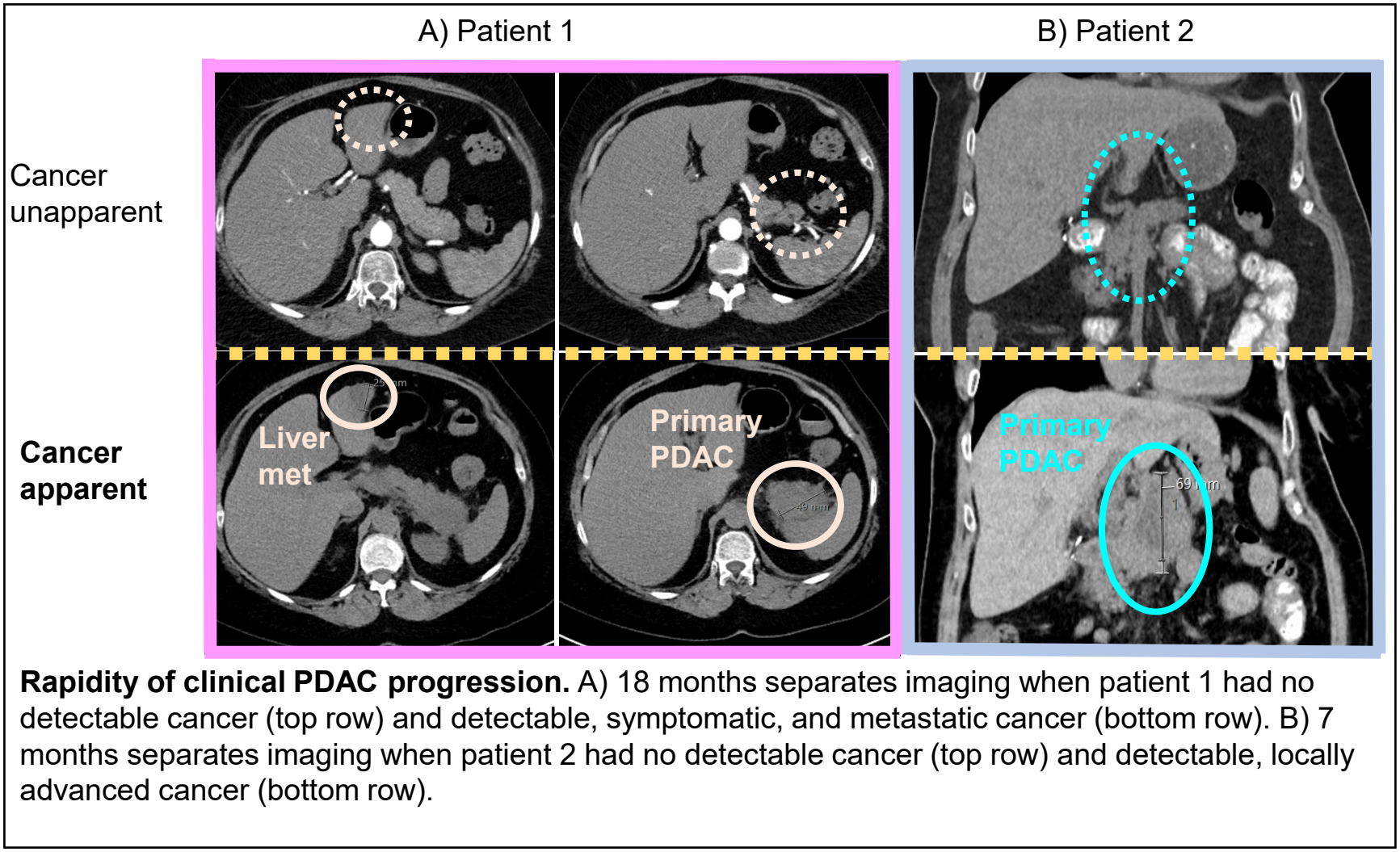
Stage distribution



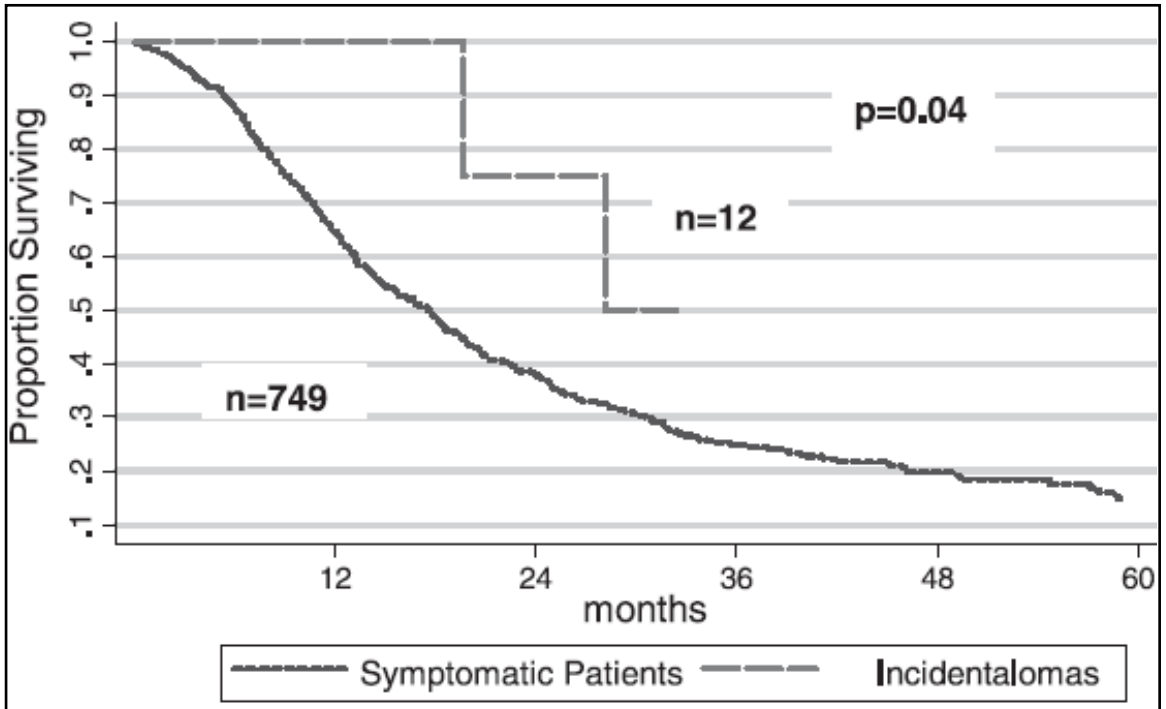
CA Cancer J Clin 2024

5 year survival for localized and metastatic cancer

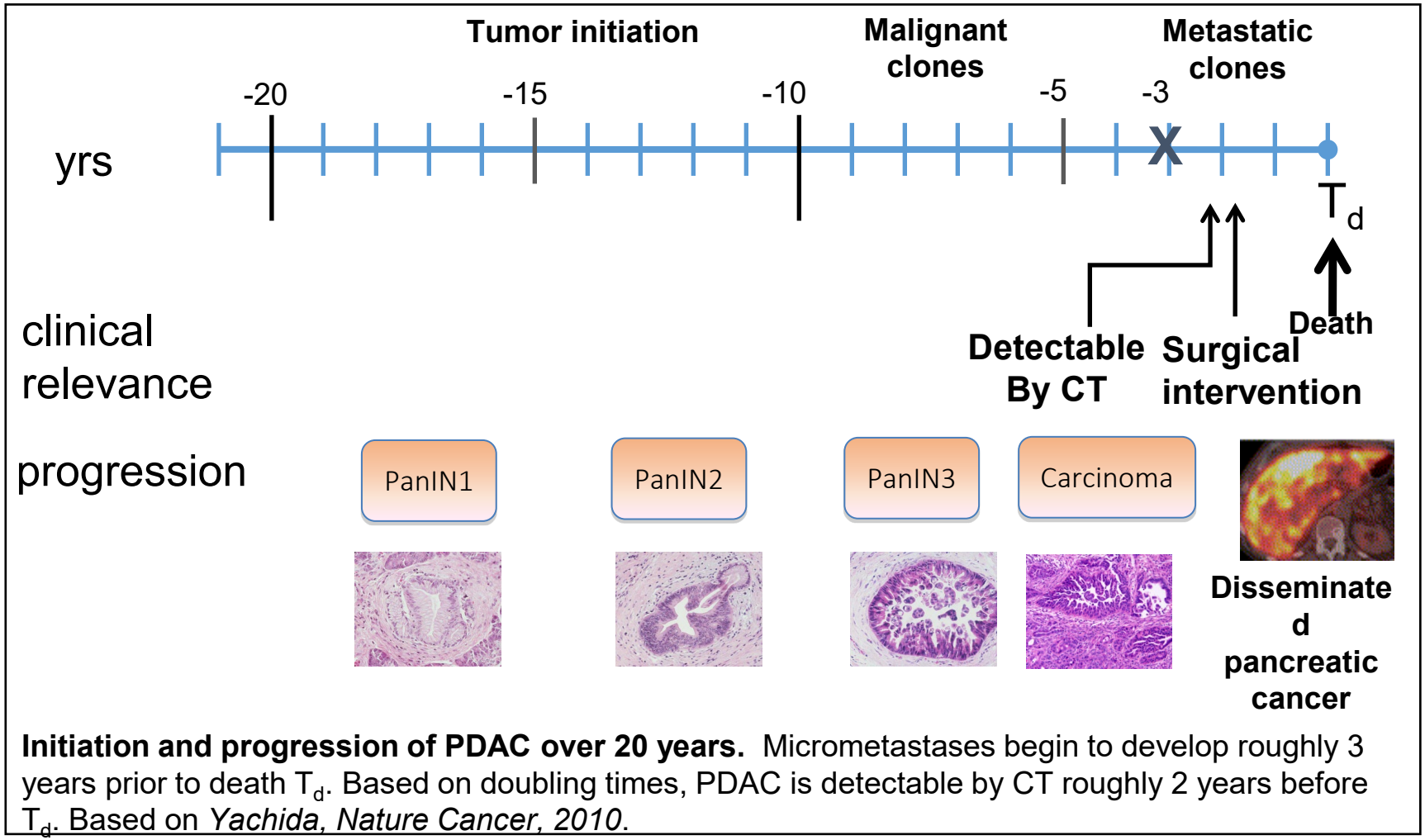
Cancer	Localized	Metastatic
Breast	99%	30%
Prostate	>99%	32%
Lung	61%	7%
Colorectal	91%	14%
Melanoma	100%	32%
Bladder	70%	8%
Kidney	93%	25%
NHL	86%	67%
Uterine	95%	18%
Pancreas	44%	3%



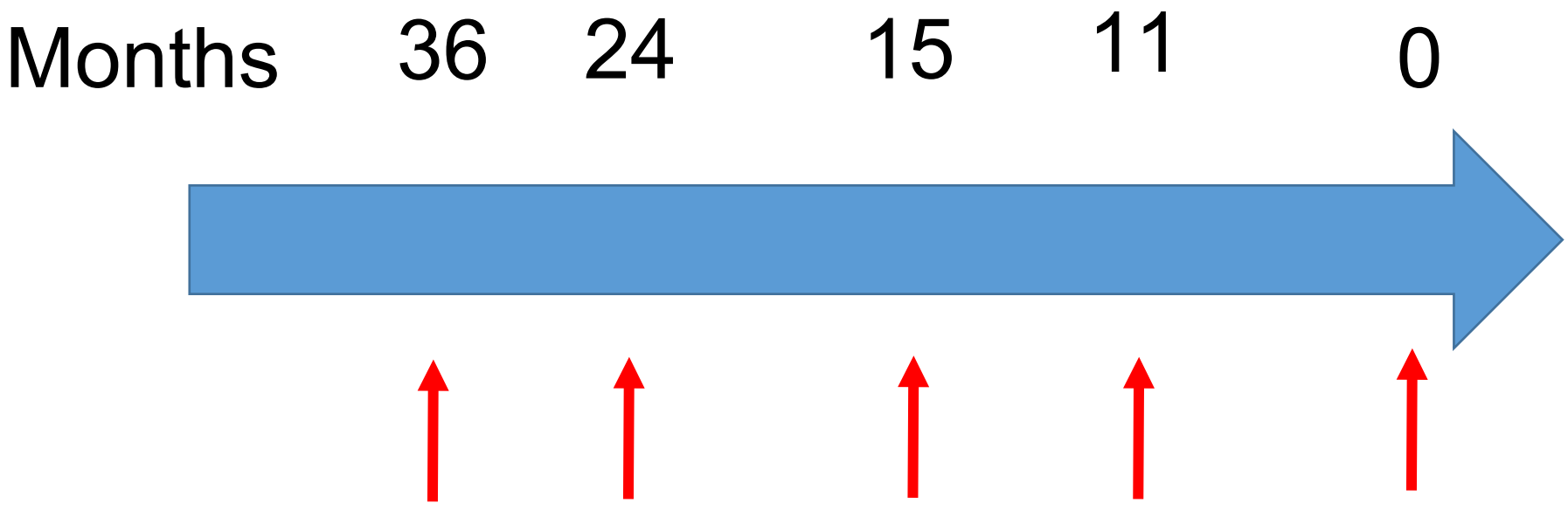
Rapidity of clinical PDAC progression. A) 18 months separates imaging when patient 1 had no detectable cancer (top row) and detectable, symptomatic, and metastatic cancer (bottom row). B) 7 months separates imaging when patient 2 had no detectable cancer (top row) and detectable, locally advanced cancer (bottom row).



Survival benefit of early detection of asymptomatic PDAC.
Winter et al. Ann of Surgery, 2006.



Initiation and progression of PDAC over 20 years. Micrometastases begin to develop roughly 3 years prior to death T_d. Based on doubling times, PDAC is detectable by CT roughly 2 years before T_d. Based on *Yachida, Nature Cancer, 2010*.


Months
36
24
15
11
0
Limits of detection
Localized
Locally Advanced
Metastatic
Death
JAMA Oncology 2021; 7(3):421 (SWOG STUDY)
JAMA. 2016; 315(17):1844.
NEJM. 2011; 64;1817

Performance measures for cancer screening tests

Screening test result	Cancer	No Cancer	Total
Positive	a *true positives*	b *false positives*	a+b *all positives*
Negative	c *false negatives*	d *true negatives*	c+d *all negatives*
Total	a+c *cancers present*	b+d *cancers not present*	a+b+c+d *all screenees*

PPV: a/(a+b)

NPV: d/(c+d)

Sensitivity: a/(a+c)

Specificity: d/(b+d)

Positivity rate: (a+b)/(a+b+c+d)

Prevalence: (a+c)/(a+b+c+d)

FNR: c/(a+c)

FPR: b/(b+d)

Negativity rate: (c+d)/(a+b+c+d)

Breast cancer screening

Sensitivity	82%
Specificity	91%
PPV	4%
NPV	>99%
FPR	9%
FNR	18%
Positivity rate	10%
Negativity rate	90%

Pam Marcus. Assessment of cancer screening: a primer

Simulation of PPV

Prevalence is 500/100,000

Sensitivity/Specificity	**90%**	**95%**	**99%**
90%	4.3%	4.6%	4.7%
95%	8.3%	8.7%	9.0%
99%	31.1%	32.3%	33.2%

#	Cancer	Prevalence/100,000
1	Breast	130
2	Prostate	116
3	Lung	30
4	Colorectal	30
5	Melanoma	21
6	Bladder	10
8	Kidney	15
7	NHL	19
9	Uterine	28
10	Pancreas	5

Simulation of test needed for pancreatic cancer

	PDAC	No PDAC	
Test pos	60,000	45,000	105,000
Tes neg	30,000	109,865,000	109,895,000
	90,000	109,910,000	110,000,000

PPV = 57%

NPV = 100%

Sensitivity = 67%

Specificity = 99.96%

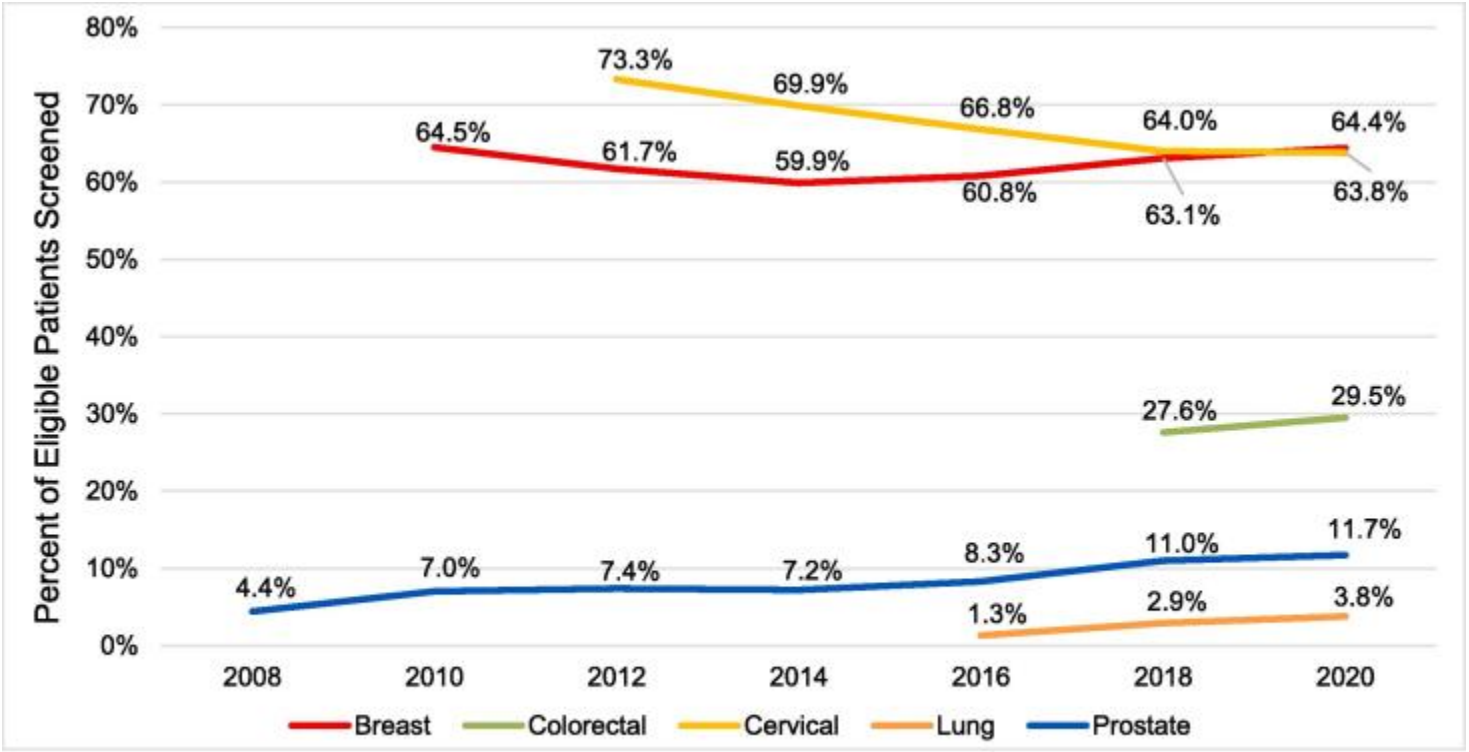
Prevalence PDAC = 0.08%

US Preventive Task Force Recommendations

		PPV
Mammography (40-74 yr)	every 2 years	4%
Pap smear (21-65)	every 3-5 years	18%
Colonoscopy (45-75)	every 10 years	100%
Low dose chest CT (50-80)	yearly (select populations)	10%
Prostate-specific antigen	individualized	25%

USPTF

Compliance with screening



*The time points for which screening adherence was assessed varied by cancer type due to an extended look-back period (ie, 10 years for colorectal cancer screening, 5 years for cervical cancer screening), date of USPSTF recommendation implementation, or the availability, or lack thereof, of CPT codes for specific screening modalities

Cervix

Breast

CRC

Prostate

Lung

Kim et al. Prev Med Rep 2022

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 OCTOBER 27, 2022 VOL. 387 NO. 17

Effect of Colonoscopy Screening on Risks of Colorectal Cancer and Related Death

M. Bretthauer, M. Løberg, P. Wieszczy, M. Kalager, L. Emilsson, K. Garborg, M. Rupinski, E. Dekker, M. Spaander, M. Bugajski, Ø. Holme, A.G. Zauber, N.D. Pilonis, A. Mroz, E.J. Kuipers, J. Shi, M.A. Hernán, H.-O. Adami, J. Regula, G. Hoff, and M.F. Kaminski, for the NordICC Study Group*

ABSTRACT

Table 2. Primary and Secondary End Points.

End Point	Invited Group		Usual-Care Group		Risk Difference (95% CI)	Risk Ratio (95% CI)
	Participants	10-Yr Risk (95% CI)	Participants	10-Yr Risk (95% CI)		
	number	*percent*	*number*	*percent*	*percentage points*	
Colorectal cancer	259	0.98 (0.86 to 1.09)	622	1.20 (1.10 to 1.29)	−0.22 (−0.37 to −0.07)	0.82 (0.70 to 0.93)
Death						
From colorectal cancer	72	0.28 (0.21 to 0.34)	157	0.31 (0.26 to 0.35)	−0.03 (−0.11 to 0.05)	0.90 (0.64 to 1.16)
From any cause	3036	11.03 (10.66 to 11.40)	6079	11.04 (10.78 to 11.30)	−0.01 (−0.47 to 0.44)	0.99 (0.96 to 1.04)

The NEW ENGLAND JOURNAL of MEDICINE

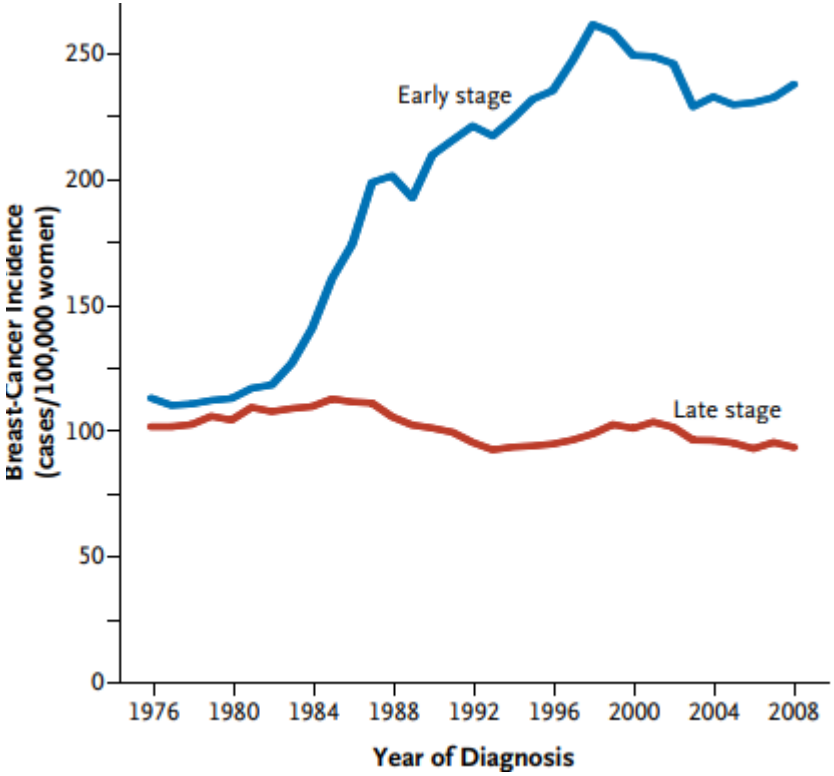
ORIGINAL ARTICLE

Effect of Three Decades of Screening Mammography on Breast-Cancer Incidence

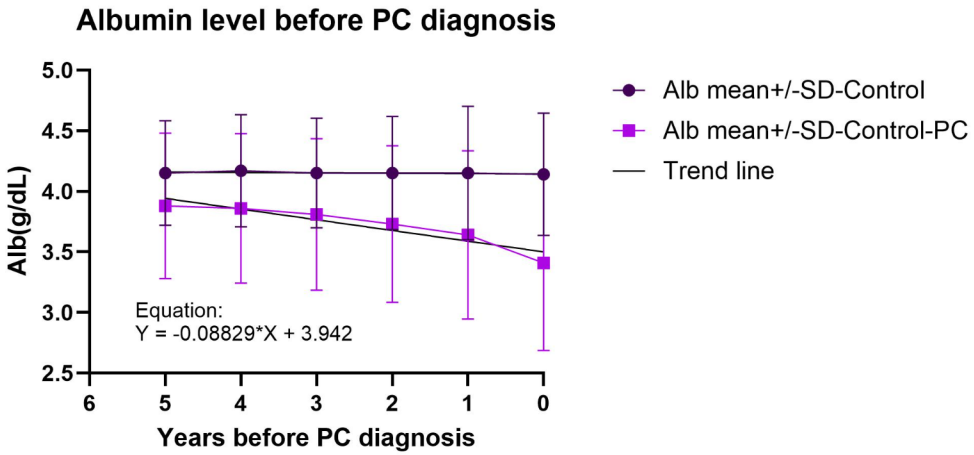
Archie Bleyer, M.D., and H. Gilbert Welch, M.D., M.P.H.

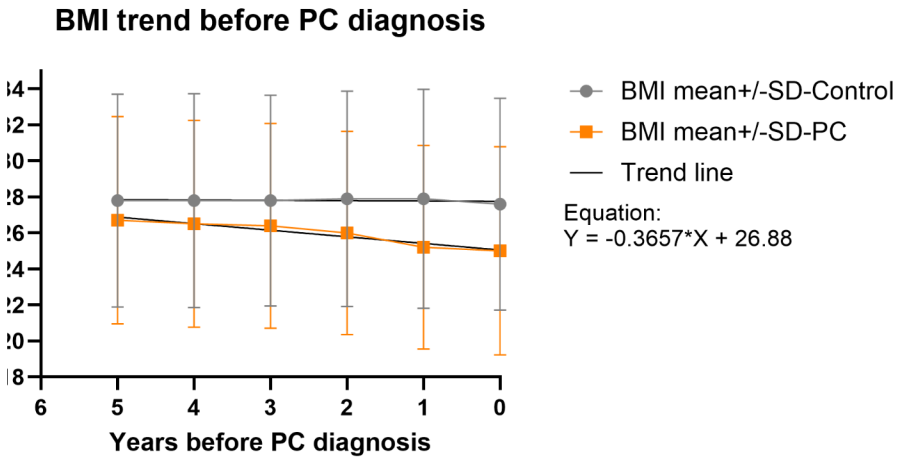
Table 1. Absolute Change in the Incidence of Stage-Specific Breast Cancer among Women 40 Years of Age or Older after the Introduction of Screening Mammography.*

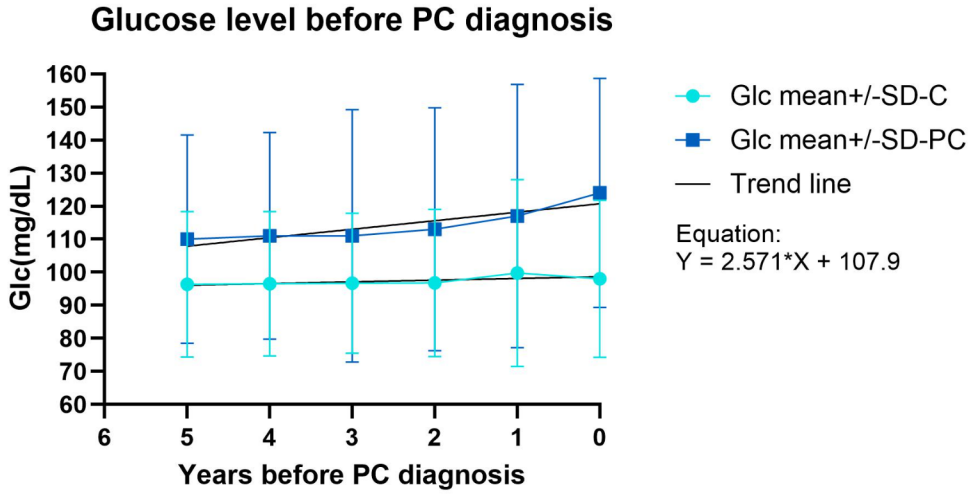
Variable	Annual Breast-Cancer Incidence			Women Affected over the Three Decades†
	Before Mammography (1976–1978)	Three Decades Later (2006–2008)	Absolute Change	
	number of cases per 100,000 women			*estimated number of women*
Increase in cases of early-stage breast cancer				
DCIS	7	56	50	573,000
Localized disease	105	178	72	1,012,000
Total	112	234	122	1,585,000
Decrease in cases of late-stage breast cancer				
Regional disease	85	78	–8‡	59,000
Distant disease	17	17	0§	8,000
Total	102	94	–8	67,000

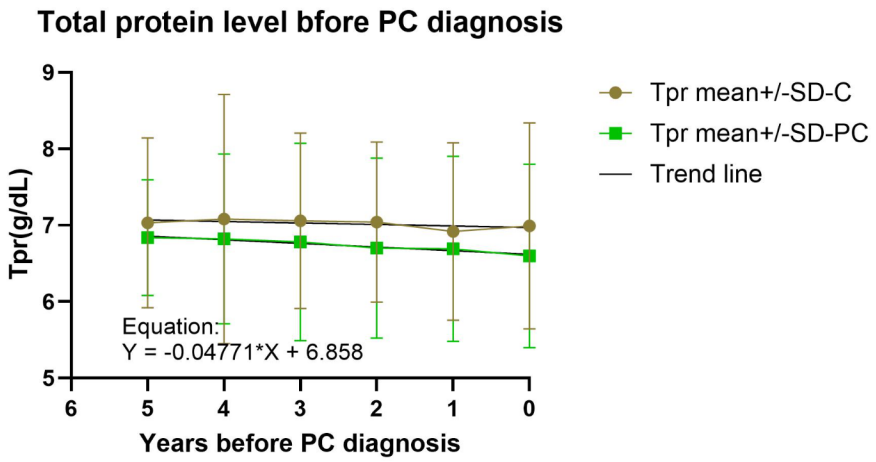


The promise of early detection: Pancreatic cancer

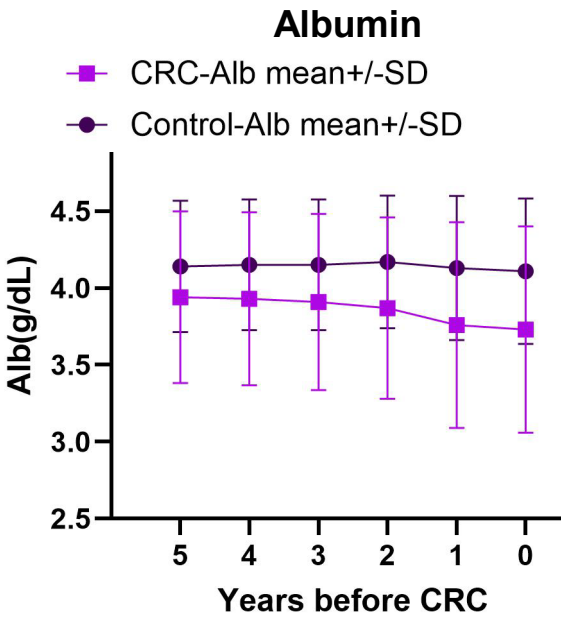


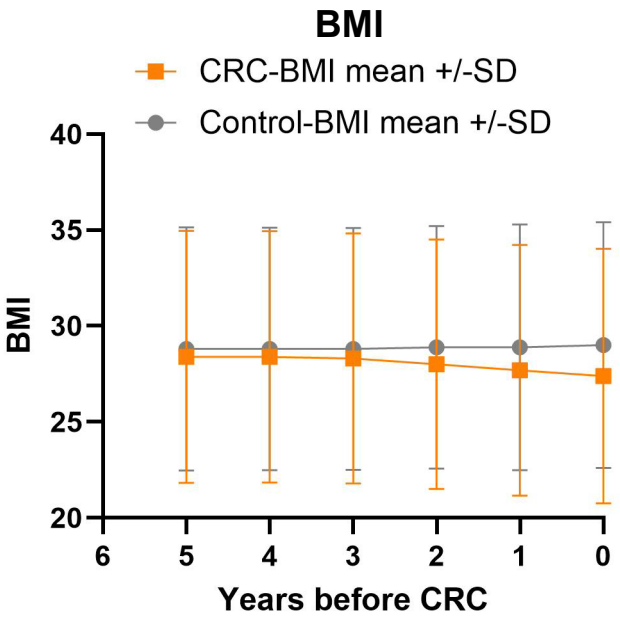


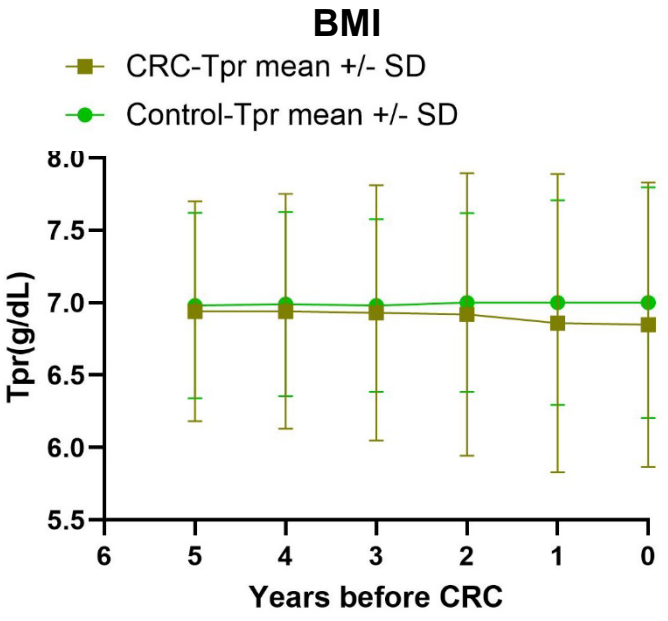


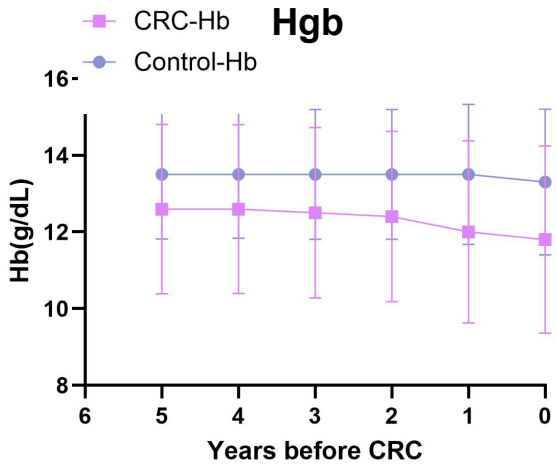


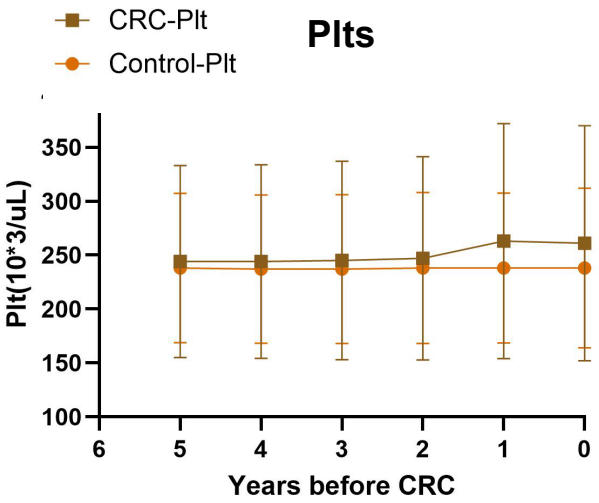
The promise of early detection: CRC







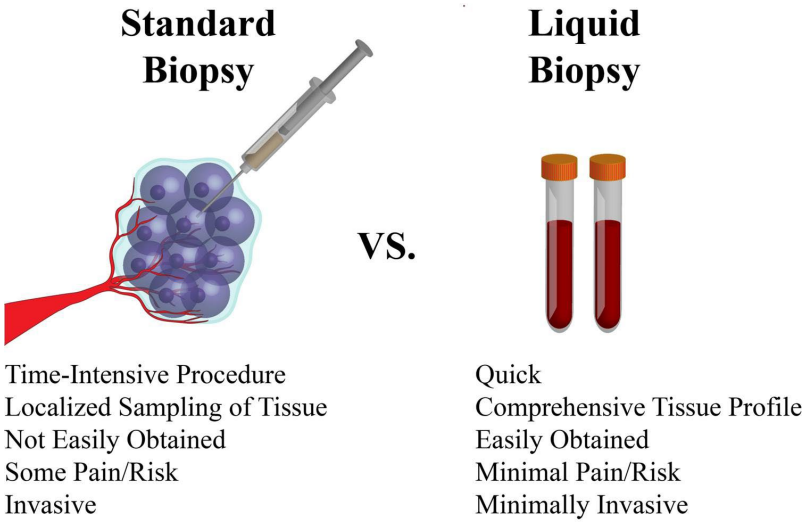




Liquid biopsy: a non-invasive laboratory test that analyzes a biological sample to detect cancer cells or tumor-material

- Google AI

- Fluids may include blood, urine, saliva, CSF
- Analytes may include DNA, RNA, protein, metabolites



https://www.gene-quantification.de/liquid-biopsy-index.html

MCED: Multi-cancer early detection test

Selected pan-cancer liquid biopsies – progress update				
Company	**Liquid biopsy**	**Use**	**Status in US**	**Company notes**
Guardant Health	Guardant360	Helps assign targeted therapy	Approved Aug 7, 2020, price approx $6,800	$550m VC funding; floated in 2018
Foundation Medicine (Roche)	FoundationOne Liquid CDx	Helps assign targeted therapy	Approved Aug 27, 2020, price $5,800	$115m VC funding; bought by Roche for $2.5bn in 2015
Grail	Galleri	Screening for early detection and identification of tumour origin	Launched as LDT Jun 4, 2021, price $949	$2.1bn VC funding; bought by Illumina for $8bn in 2020
	Unnamed	Postsurgical, detects disease recurrence	In development	
Thrive Earlier Detection (Exact Sciences)	CancerSeek	Early detection	FDA breakthrough device status	$367m VC funding; bought by Exact Sciences in 2020 for $1.7bn
Natera	Signatera	Postsurgical, detects disease recurrence	FDA breakthrough device status	$152m in VC funding; floated in 2015
Archer DX (Invitae)	Stratafide	Helps assign targeted therapy	FDA breakthrough device status	$150m VC funding; bought by Invitae in 2020 for $1.4bn

https://www.evaluate.com/vantage/articles/news/snippets/grail-launches-pan-cancer-screen-those-who-can-pay-out-pocket

THE LANCET

Blood-based tests for multicancer early detection (PATHFINDER): a prospective cohort study

Prof Deb Schrag, MD • Prof Tomasz M Beer, MD • Charles H McDonnell III, MD • Lincoln Nadauld, MD • Christina A Dilaveri, MD • Robert Reid, MD • et al. Show all authors

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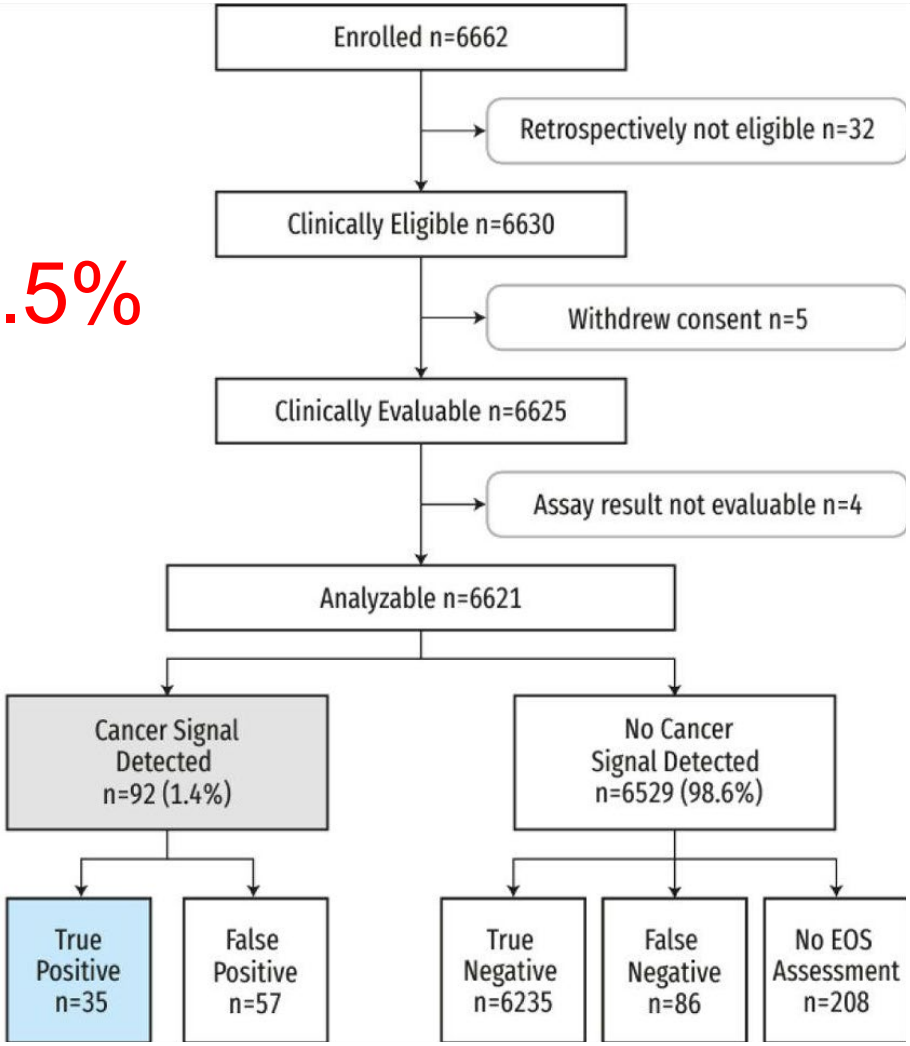

Multi-cancer early detection test in symptomatic patients referred for cancer investigation in England and Wales (SYMPLIFY): a large-scale, observational cohort study

Brian D Nicholson, Jason Oke, Pradeep S Virdee, Dean A Harris, Catherine O'Doherty, John ES Park, Zaed Hamady, Vinay Sehgal, Andrew Millar, Louise Medley, Sharon Tonner, Monika Vargova, Lazarina Engonidou, Kaveh Riahi, Ying Luan, Sara Hiom, Harpal Kumar, Harit Nandani, Kathryn N Kurtzman, Ly-Mee Yu, Clare Freestone, Sarah Pearson, FD Richard Hobbs, Rafael Perera, Mark R Middleton

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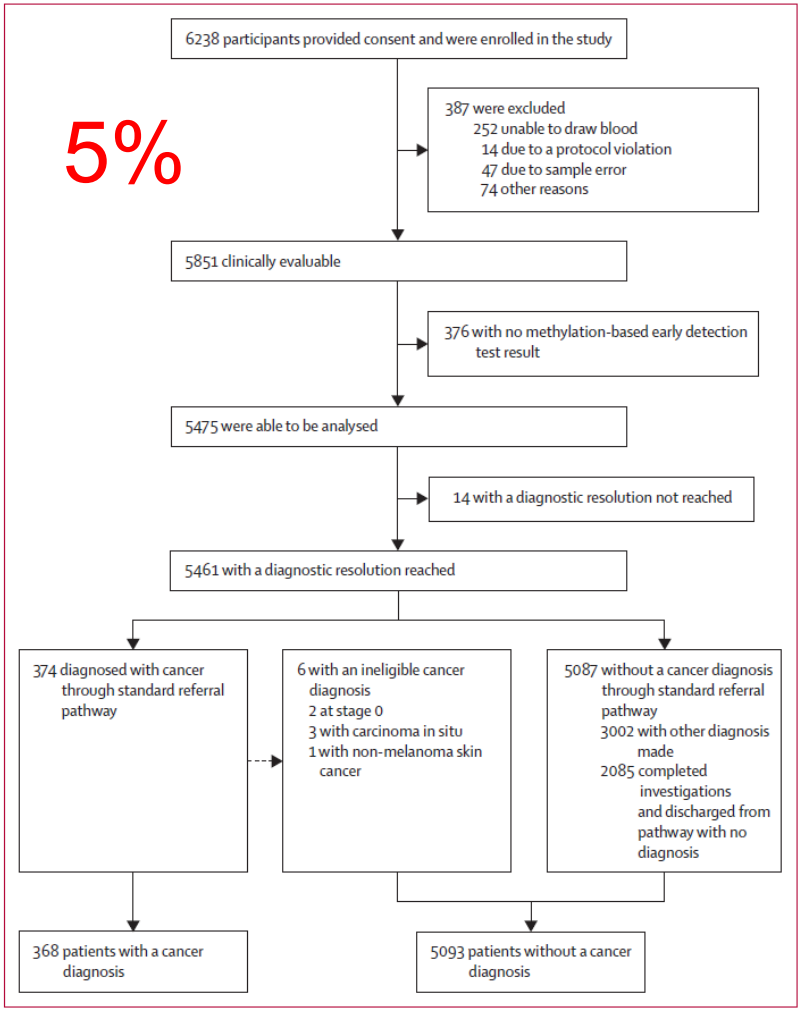


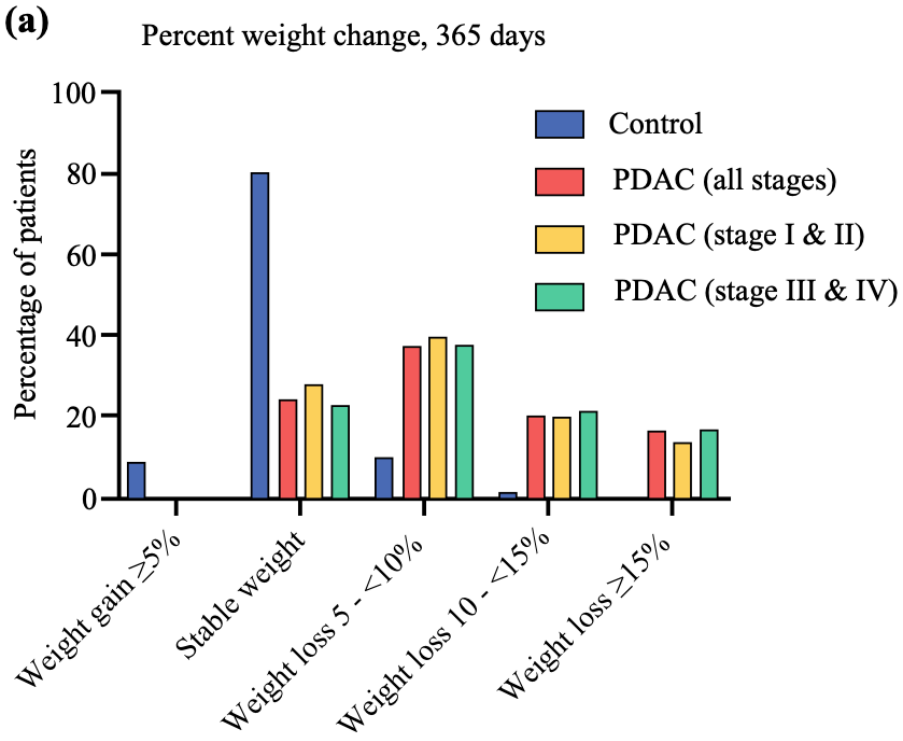
- MCED, best in class
- Detects over 50 cancers
- Costs $949
- Provides top 3 likely matches

<u>Performance metrics</u>
Sensitivity 51%
Specificity 99.5%
>PPV 44%

Annals of Oncology 2021

Weight Loss as an Untapped Early Detection Marker in Pancreatic and Periampullary Cancer

Jonathan J. Hue, MD[1], Kavin Sugumar, MD[1], Ravi K. Kyasaram, MS[1], John Shanahan, BA[1], Joshua Lyons, MD[1], Lee M. Ocuin, MD[2], Luke D. Rothermel, MD[1], Jeffrey M. Hardacre, MD[1], John B. Ammori, MD[1], Goutham Rao, MD[3], Jordan M. Winter, MD[1], and Sarah C. Markt, ScD, MPH[4]



Patient-centered Weight Tracking as an Early Cancer Detection Strategy

Jonathan J. Hue[1], Sarah C. Markt[2], Goutham Rao[3], Jordan M. Winter[1]

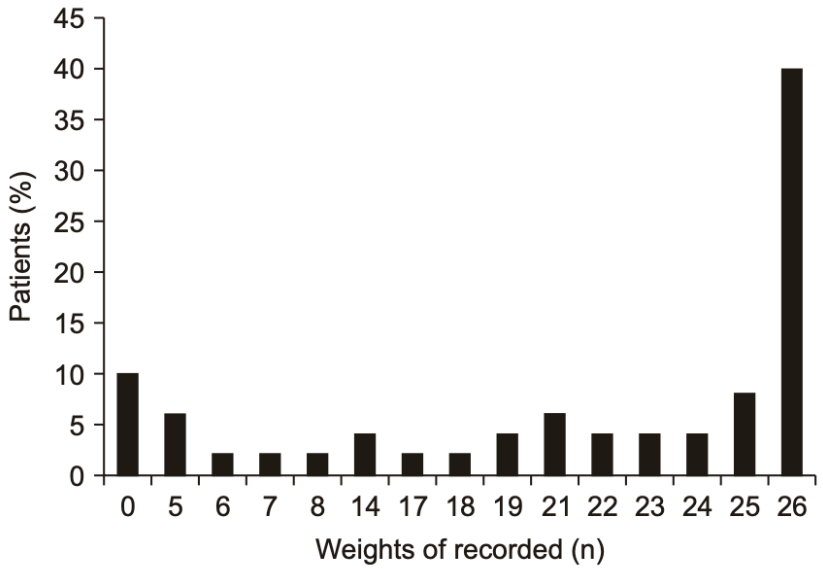


Figure 2. Frequency of weights recorded in the weight tracking feasibility study, University Hospitals Cleveland Medical Center Primary Care Clinic, July 2019 to January 2020.

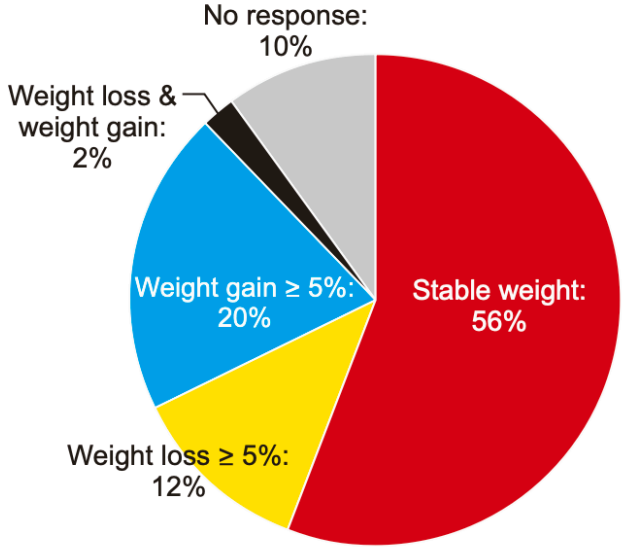


Figure 3. Summary of study population weight changes in the weight tracking feasibility study, University Hospitals Cleveland Medical Center Primary Care Clinic, July 2019 to January 2020 (intent-to-study, n = 50).

Clinical trial using UWL and liquid biopsies to detect cancer

1000 patients
>50 yrs enrolled

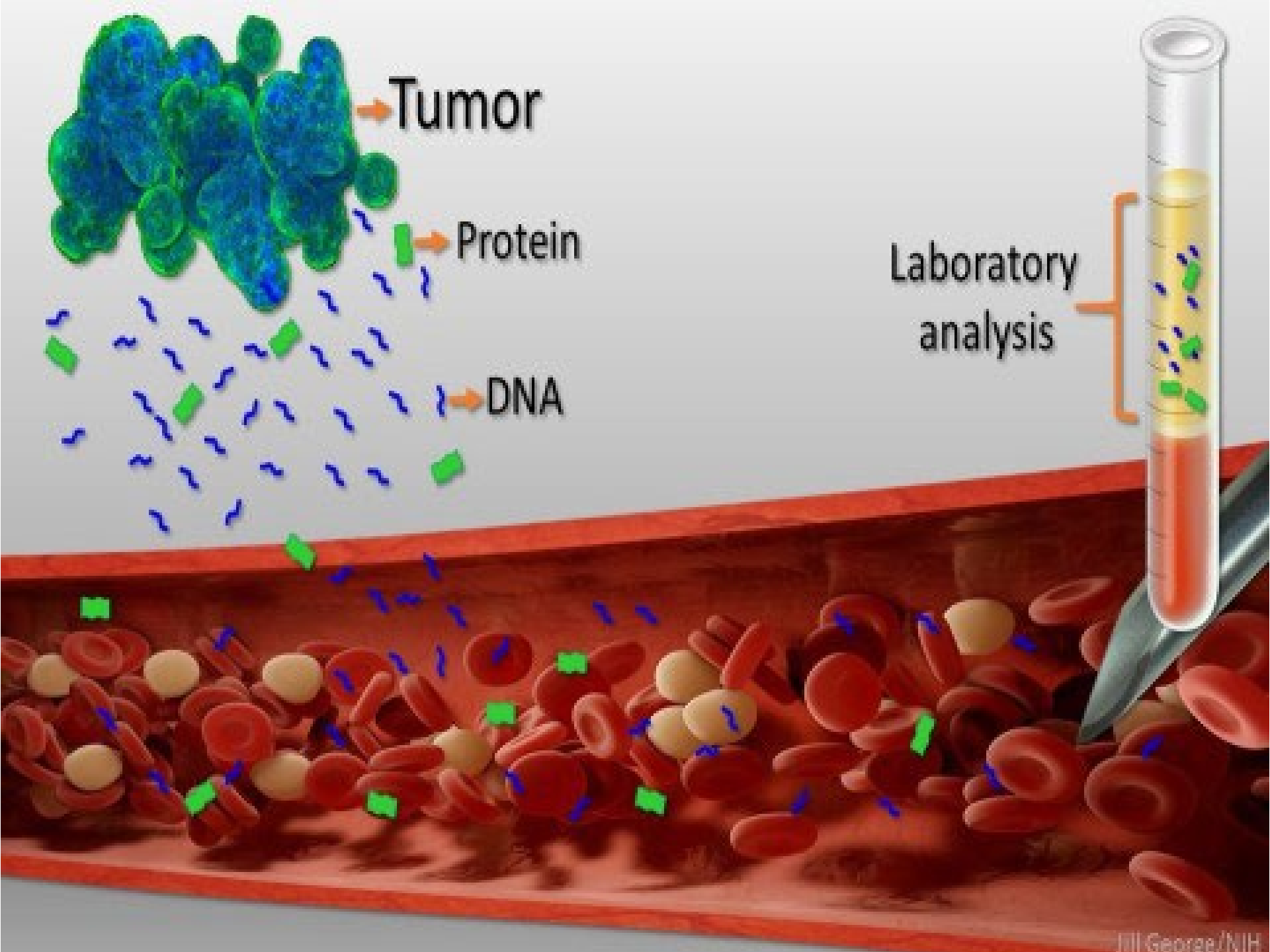
UWL (~150 over 3 years)

No UWL (850 over 3 years)

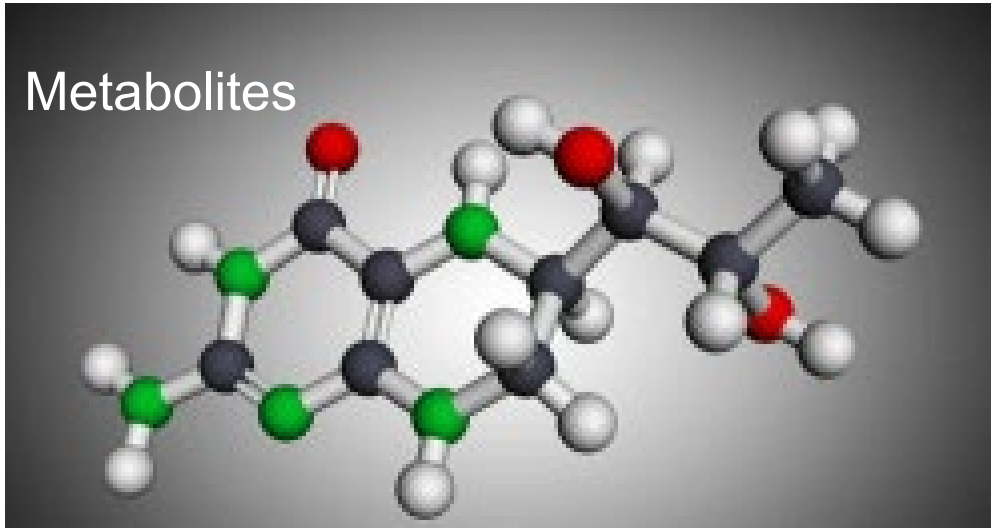
- H&P
- Diagnostic workup
- GRAIL

~ 17 of 35 cancers

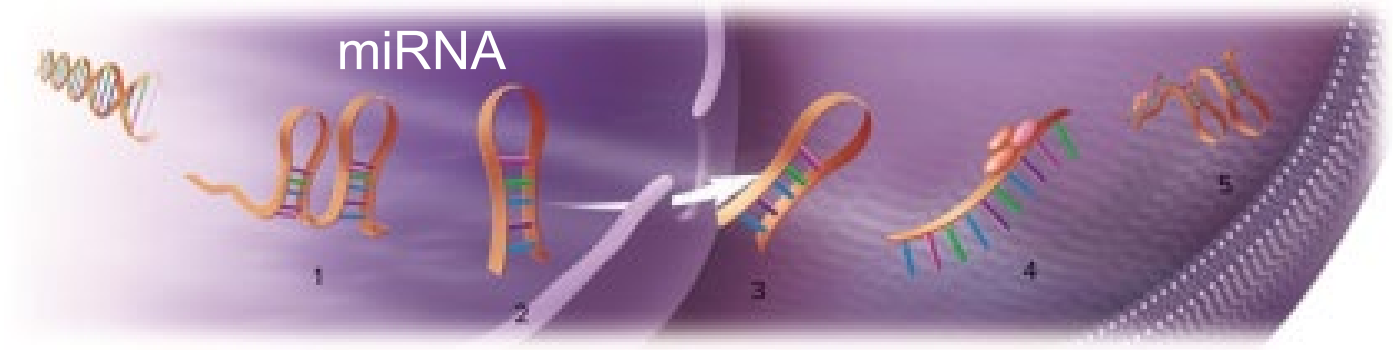

Health Monitoring
300


Tumor
Protein
DNA
Laboratory analysis
Jill George/NIH

Can any test beat methylated DNA?

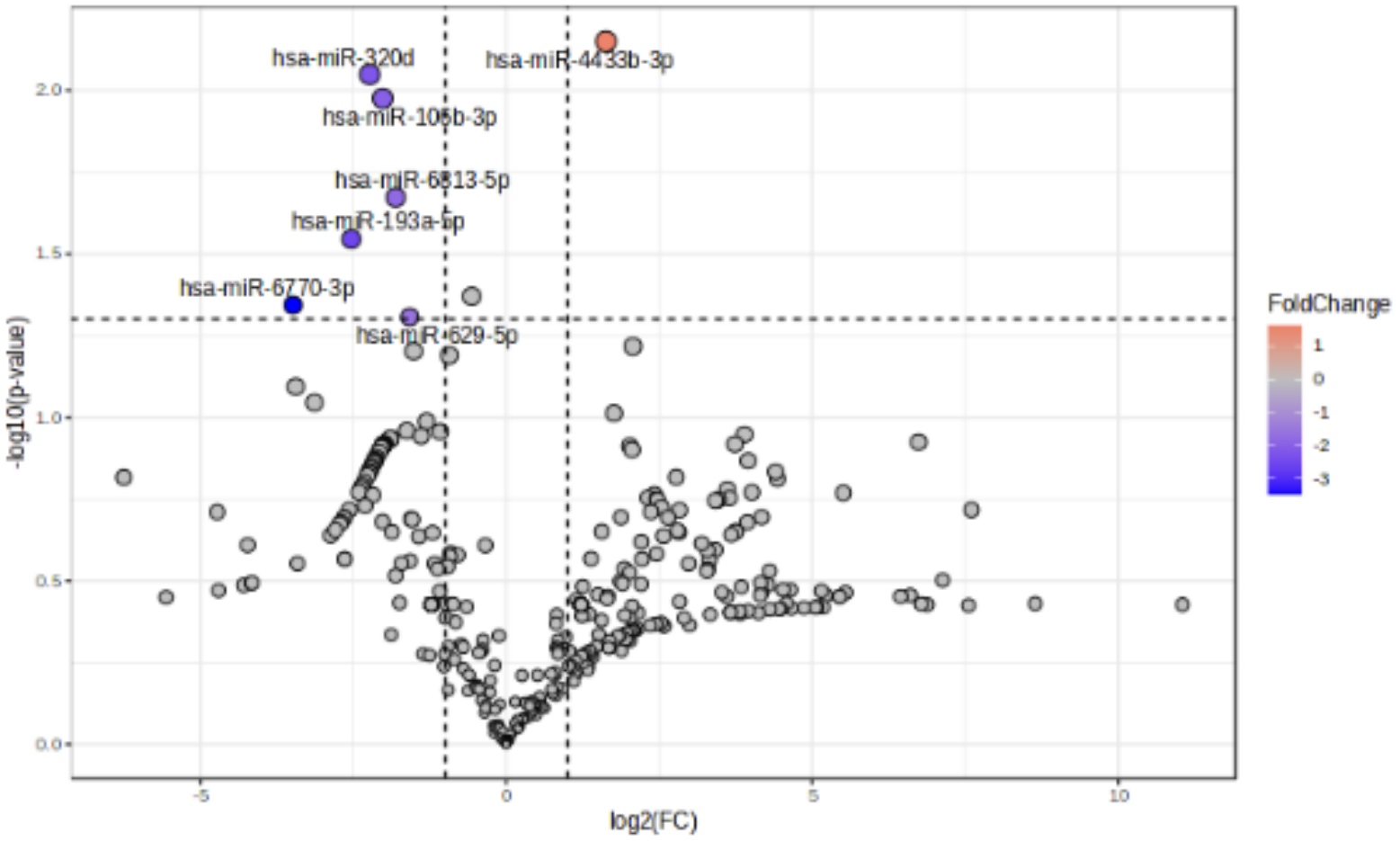


> 200,000



> 2,000

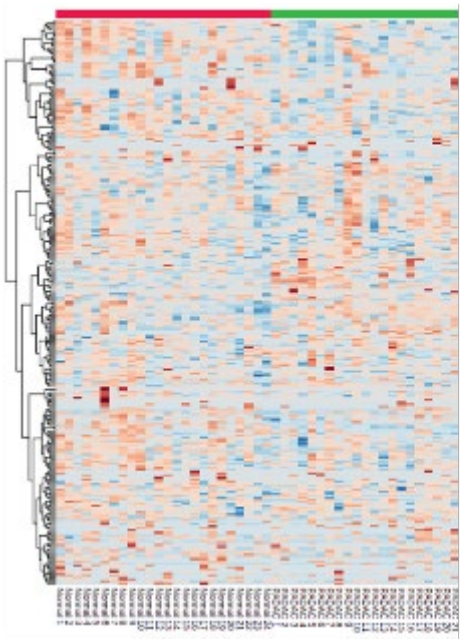
Stability of miRNAs over time



Early detection for pancreatic cancer

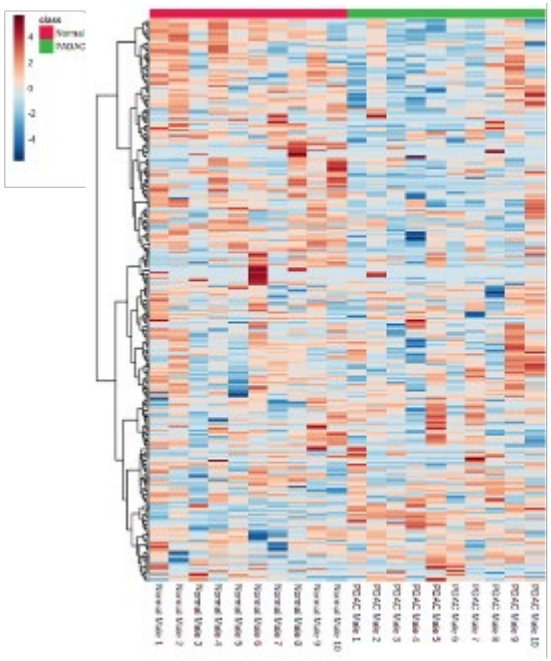
All

Non-PDAC PDAC



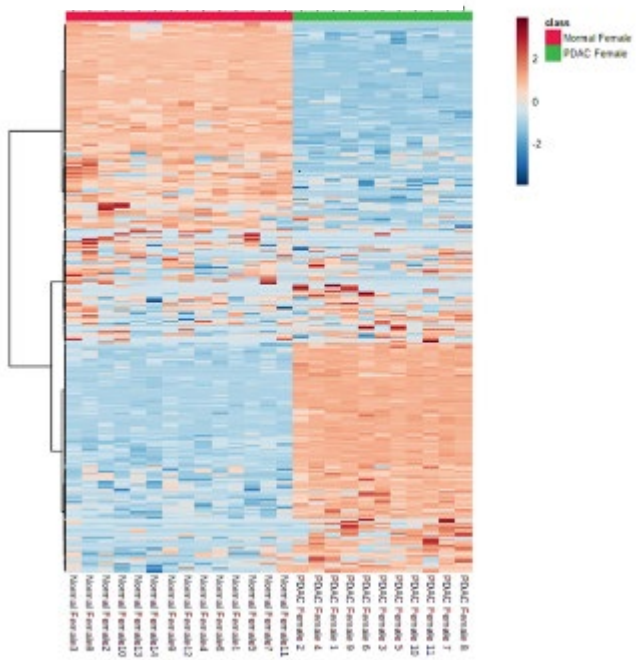
Male

Non-PDAC PDAC

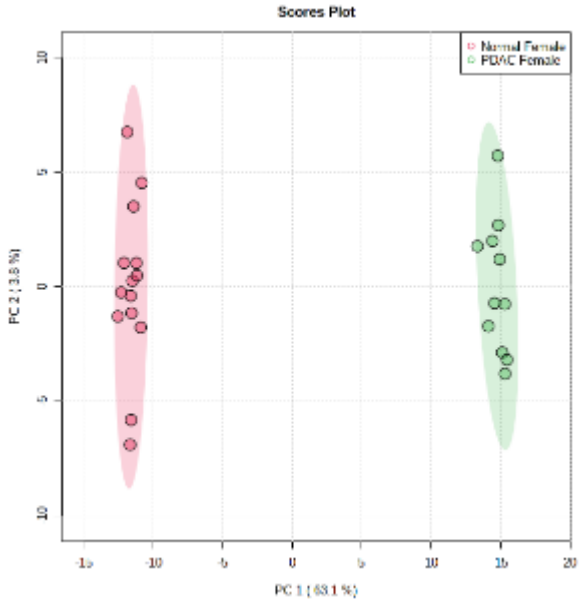


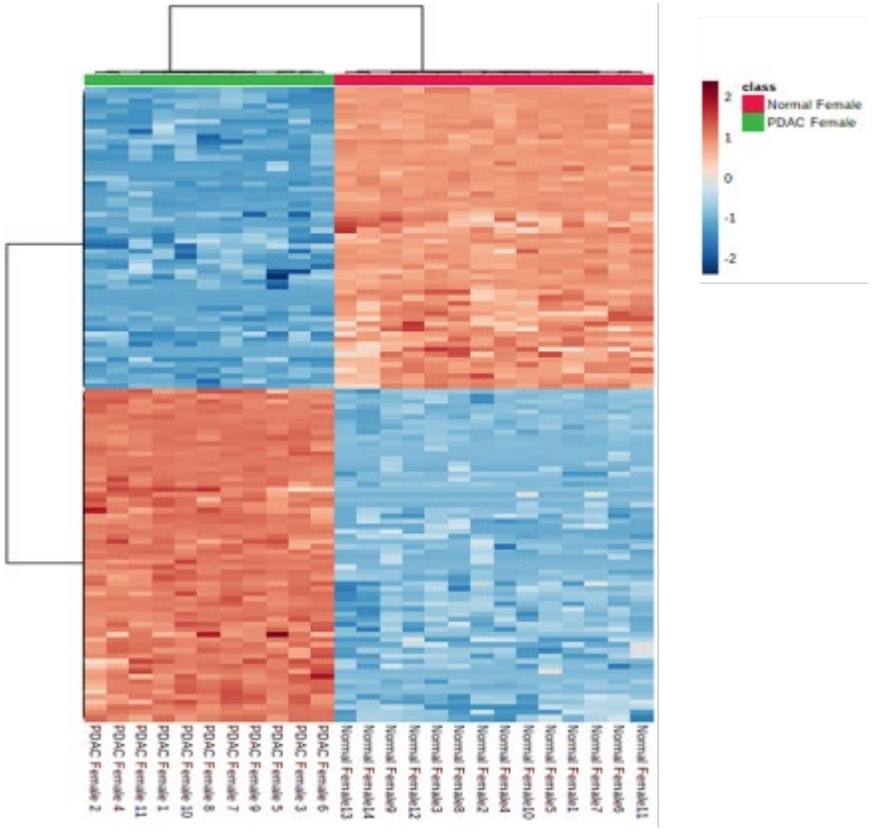
Female

Non-PDAC PDAC



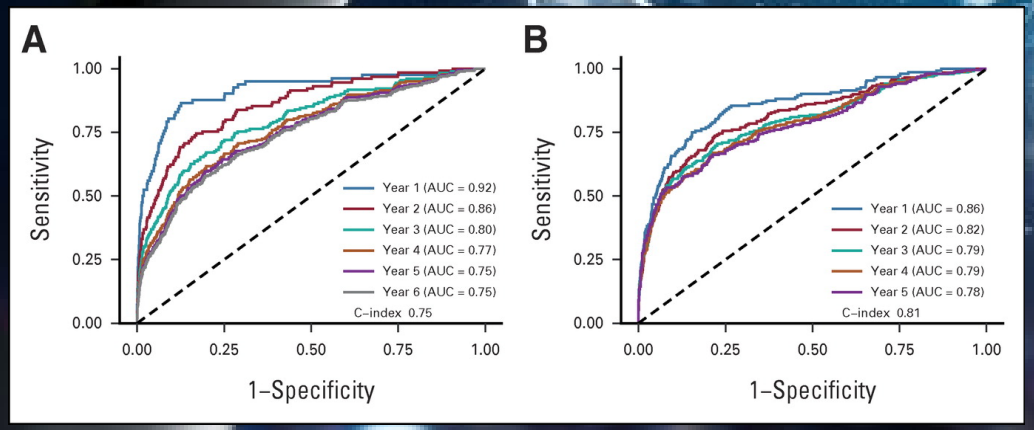
Analysis of female patients

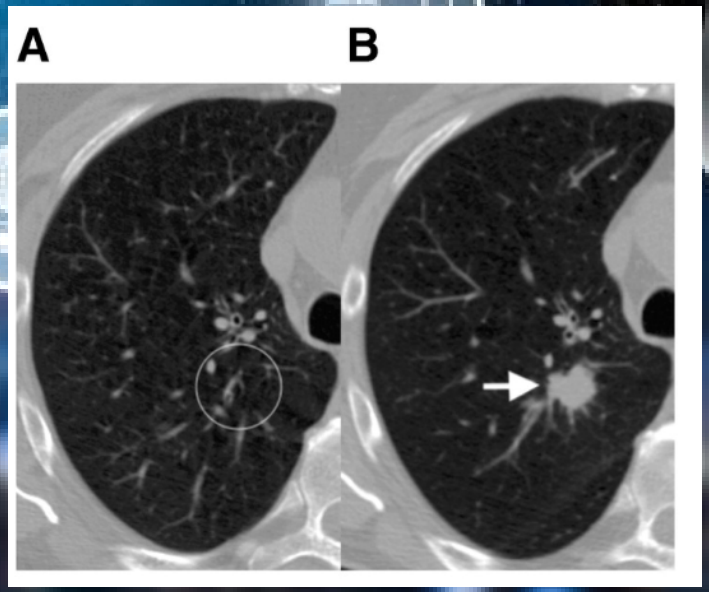




122 metabolites

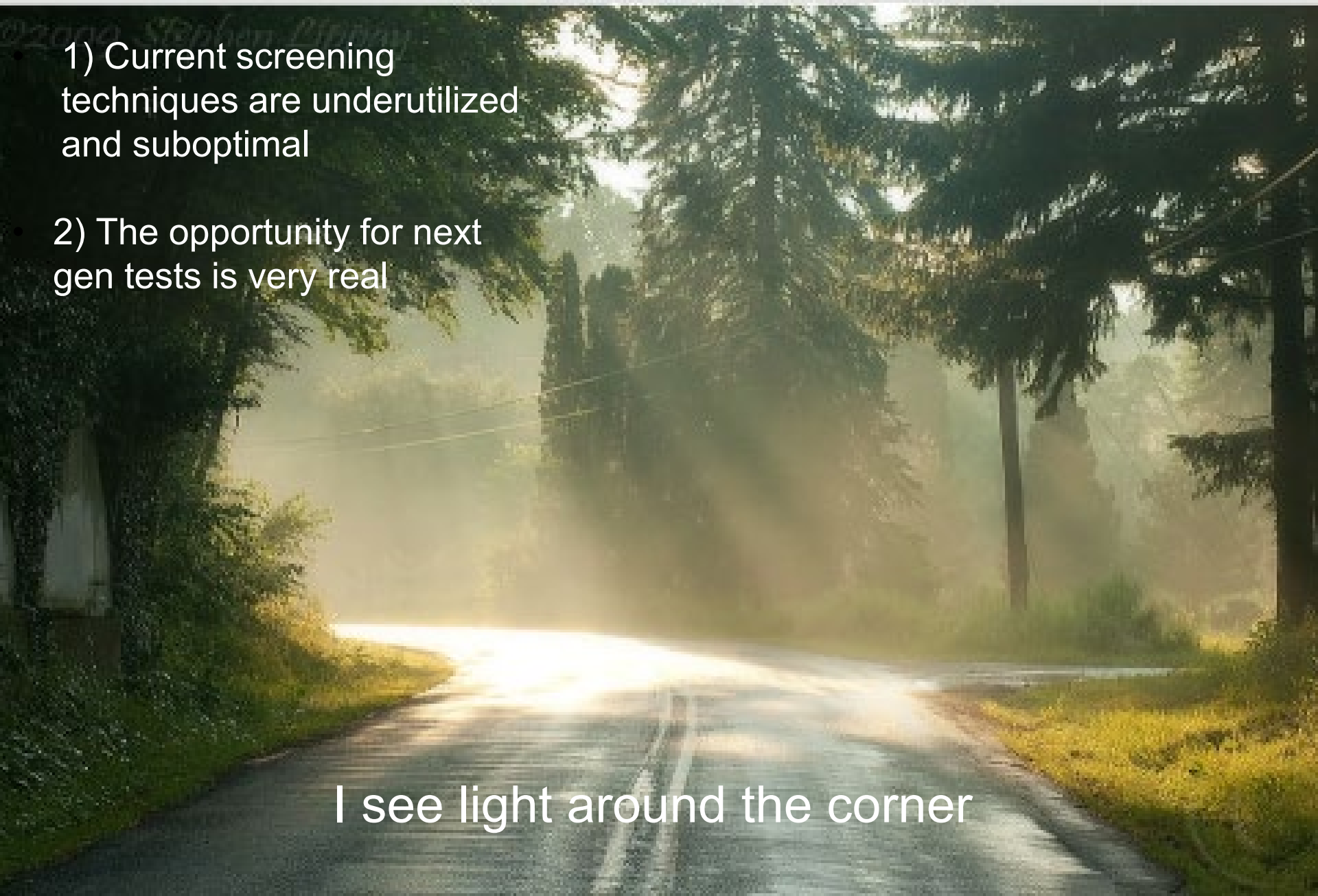
EARLY CANCER DETECTION


A
B
Sensitivity
1–Specificity
0.00
0.25
0.50
0.75
1.00
Year 1 (AUC = 0.92)
Year 2 (AUC = 0.86)
Year 3 (AUC = 0.80)
Year 4 (AUC = 0.77)
Year 5 (AUC = 0.75)
Year 6 (AUC = 0.75)
C–index 0.75
Year 1 (AUC = 0.86)
Year 2 (AUC = 0.82)
Year 3 (AUC = 0.79)
Year 4 (AUC = 0.79)
Year 5 (AUC = 0.78)
C–index 0.81


A
B

JCO, Jan 2023

In Summary



- 1) Current screening techniques are underutilized and suboptimal
- 2) The opportunity for next gen tests is very real

I see light around the corner

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