Noninvasive Multi-Cancer Screening Using Liquid Biopsy

Pros and Cons of Pan-Cancer Detection Approach: Should EDRN Increase Focus on Such an Approach?

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The Sidney Kimmel Comprehensive Cancer Center
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Disclosures

- Shareholder: PGDx, Thrive, NeoPhore, CagePharma
- BOD: Thrive.

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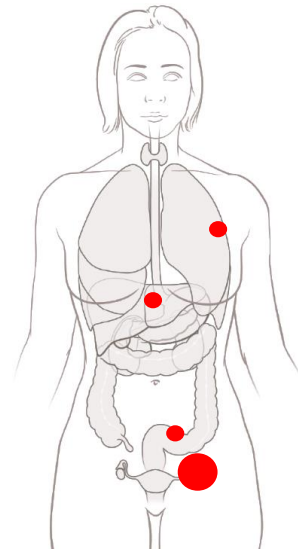
Goal for Early Detection

Identify Screen-Detected Cancers

Identify Cancers that Matter

Earlier Detection



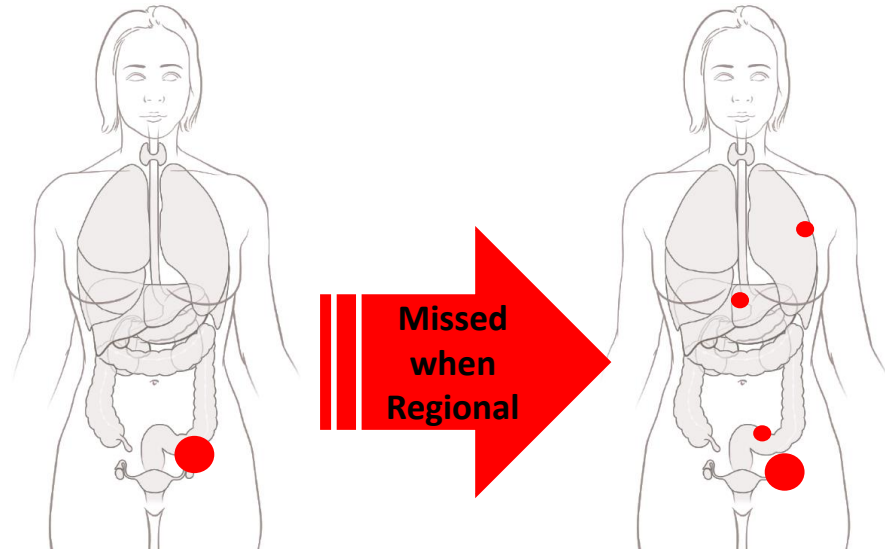
Metastatic

30% 5-year survival

58% of cases

SEER 18 2010–2016, All Races

Earlier Detection



Regional

75% 5-year survival

21% of cases

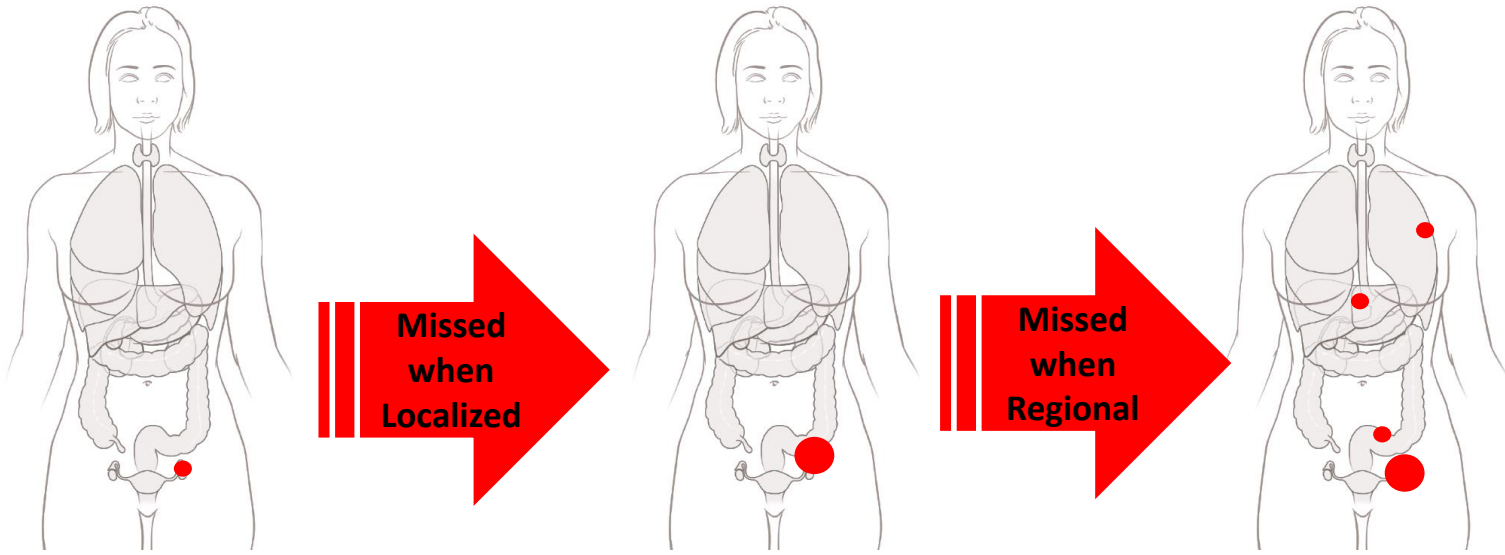
Metastatic

30% 5-year survival

58% of cases

SEER 18 2010–2016, All Races

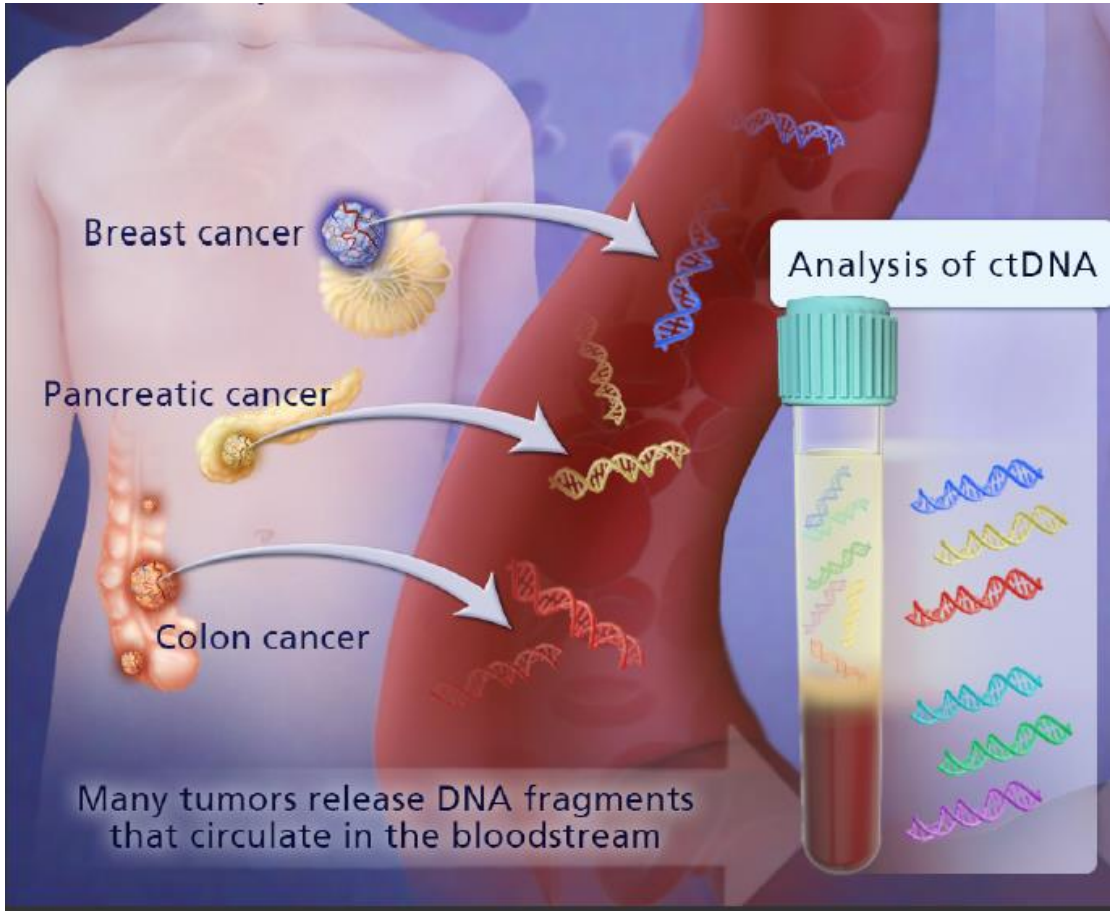
Earlier Detection



Localized	Regional	Metastatic
93% 5-year survival	**75%** 5-year survival	**30%** 5-year survival
16% of cases	**21%** of cases	**58%** of cases

SEER 18 2010–2016, All Races

Liquid Biopsy



Single Easily Accessible Medium for Multiple Cancers

Detecting Cancer with Blood Test

Single Site

- Excludes all other cancers
- Multiple single-site tests
- Not efficient for low prevalence cancers
- High risk population

VS

Multi-Cancer

- Inclusive of many cancer types including low prevalence cancers
- Single test
- Variable Performance per tumor type

Distinguishing Cancer from Non-cancer

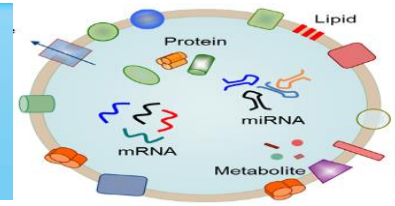
DNA Mutations

Transcripts

DNA Copy Number

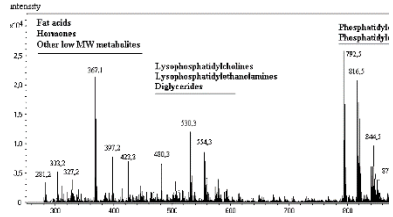
Proteins

Exosomes

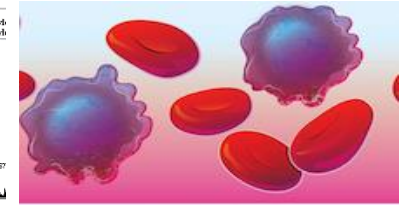


DNA Methylation

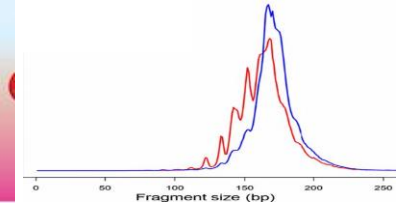
Metabolites



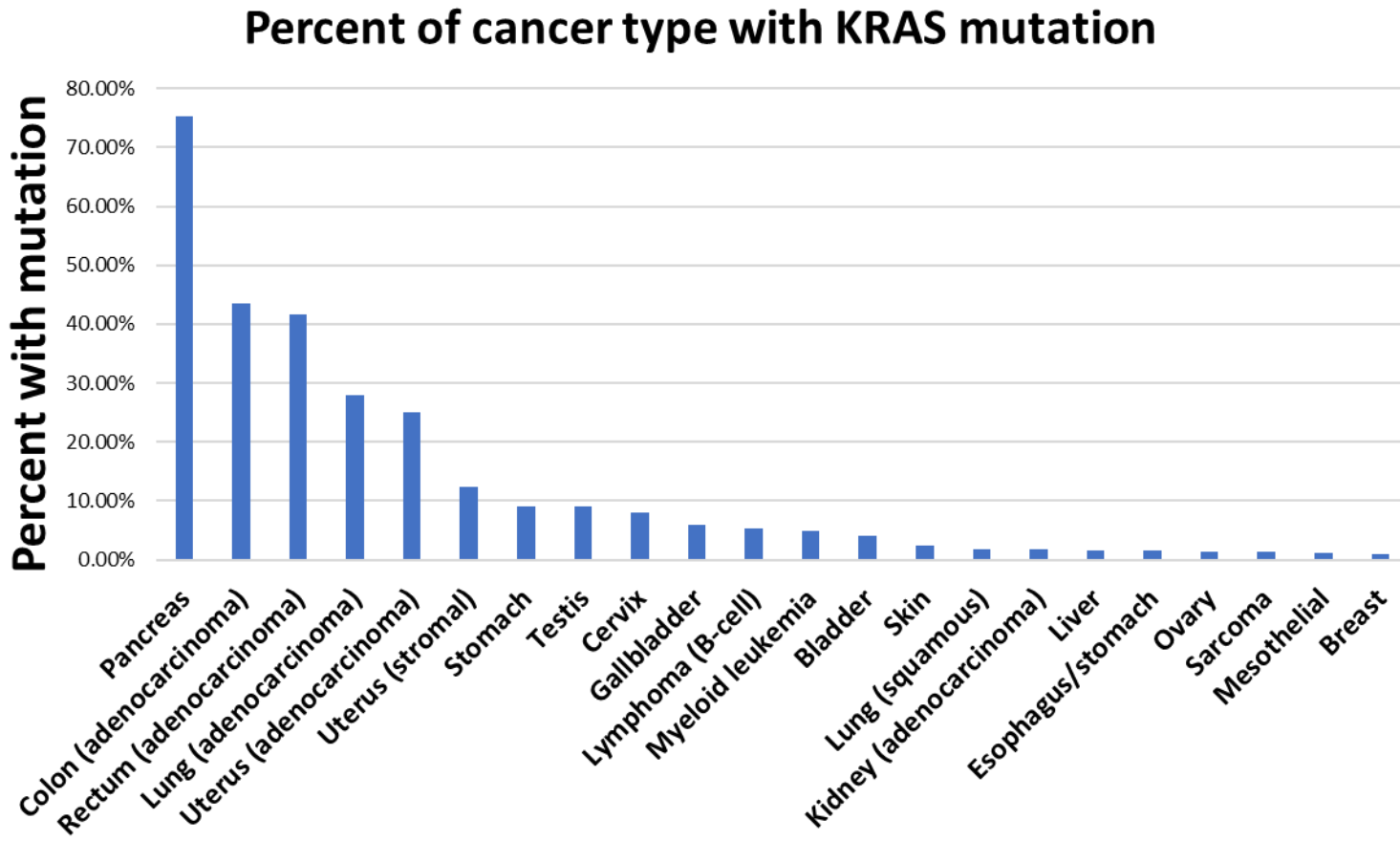
Cells



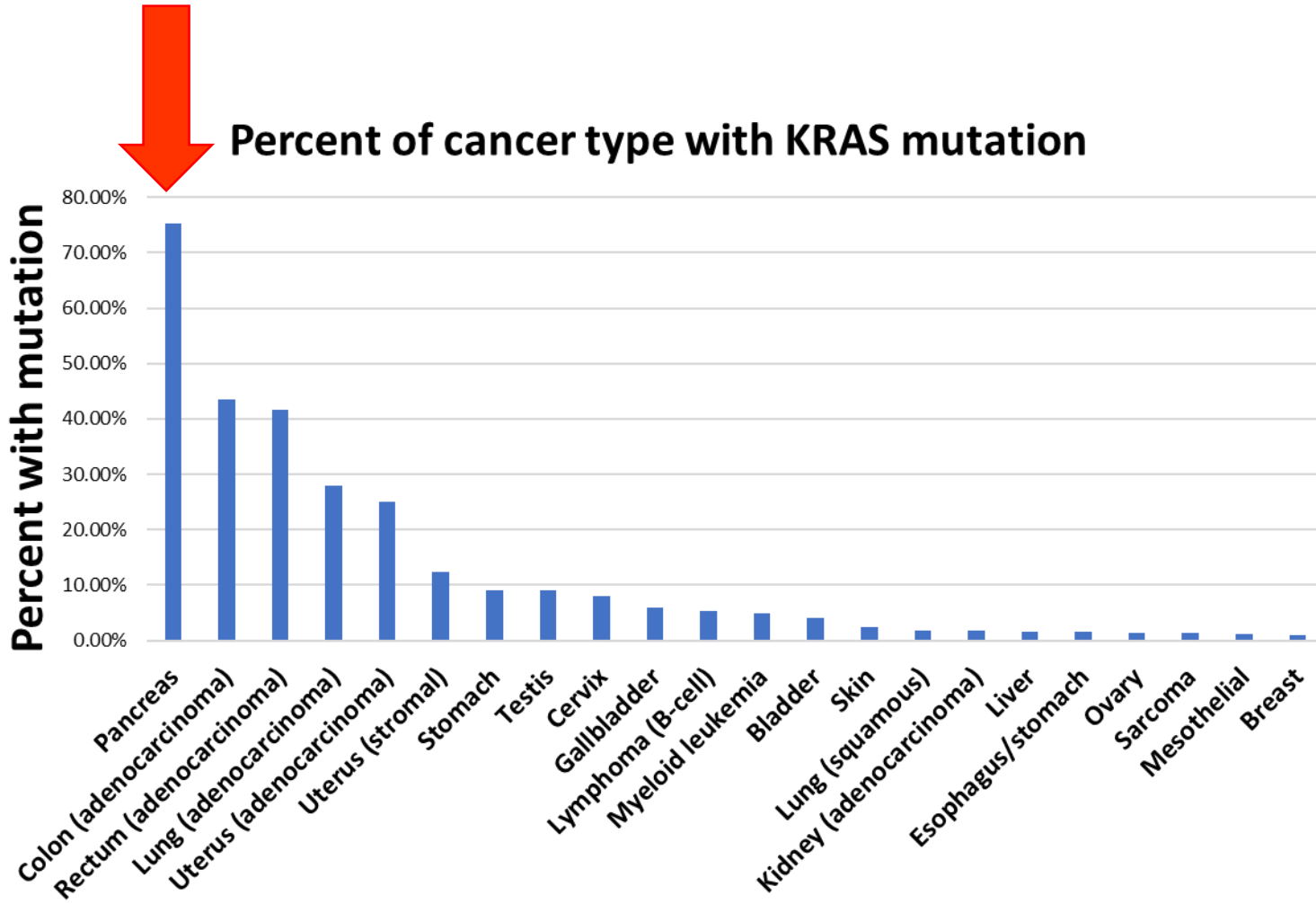
DNA Size



Many biomarkers are fundamentally cancer agnostic



Single site Pancreatic cancer test



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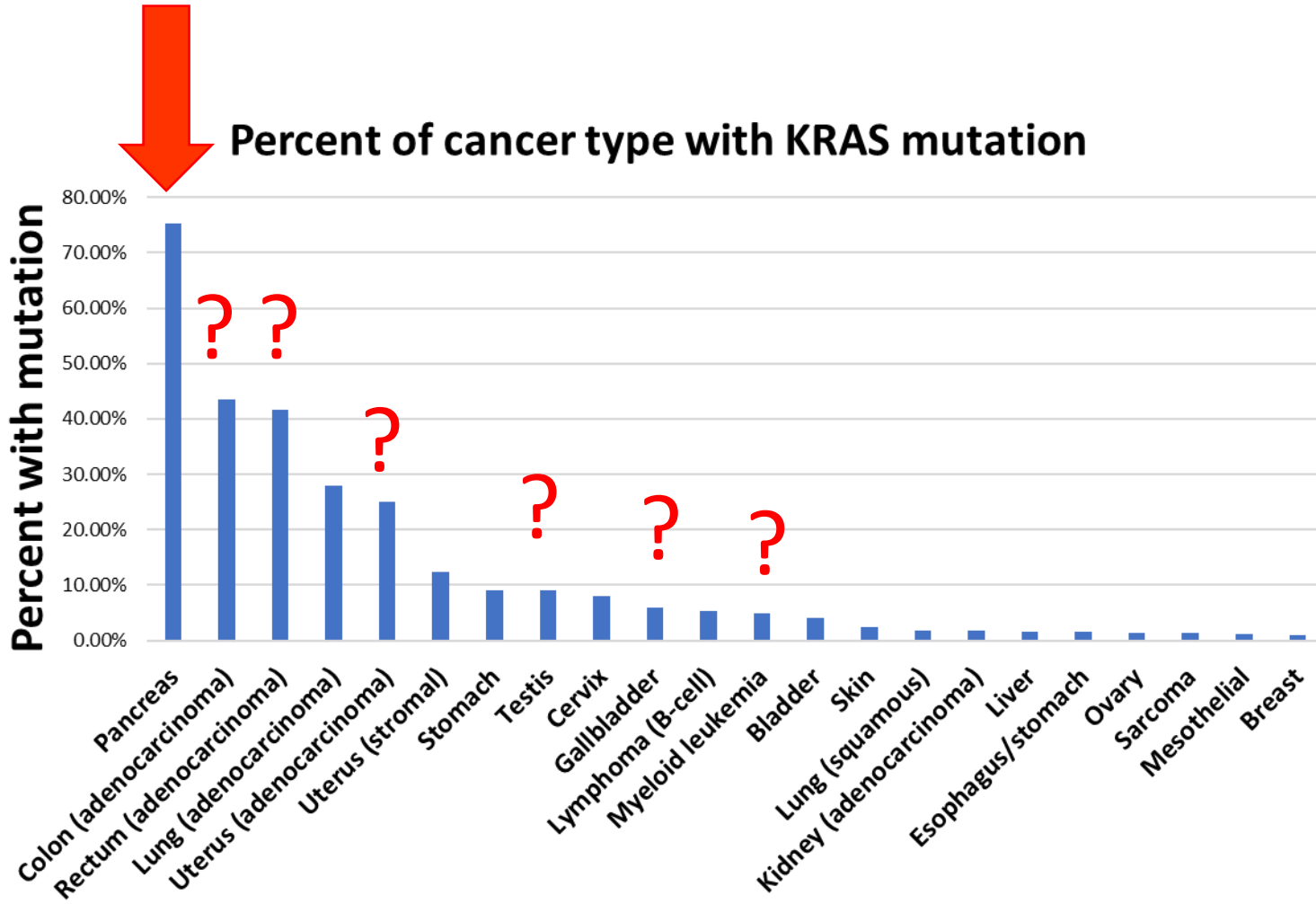
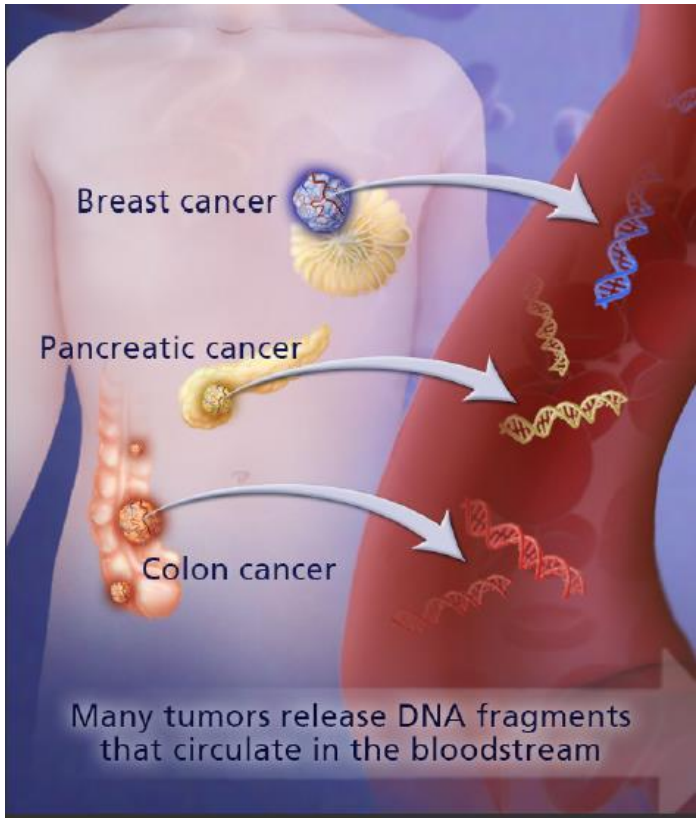


What can be detected



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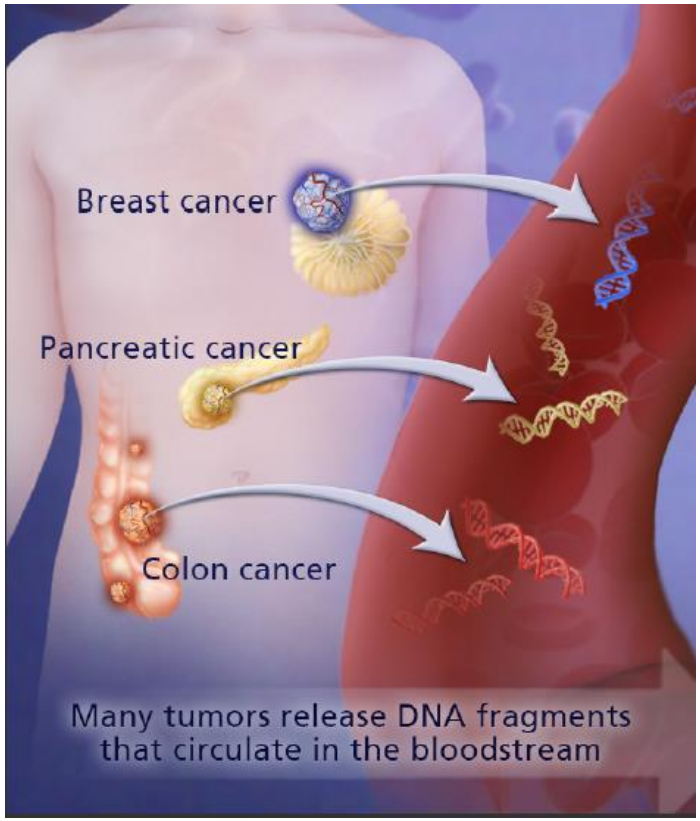

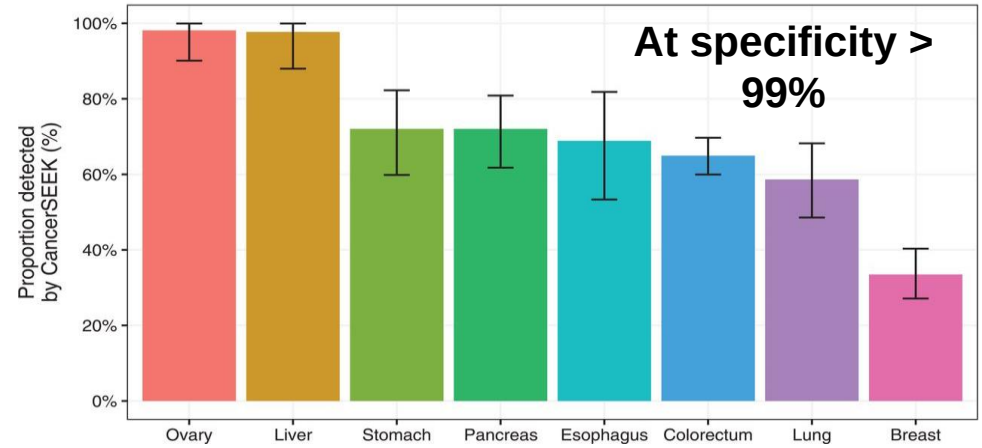

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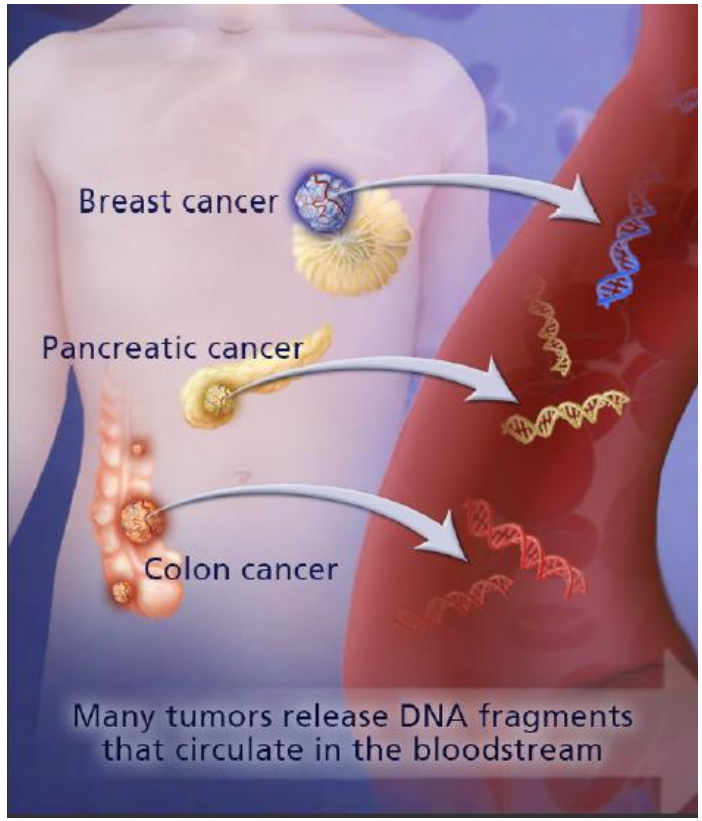
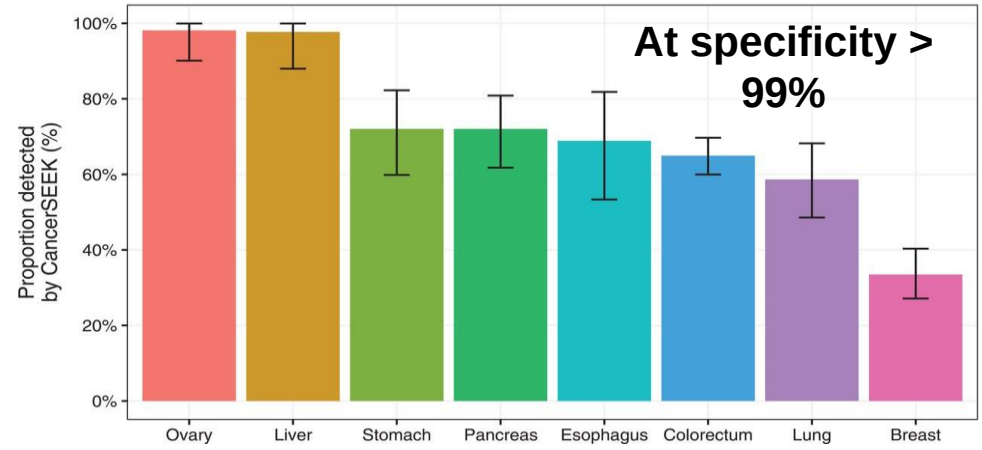
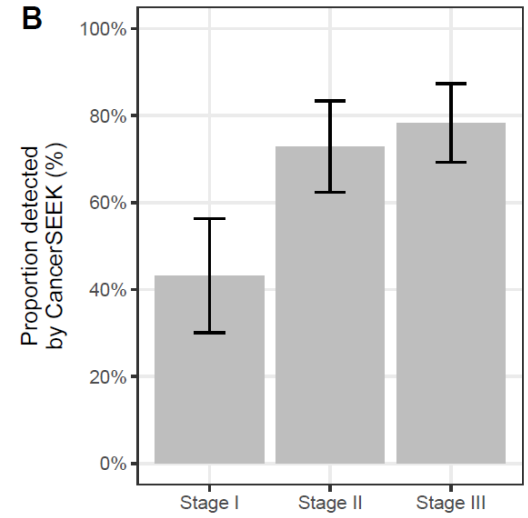




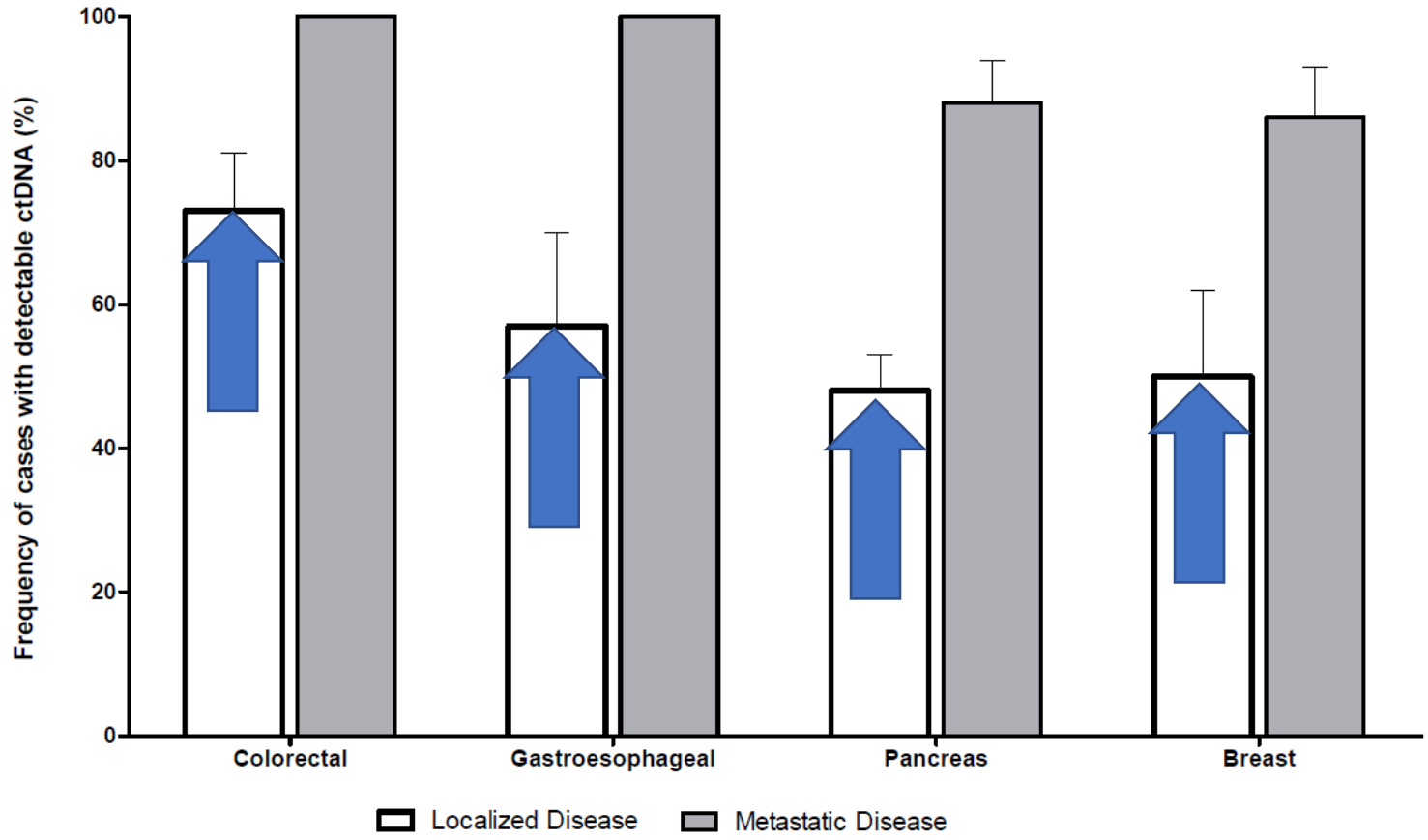


What can NOT be detected

- Biology plays a role
  - No shedding from the tumor
  - Should we detect these tumors?

- Detection of precancerous lesions is not sensitive
  - Unintendedly reduction of overdiagnosis?

Increase Sensitivity



Combination of Markers

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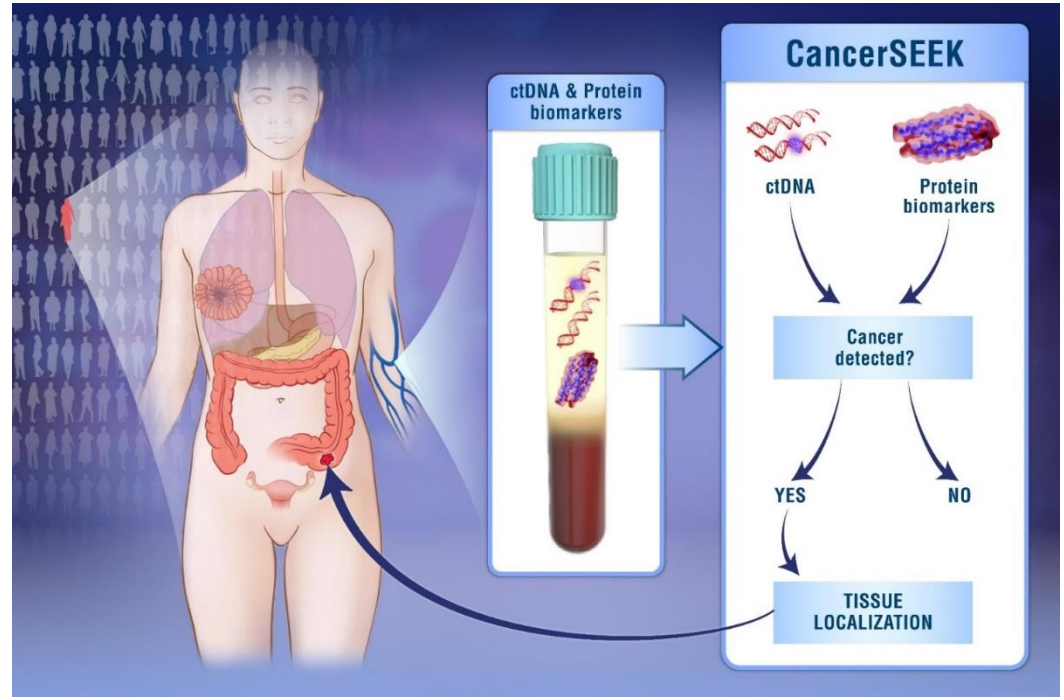


Cohen et al., *Science* , 2018

Challenges to Early Detection

- Social – Society and individuals tend to give priority to reactive rather than proactive solutions.

- Psychological – Communication of a result is important:
  - Positive - Anxiety or even depression upon delivering test results.
  - Negative result - Individuals should not made believe that they are at zero risk.

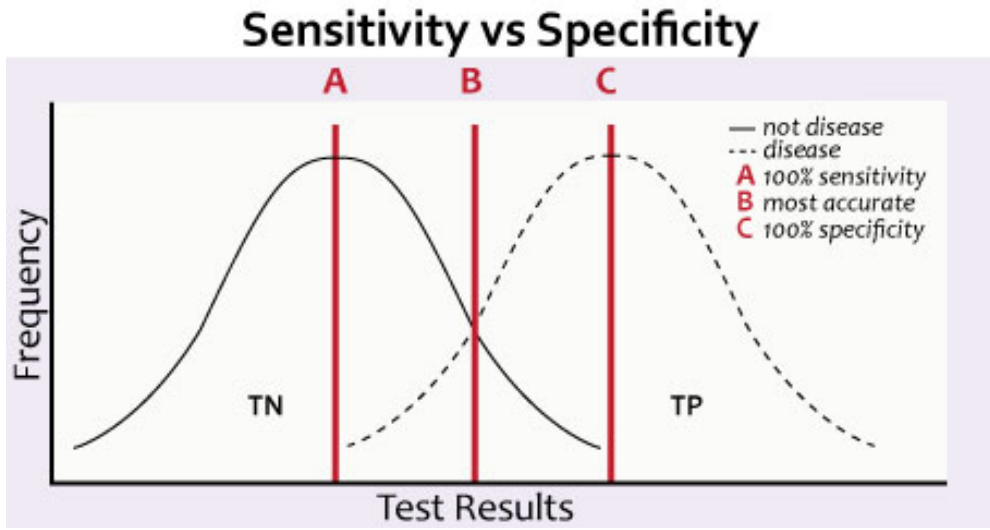
- Technical – Characteristics of the test; Location of the cancer

- Overdiagnosis – leading to Overtreatment and unnecessary follow ups – risk/benefit
- Cancers are missed – individuals that present with advanced disease - risk due to underdiagnosis

- Economical – Needs to be cost effective to administer across the population.

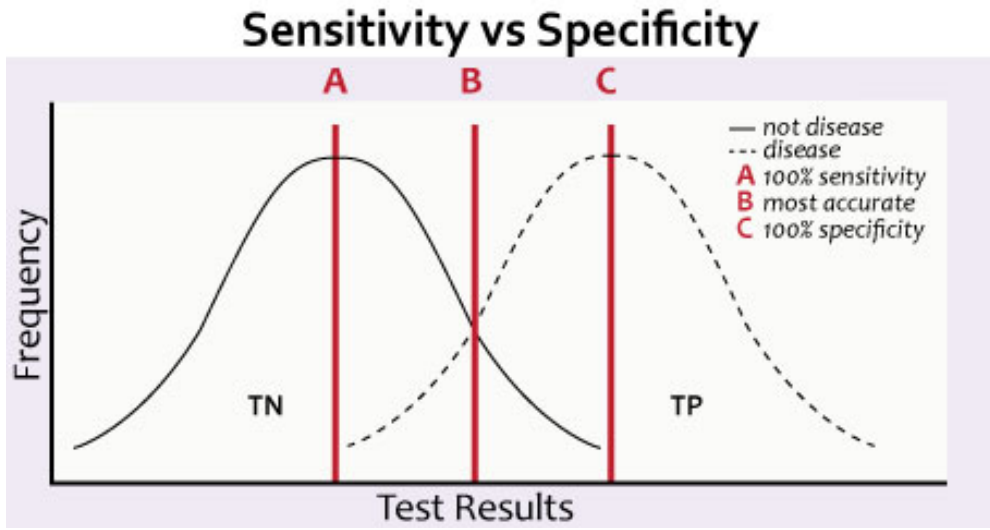
- Practical – Needs to be readily deliverable across the population.

Test Performance



Prevalence will determine Predictive Values

Test Performance

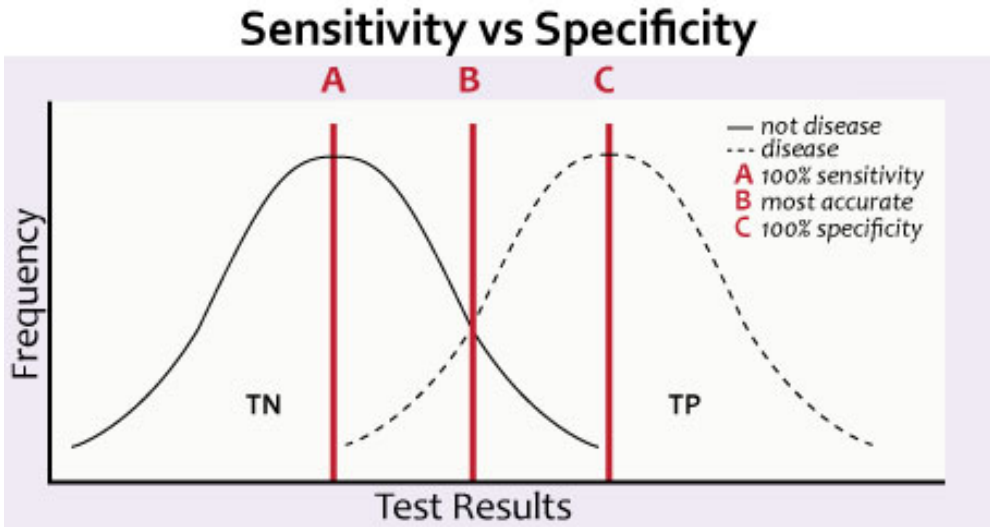


SPECIFICITY

SCREENING

Prevalence will determine Predictive Values

Test Performance

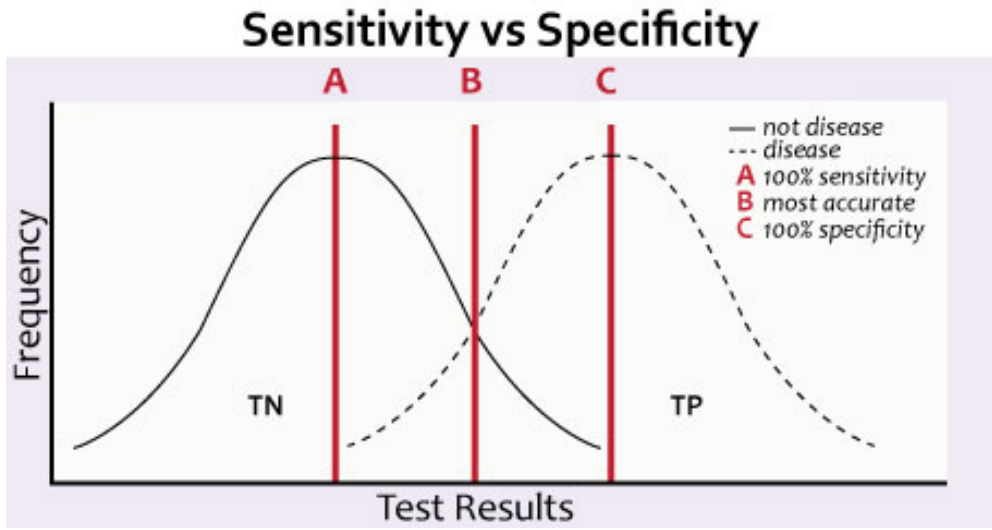


SPECIFICITY → SCREENING

SENSITIVITY → DIAGNOSTIC

Prevalence will determine Predictive Values

Test Performance



SPECIFICITY → SCREENING

High Risk Population

SENSITIVITY → DIAGNOSTIC

Prevalence will determine Predictive Values

Prospective and Interventional

- Goal to identify screen-detected, rather than symptom-detected, cancers in the target population
- Usually smaller in size
- Usually earlier stage

- Observational studies do not report results – harm due to unnecessary invasive procedures following a test result can't be evaluated

DETECT-A
Prospective Interventional Study

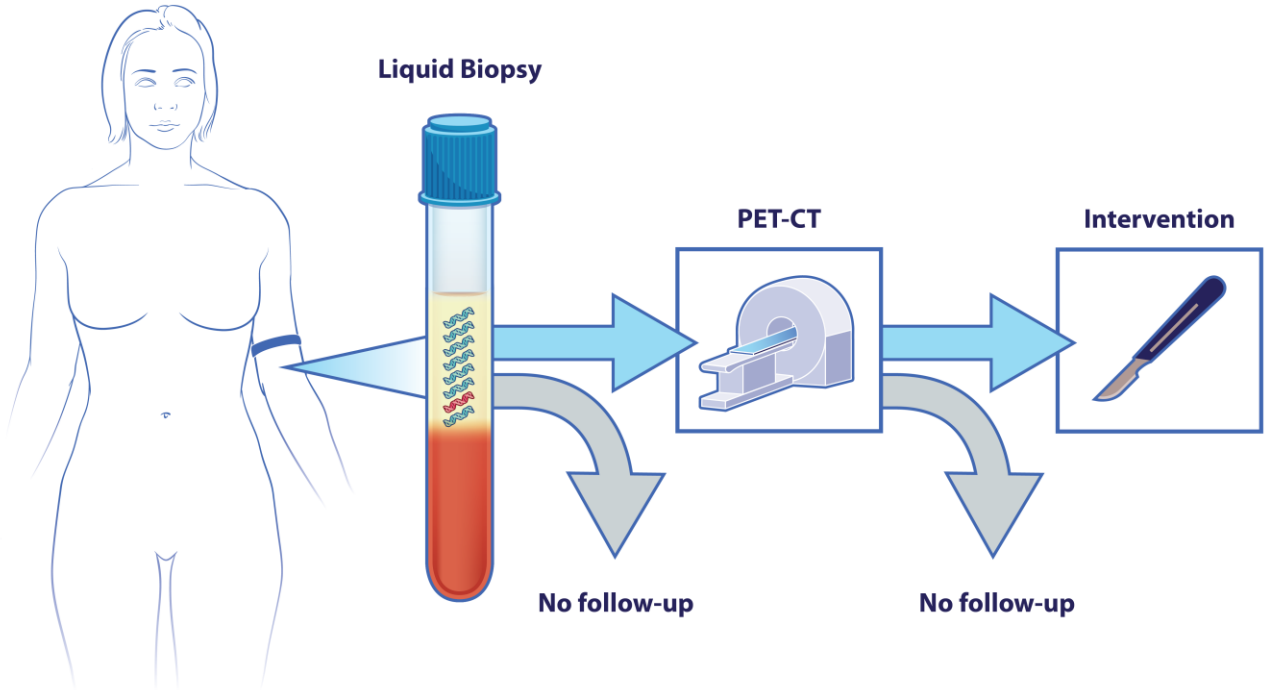
1. Can a multi-cancer blood test prospectively detect cancer in individuals whose cancer was not previously detected by other means?

2. Can such a test be used to intervene in the tumor progression process, leading to therapy with intent to cure?

3. Can such a test be incorporated into routine clinical care and not discourage participants from engaging in SOC screening?

4. Can such a test be performed safely, without incurring a large number of futile, invasive follow-up tests based on the test results?

Where We Are



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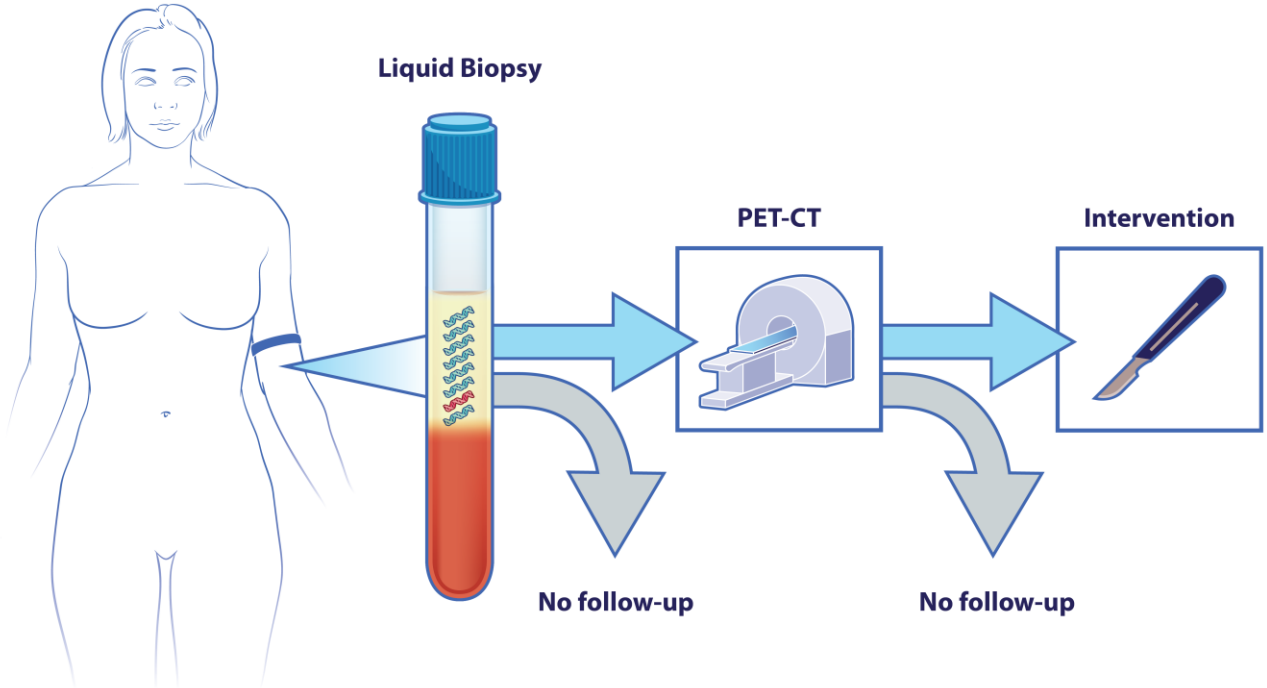
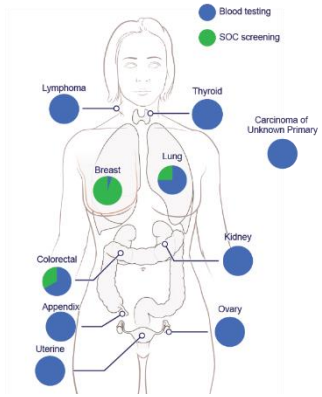


Prospective Detection



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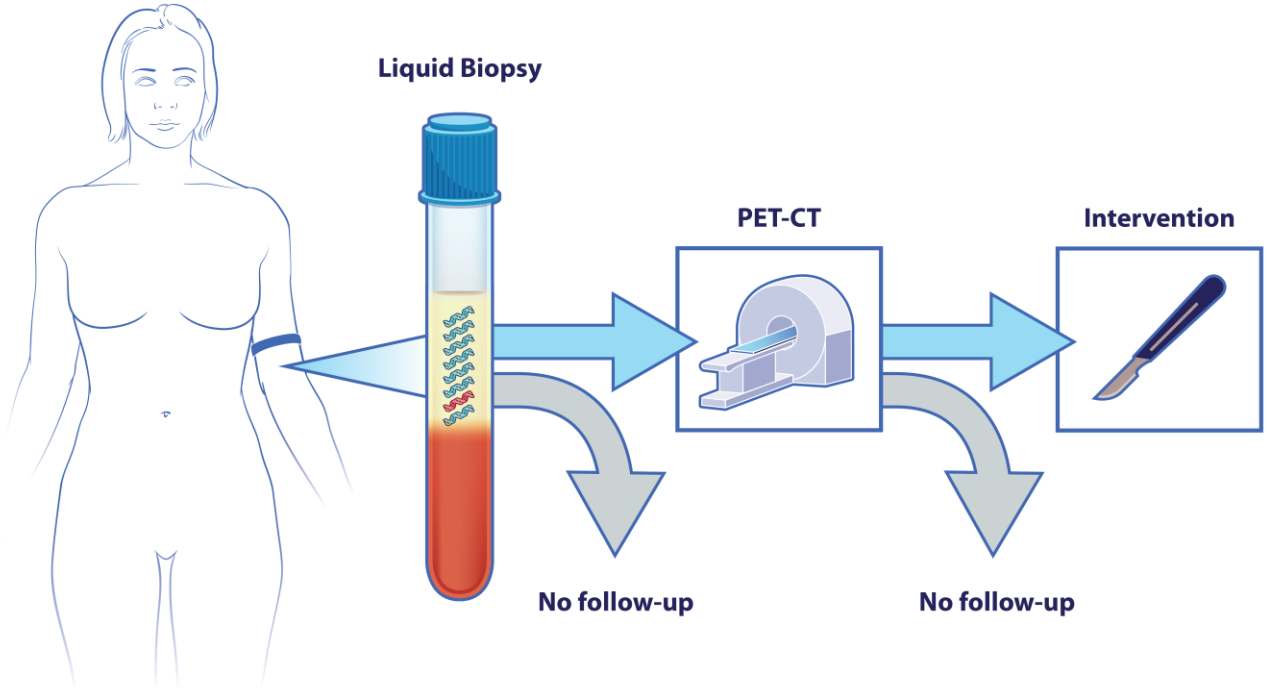

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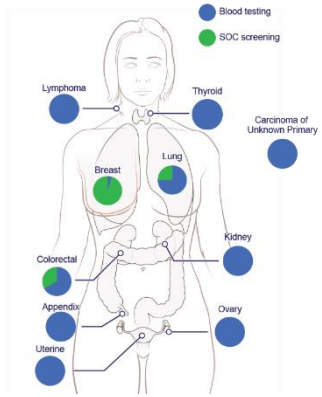
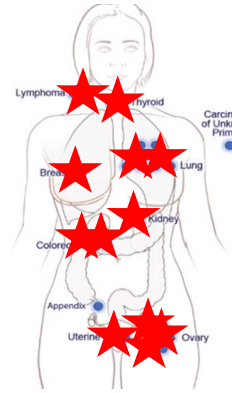
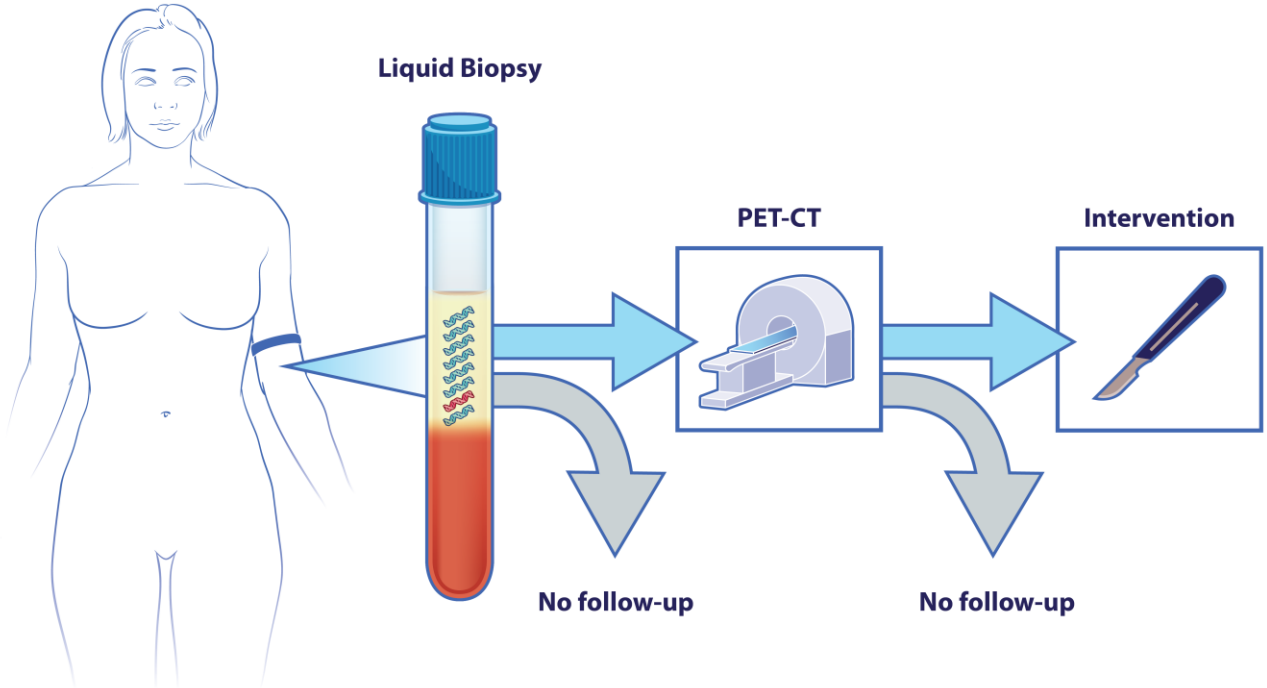


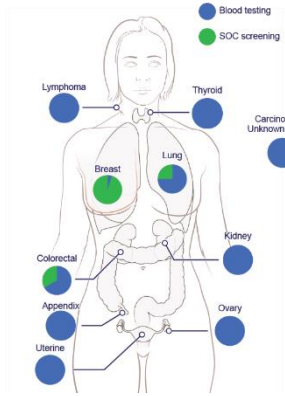


Intervention With intent-to-cure

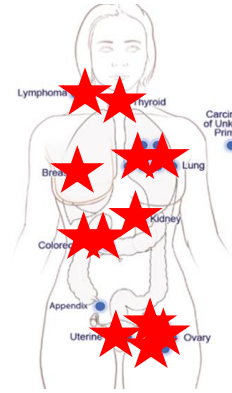
Where We Are



Prospective Detection



Complements SOC



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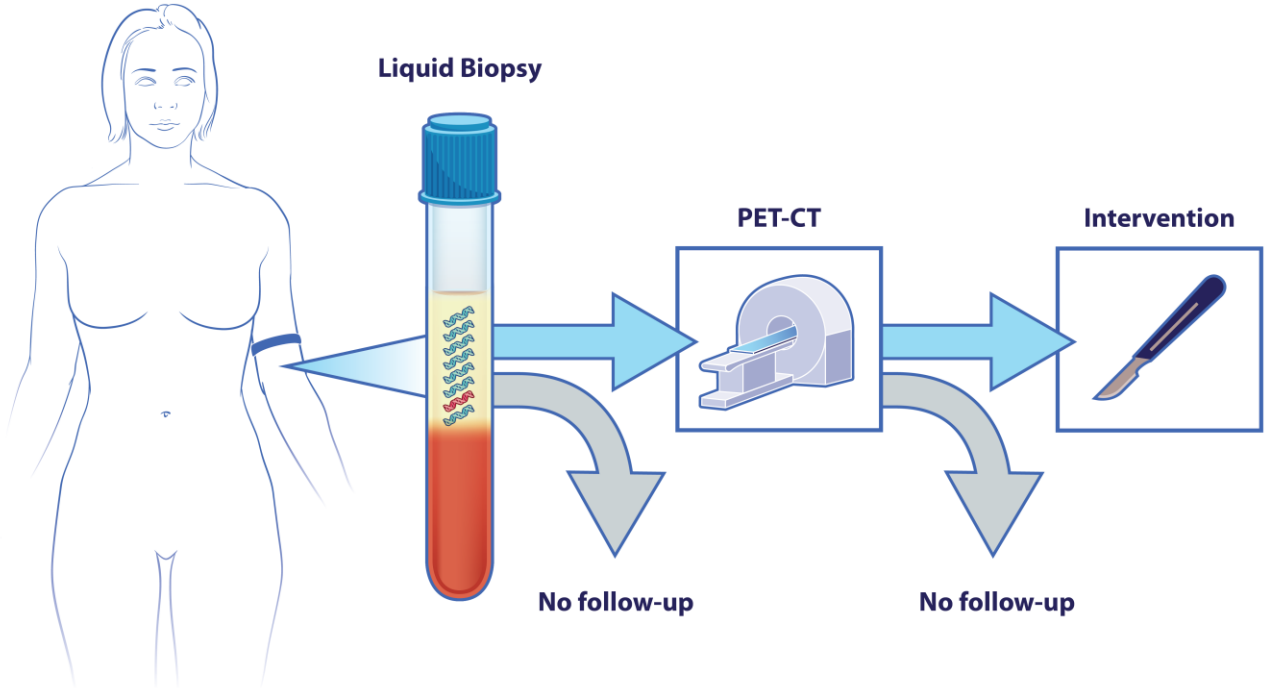

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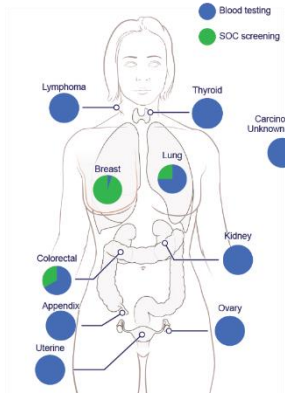

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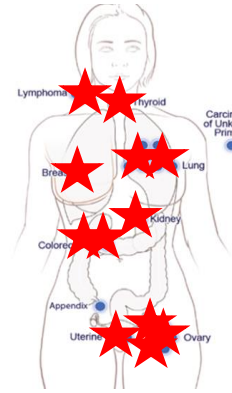

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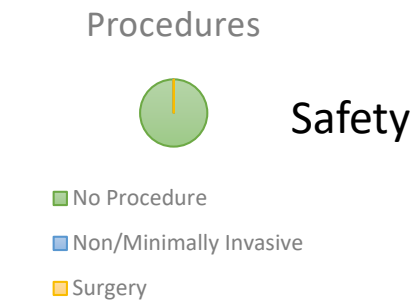


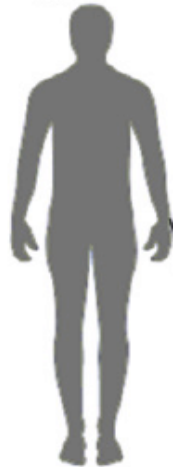
What Next

- **Randomized Prospective Interventional Studies in the target population**

- Establish Clinical Utility
  - Outcomes that can be informative within few years
- Risk-Benefit ratio
- Cost effectiveness

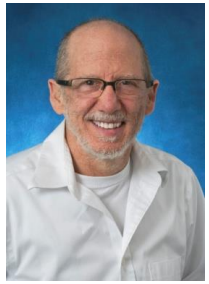
Vision

- Prevent advanced tumors by integrating such tests as part of routine screening and management



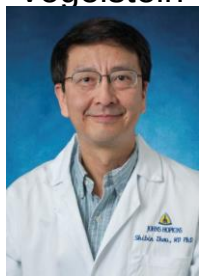
Acknowledgments

LUDWIG CANCER RESEARCH



Bert Vogelstein

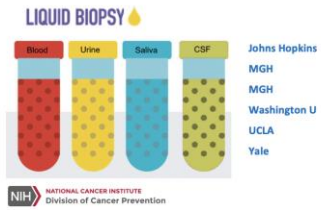
Ken Kinzler



Shibin Zhou

Chetan Bettegowda

NCI/EDRN



10,000 Women in the DETECT Study

JOHNS HOPKINS UNIVERSITY

CURE PANCREATIC CANCER
LUSTGARTEN FOUNDATION

Anne Marie O'Broin Lennon

Cristian Tomasetti

Ralph Hruban

Elliot Fishman

Adam H. Buchanan
David Ledbetter
and the team from

Geisinger

Fred Sanfilippo
and

The Marcus Foundation, Inc.

Thrive.
Earlier Detection

hhmi