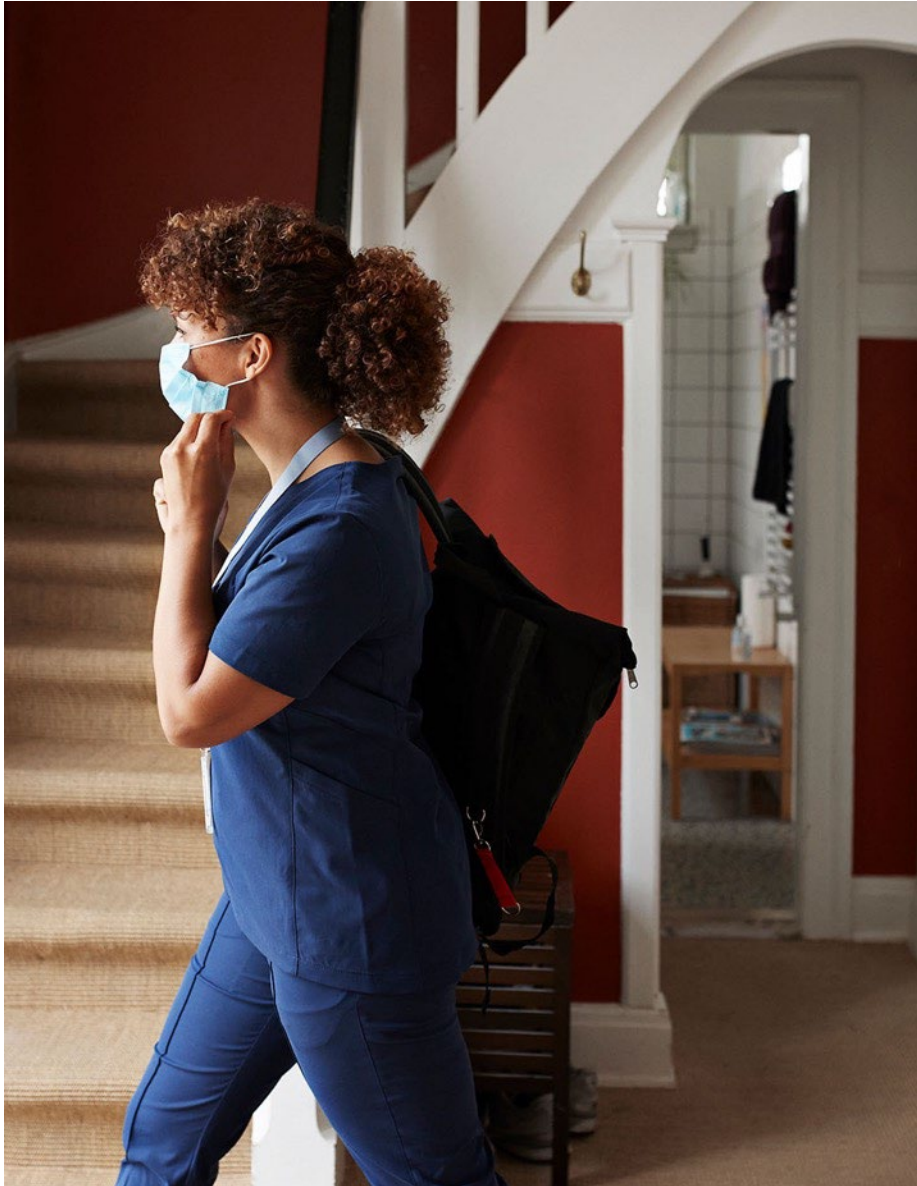


UK NSC MCDs Seminar, 27 February 2025

# Where are we now? A focus on multi-cancer detection tests

Dr Jessica Lloyd, Strategic Evidence Manager,  
Evidence and Implementation Department,  
Cancer Research UK



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in the UK

**02** What are MCDs?

**03** MCDs across the  
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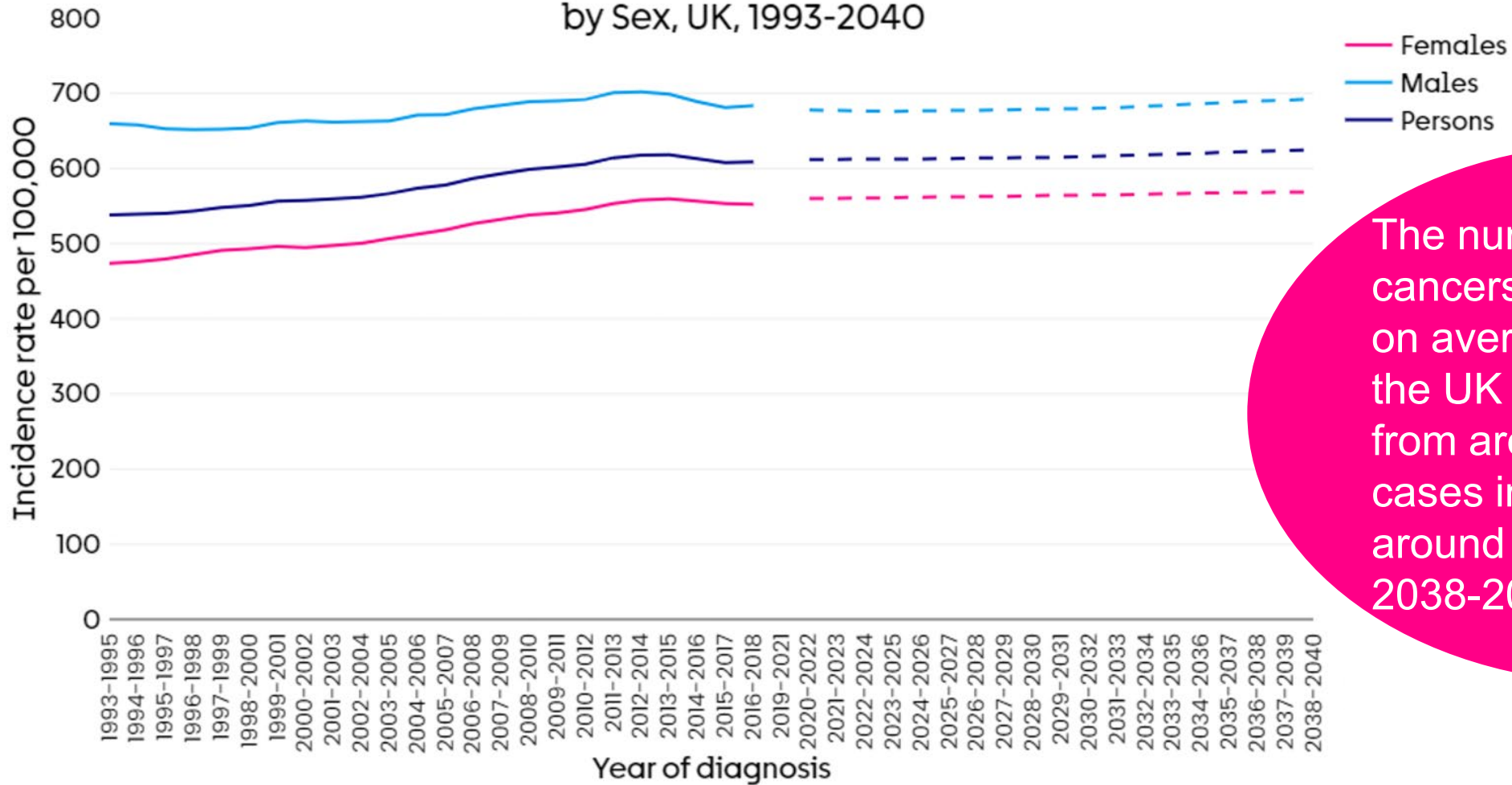
**05** Evidence: published  
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**06** Key  
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# Cancer outcomes in the UK

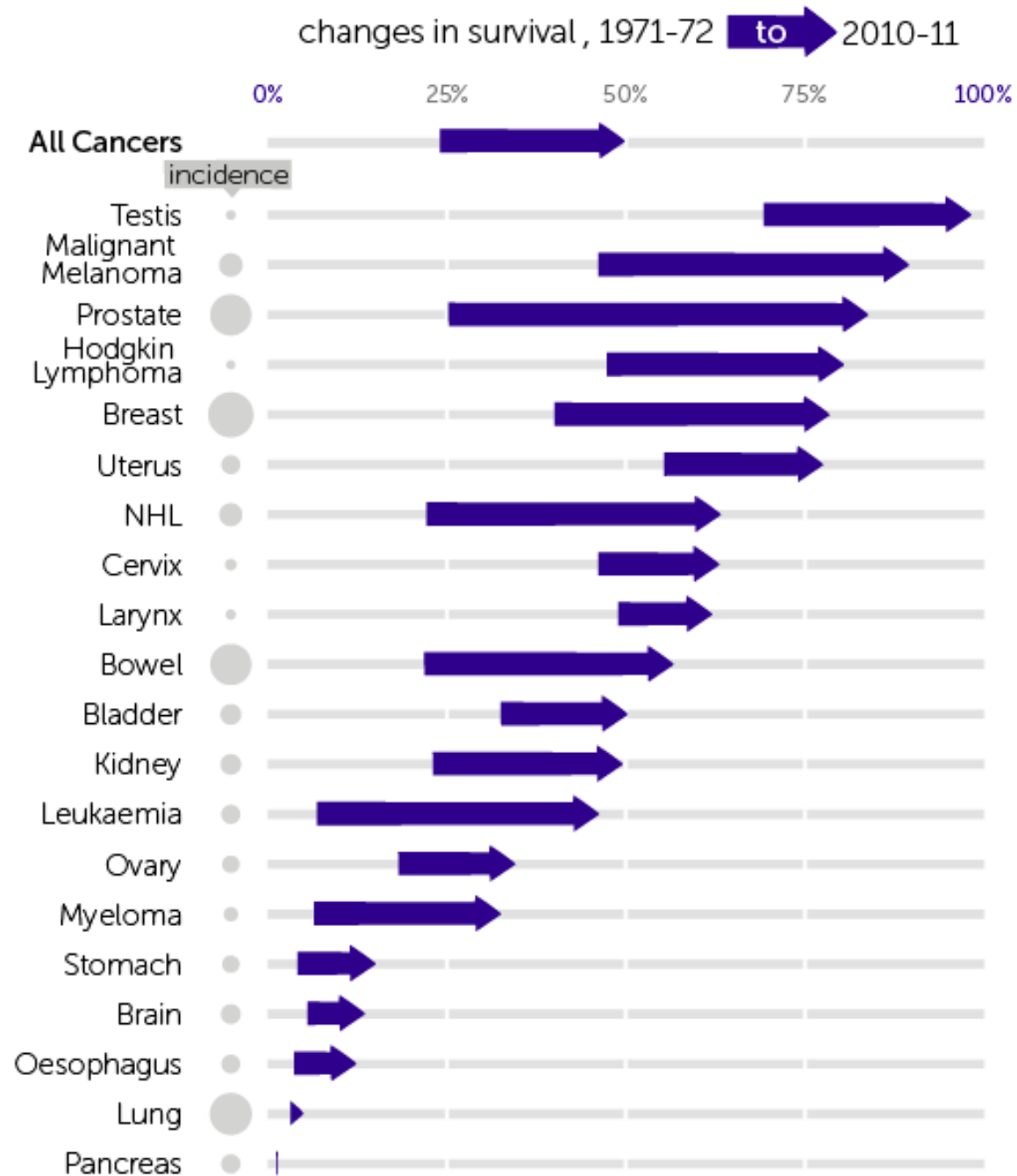
# Cancer incidence is growing...

All Cancers Combined (Excluding NMSC),  
Observed and Projected Age-Standardised Incidence Rates,  
by Sex, UK, 1993-2040



The number of new all cancers combined cases on average each year in the UK is projected to rise from around 420,000 cases in 2023-2025 to around 506,000 cases in 2038-2040 [1].

Net survival increased substantially during the 40-year period 1971–2011, both in England and in Wales [2].



# Colon cancer

5-year survival changes, 1995-1999 to 2010-2014



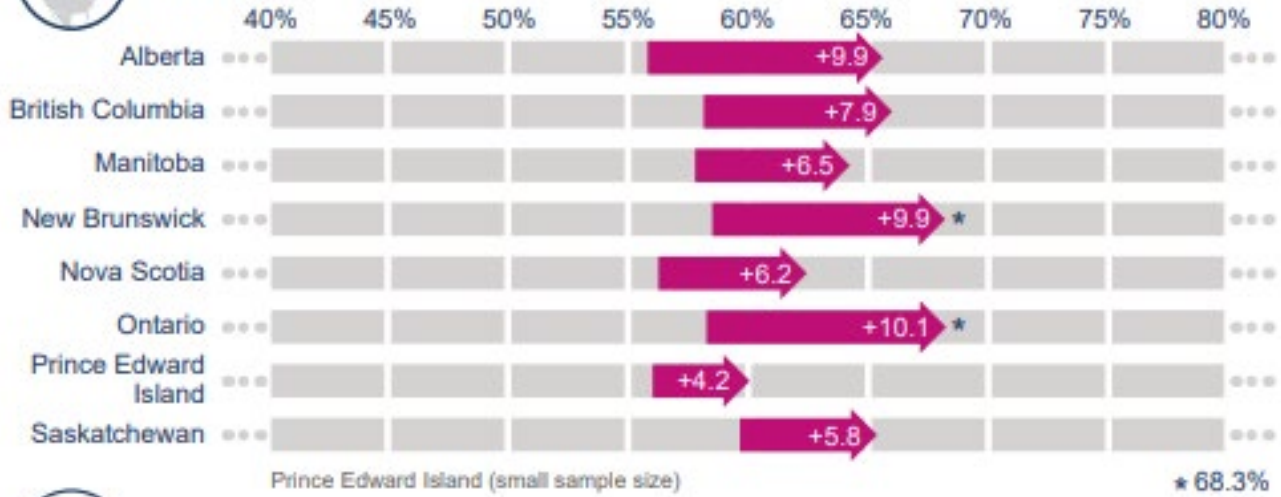
\* = Highest 2010-2014 survival for this country



## Australia



## Canada

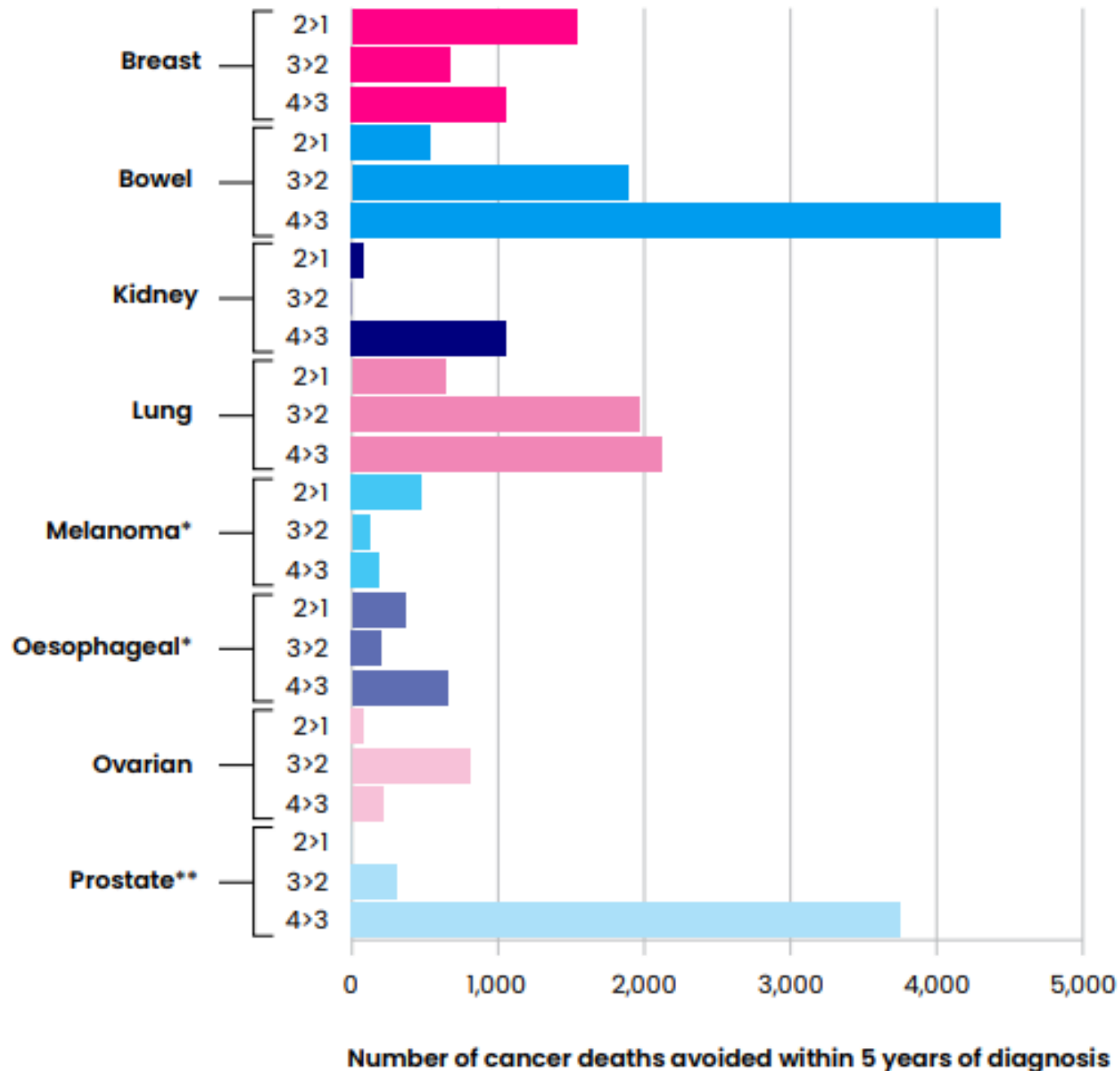


## UK



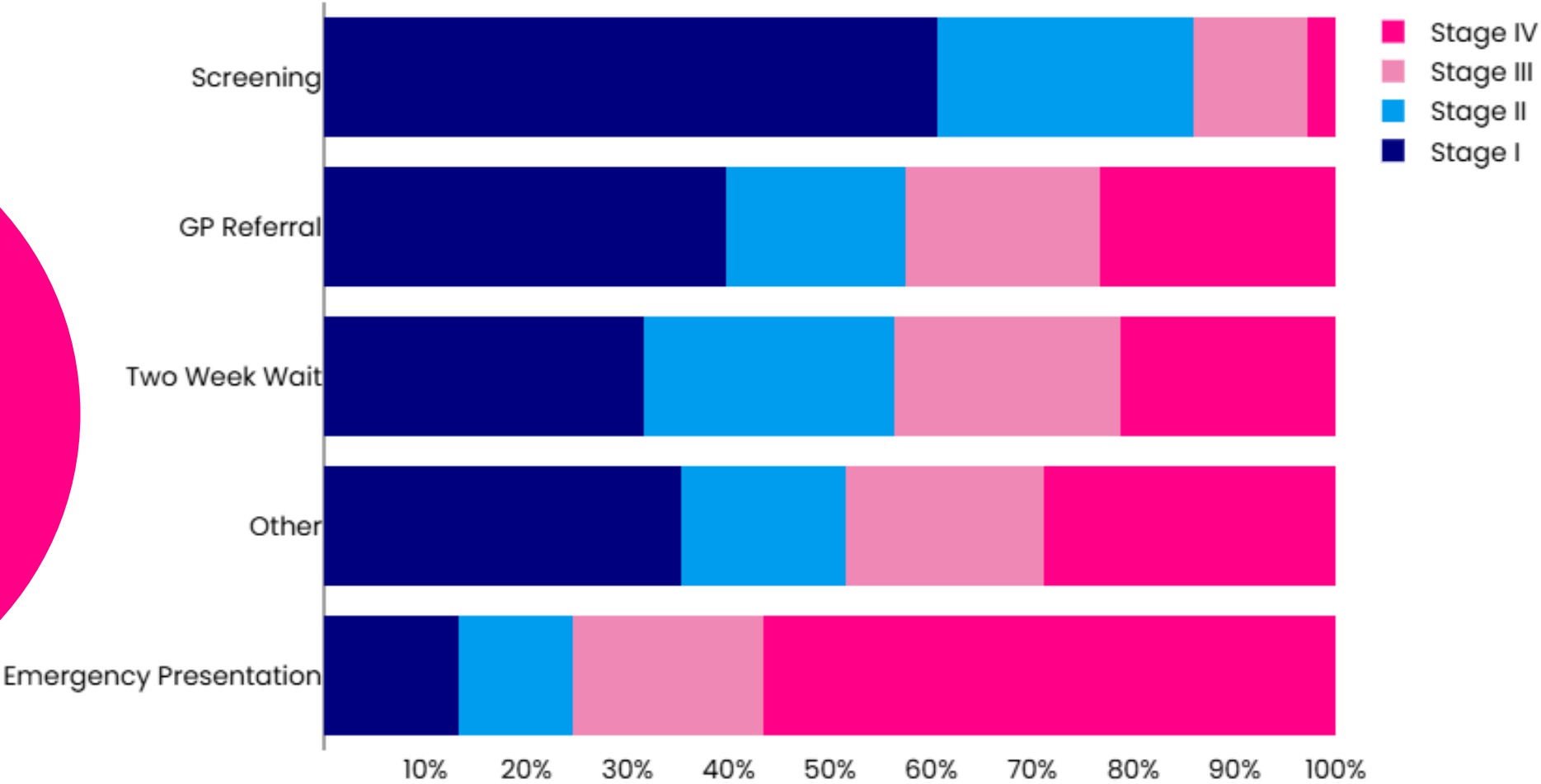
International Cancer Benchmarking Partnership (ICBP) shows that the UK lags behind many comparable countries [3].





We want to save lives through meaningful earlier diagnosis (?)

### Proportion of Cancer Cases by Presentation Route and Known Stage at Diagnosis All Cancers Combined, England, 2020



About 90% of cancers detected through screening are diagnosed at an earlier stage [4]

Proportion of Cases by Known Stage





EARLY DETECTION AND  
DIAGNOSIS OF CANCER

---

# A ROADMAP TO THE FUTURE

“Earlier diagnosis of cancer can be transformative of peoples lives, and we need to continue to undertake the planning and research to achieve it.”

**Professor Chris Whitty [5]**



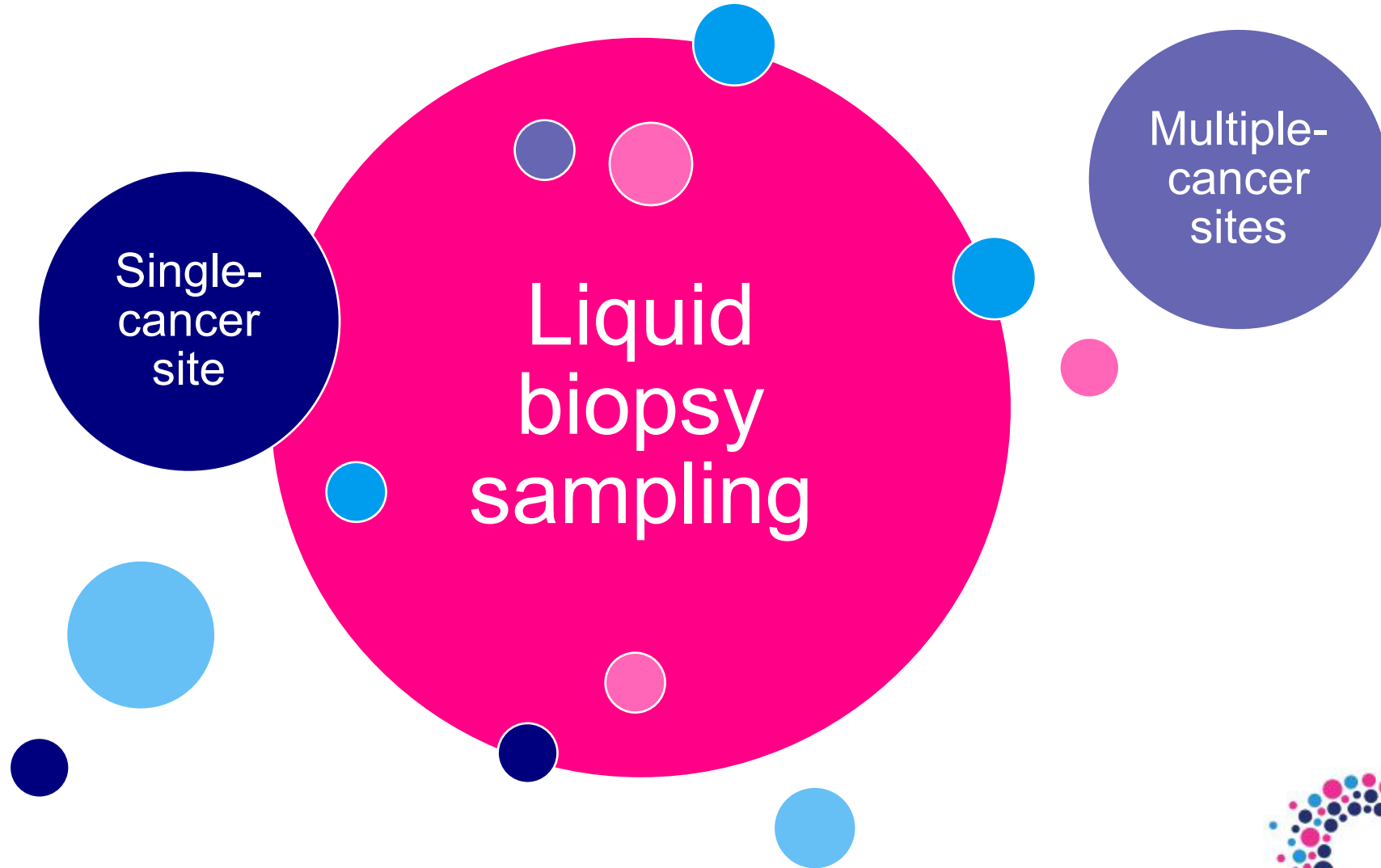
# What are MCDs?

# **Multi-cancer detection (MCD) tests**

Detect the presence of biomarkers that are associated with more than one cancer type in a single sample collected by a non-invasive method

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**MCDs use liquid  
biopsy technology**



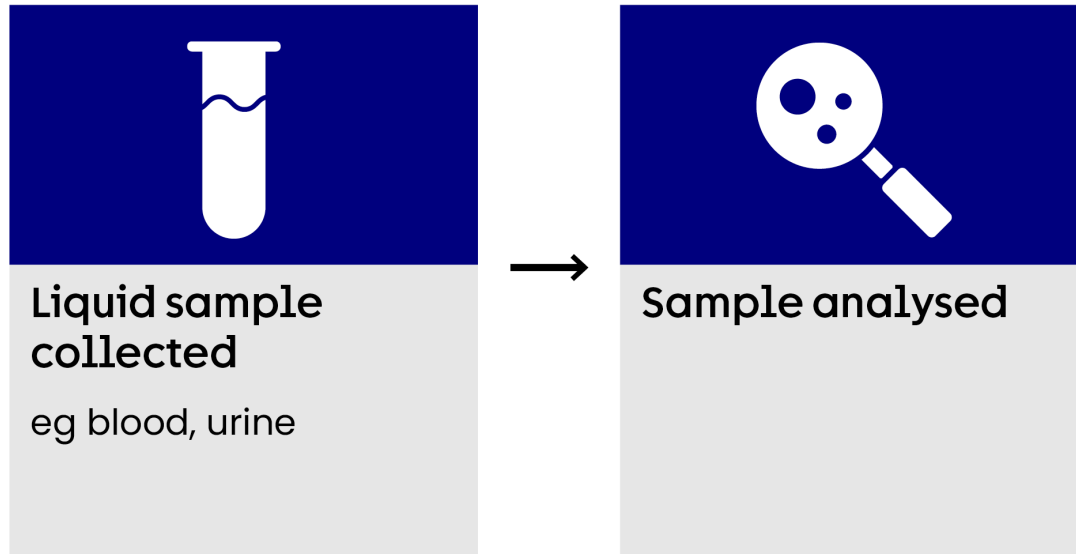
# What is an MCD?



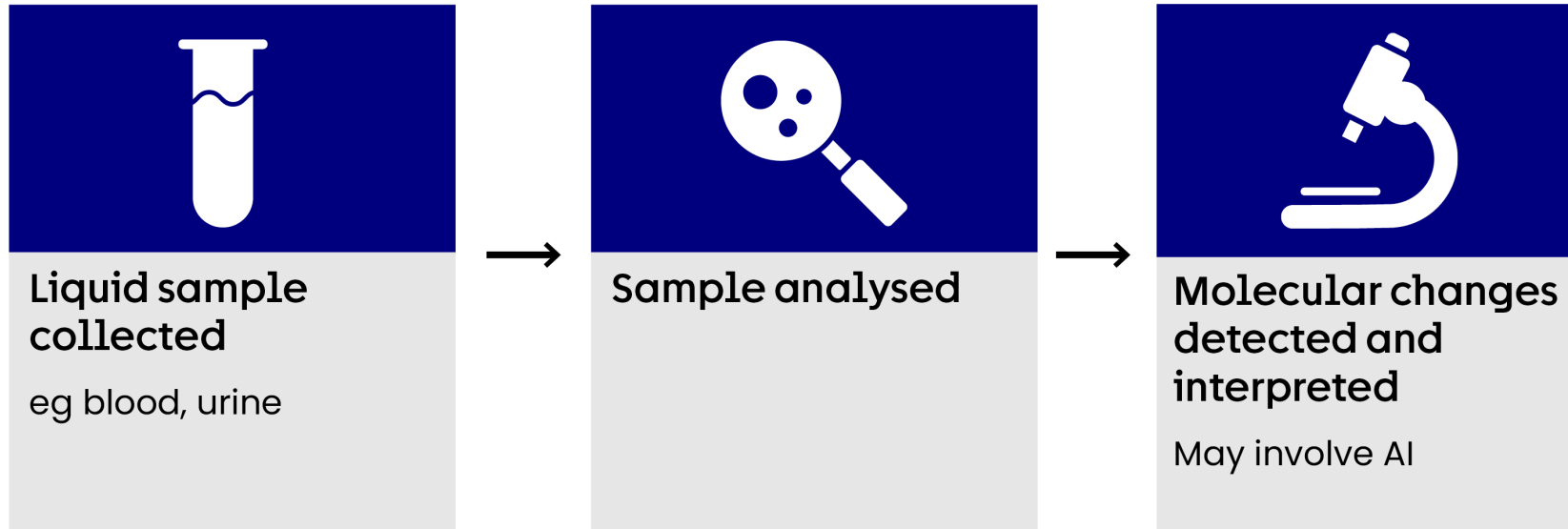
Liquid sample  
collected

eg blood, urine

# What is an MCD?

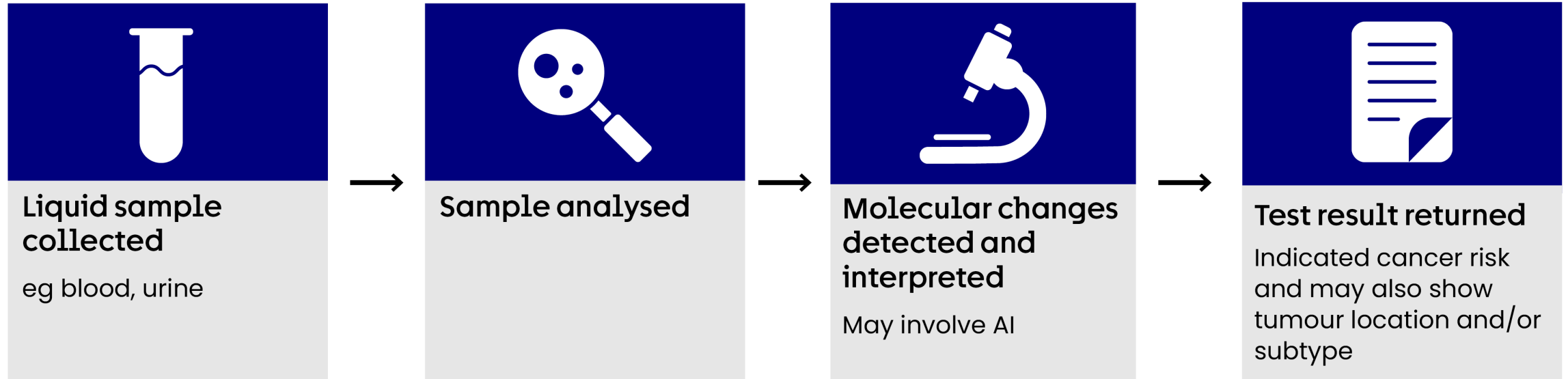


# What is an MCD?





# What is an MCD?



# Possible advantages of MCDs?

**Non-invasive**



Sample collection considered non-invasive

**More acceptable**



Seen as more acceptable by patients

**Widen Access**



Easier to access some other screening tests

**Turn around time**



Receive results faster

**Multiple cancers detected with one test**



# Use of MCDs across the cancer pathway

# Potential for impact across the cancer pathway

**Risk stratification**

**Asymptomatic  
screening**



**More screening  
diagnosis**



**Earlier help-seeking for  
symptoms**



**Earlier referral  
for tests**



**Prompt testing  
and reporting,  
accurate staging**



**Optimal  
treatment  
decisions**

Pre-  
cancerous  
indicator

Development  
of cancer

Symptom

Clinical  
presentation

Investigation  
of related  
symptoms

Referral to  
secondary  
care

Specialist  
visit

Diagnosis/  
referral to  
treatment

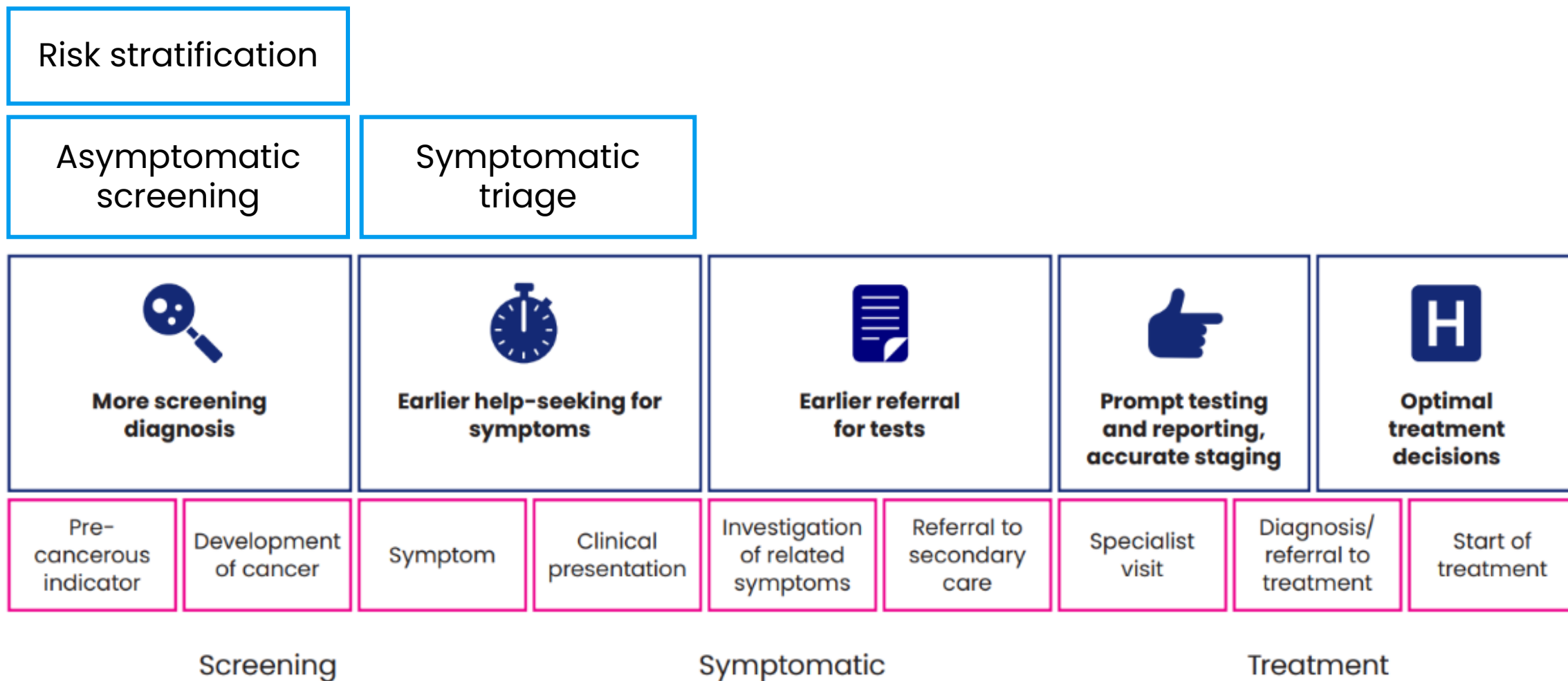
Start of  
treatment

Screening

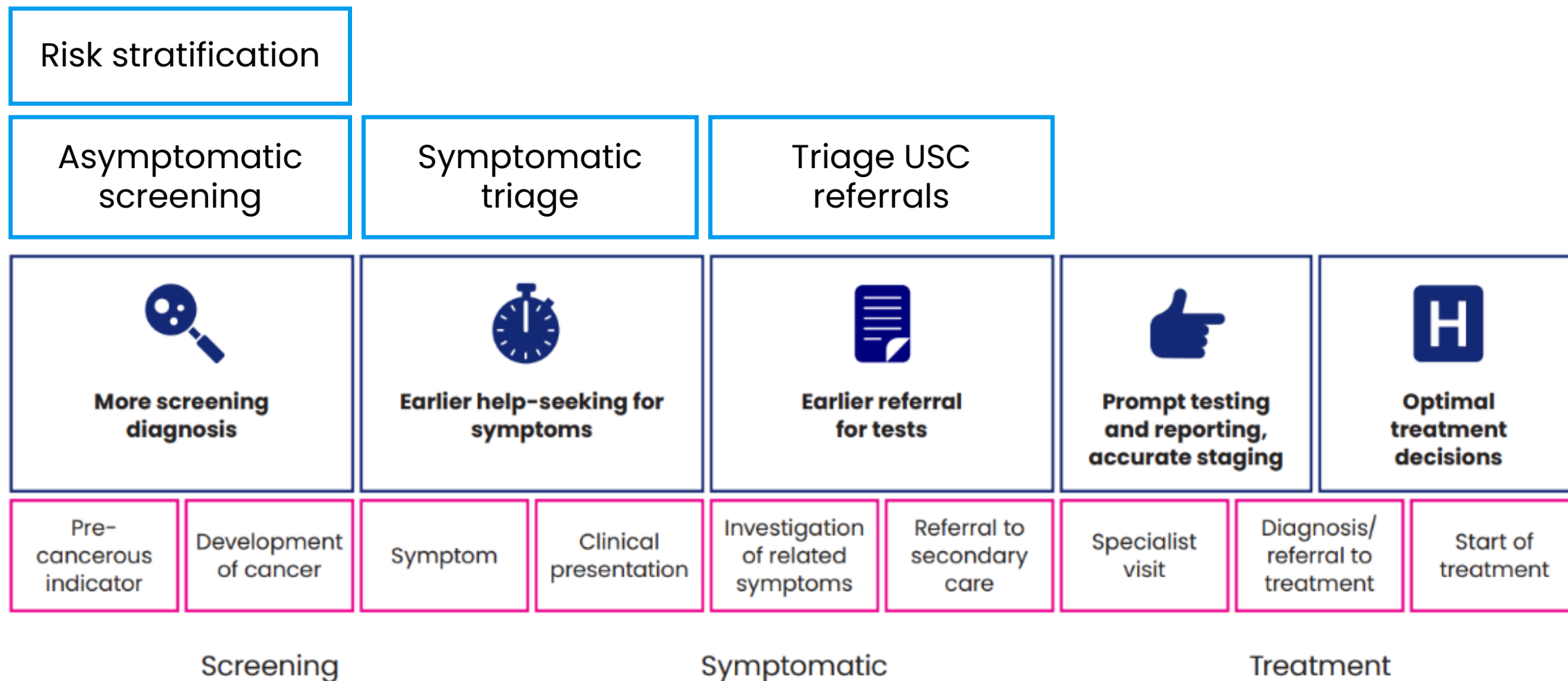
Symptomatic

Treatment

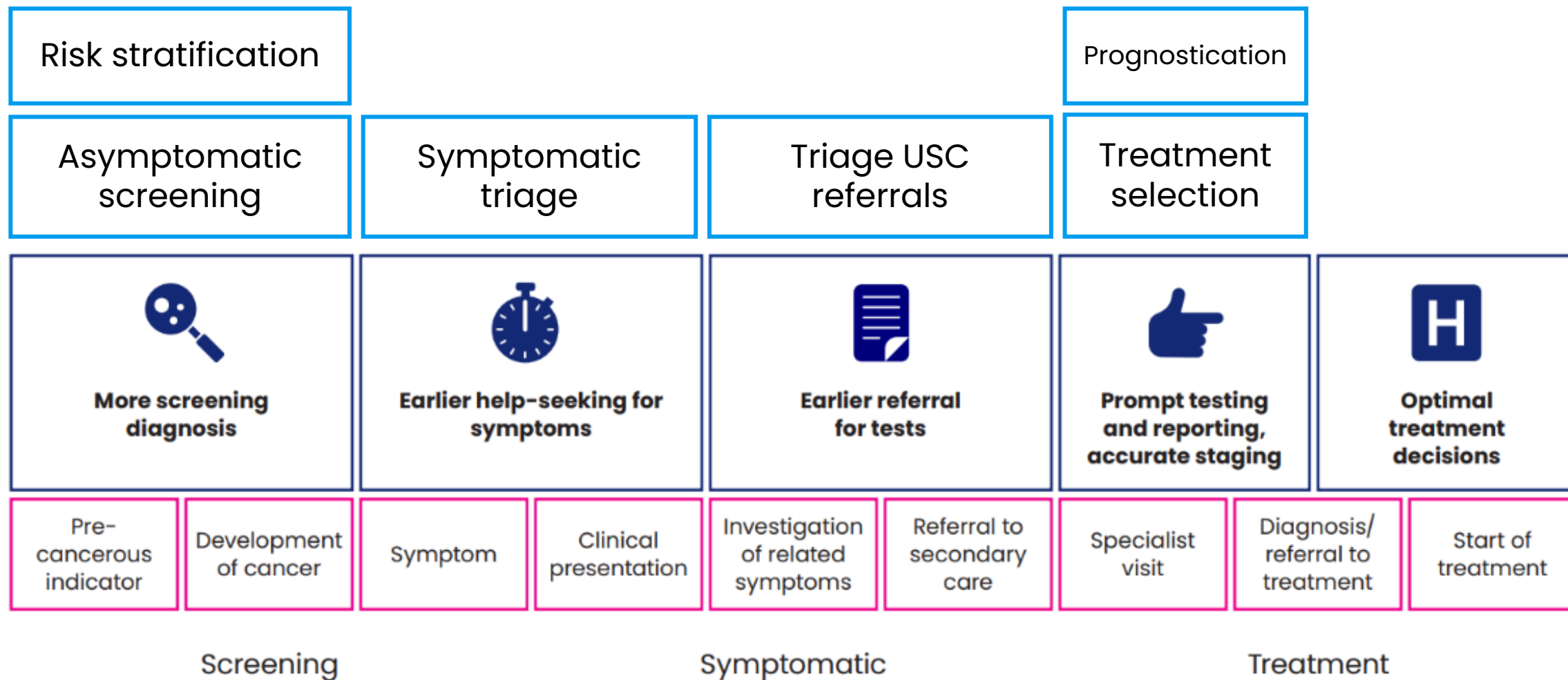
# Potential for impact across the cancer pathway



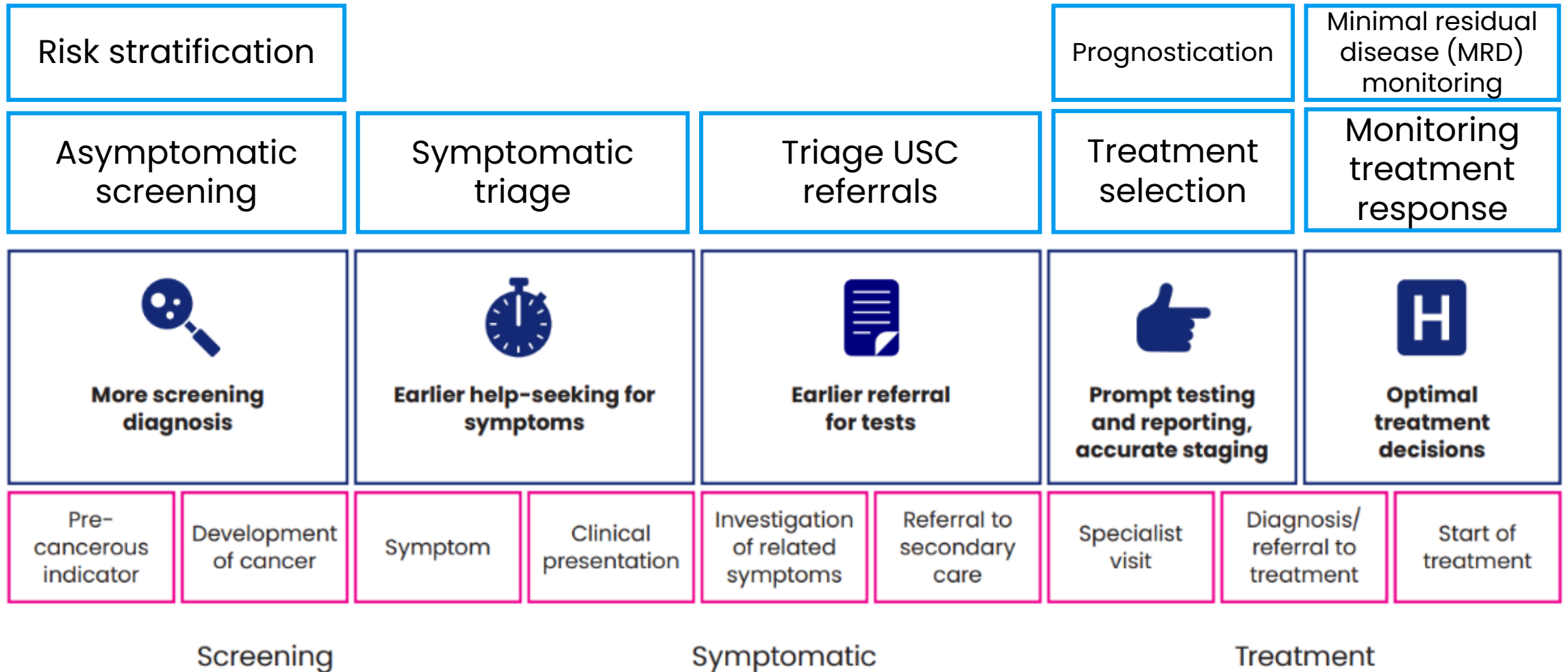
# Potential for impact across the cancer pathway



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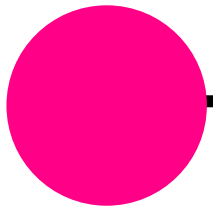


# Potential for impact across the cancer pathway





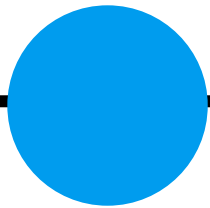
# CRUK Content: MCT Explainer Series



June 2024

One test to detect multiple cancers – where are we now?

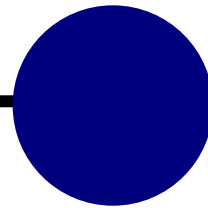
[6]



September 2024

Multi-cancer earlier detection tests: implications for screening programmes

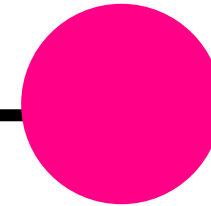
[7]



February 2025

Could multi-cancer tests help GPs spot cancer?

[8]



April 2025 (TBC)

*Liquid biopsies: Towards faster cancer treatment*



---

# Multi-cancer screening

Population-based  
screening  
programme for  
asymptomatic  
people to detect  
multiple-cancers

# How could MCDs be used for cancer screening?

# Multi-cancer earlier detection (MCED) test applications in screening

## Invitation to UK screening

Current site-specific programmes



## Screening test

Current test (eg FIT or mammography)



## Screening result

 Negative



Invited to screening at next interval

 Positive



Referred for diagnostic investigation

This not an exhaustive list of potential uses of MCEDs in screening

# 1. Risk Stratification using MCDs

Risk stratified screening tailors the frequency of screening intervals and the types of screening tests offered to a person's risk of developing cancer.



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Cancer risk can be calculated using different information, including medical history, lifestyle, socioeconomic status, and clinical indicators from other tests.



# 1. Risk Stratification using MCDs

Risk stratified screening tailors the frequency of screening intervals and the types of screening tests offered to a person's risk of developing cancer.

Cancer risk can be calculated using different information, including medical history, lifestyle, socioeconomic status, and clinical indicators from other tests.

Results of MCD analysis could potentially contribute to risk assessment.



# Multi-cancer earlier detection (MCED) test applications in screening

Invitation to UK screening 

Current site-specific programmes



Screening test 

Current test (eg FIT or mammography)



 MCED supports current test

2



Screening result 

 Negative



Invited to screening at next interval

 Positive



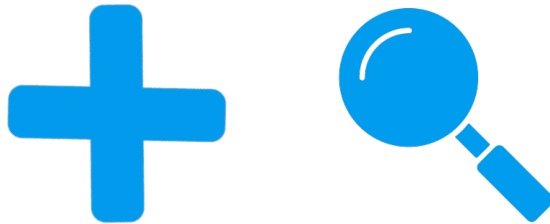
Referred for diagnostic investigation

This not an exhaustive list of potential uses of MCEDs in screening



## 2. The MCD supports current screening tests

MCEDs could be used as an additional screening test within the current programmes.



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MCEDs could be used as an additional screening test within the current programmes.

By combining MCEDs with the existing test, it may be possible to give better information at the time of screening.

For example, mammography could potentially be improved if the MCED could support differentiate between sub-types of breast cancer.



# Multi-cancer earlier detection (MCED) test applications in screening

Invitation to UK screening 

Current site-specific programmes



Screening test 

Current test (eg FIT or mammography)



Screening result 

 Negative



Invited to screening at next interval

 **MCED replaces current test**



3

 Positive



Referred for diagnostic investigation

This not an exhaustive list of potential uses of MCEDs in screening

### 3. MCD replaces current screening test

Many MCDs are based on a blood draw.



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They have a potential advantage (if they perform well), as in comparison to certain tests, they may be cheaper, easier to administer and more accessible to patients.



### 3. MCD replaces current screening test

Many MCDs are based on a blood draw.

They have a potential advantage (if they perform well), as in comparison to certain tests, they may be cheaper, easier to administer and more accessible to patients.

That may also make them more acceptable to the public and increase uptake in cancer screening invitations.



# Multi-cancer earlier detection (MCED) test applications in screening



This not an exhaustive list of potential uses of MCEDs in screening



## 4. Multi-cancer screening programme with MCD

Screening for individual cancers means that many people require multiple appointments and tests for cancer screening.



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Screening for individual cancers means that many people require multiple appointments and tests for cancer screening.

MCEDs have the potential to be used to more efficiently screen for lots of different cancers at the same time

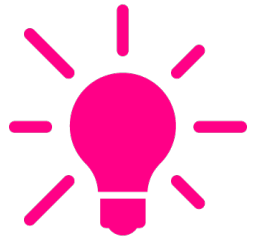


## 4. Multi-cancer screening programme with MCD

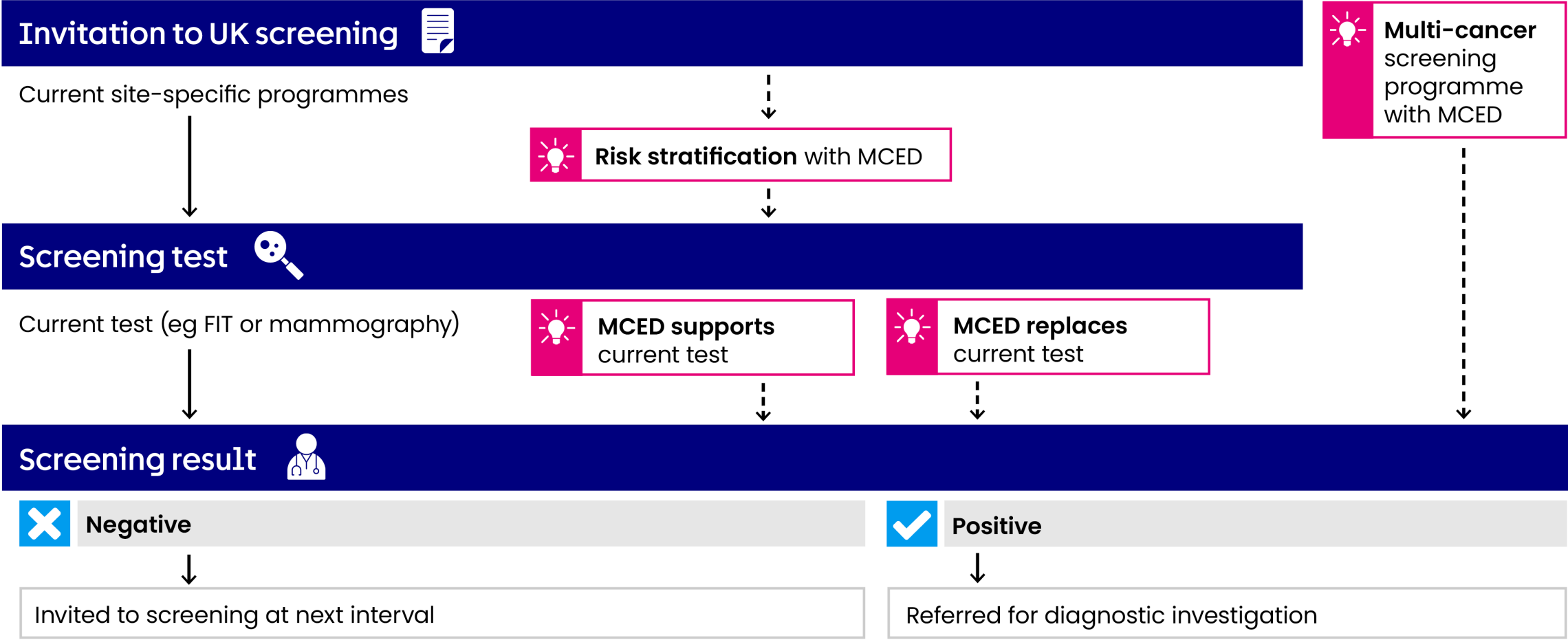
Screening for individual cancers means that many people require multiple appointments and tests for cancer screening.

MCEDs have the potential to be used to more efficiently screen for lots of different cancers at the same time

Opportunity to screen for cancers not currently offered, such as rarer cancers.



# Multi-cancer earlier detection (MCED) test applications in screening

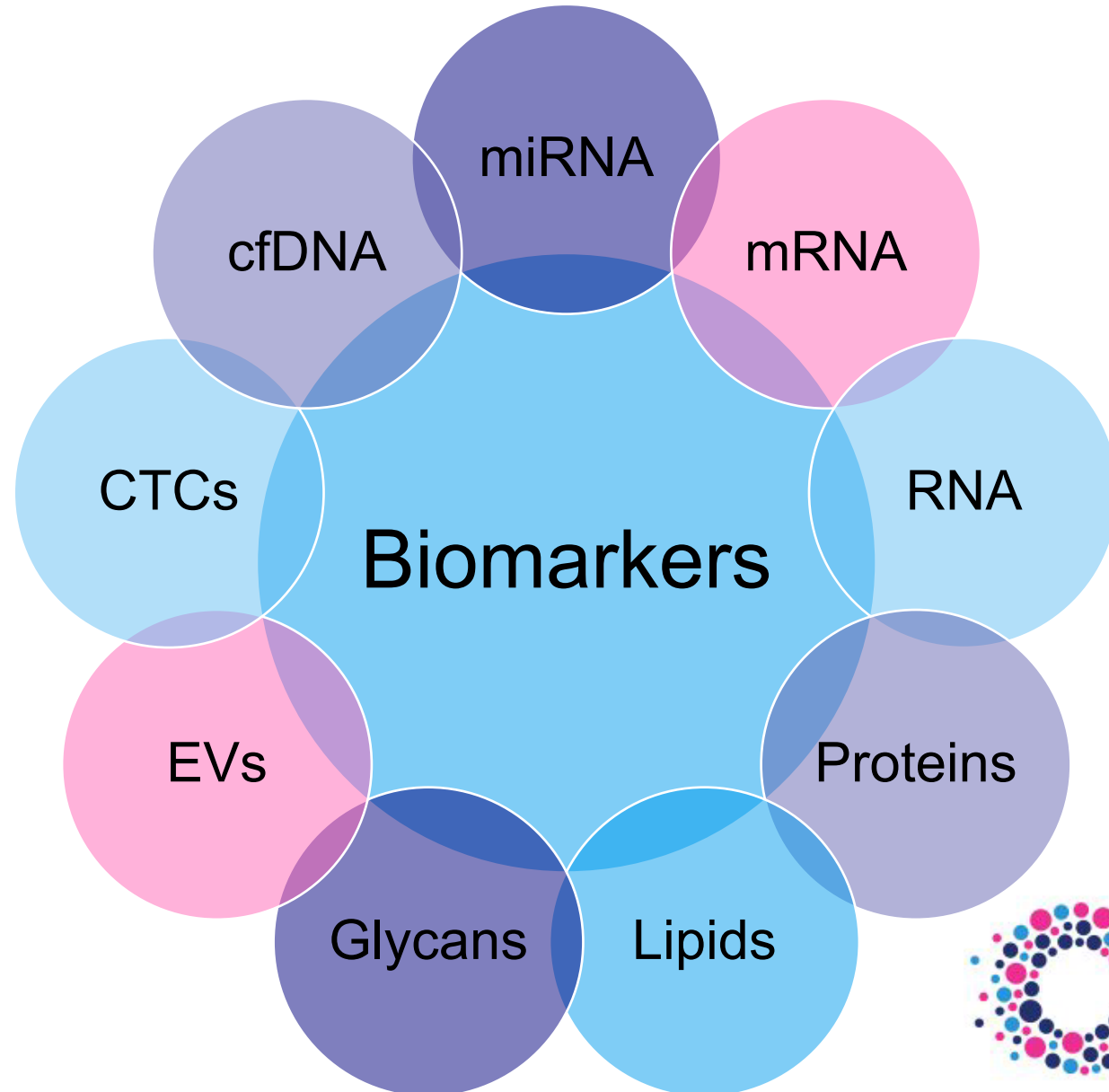


This not an exhaustive list of potential uses of MCEDs in screening

# Evidence: published & emerging

# Many different tests in development

Differ by the cancer sites detected, and the biomarkers analysed.



# What are the evidence requirements?

## Analytical Validity

Measure of how well a test can detect the biomarker in a sample.



**Precision:**  
The test provides a high degree of specificity.



**Accuracy:**  
The test measures or detects what it's intended to.



**Reliability:**  
The test regularly produces the same results.

# What are the evidence requirements?

## Analytical Validity

Measure of how well a test can detect the biomarker in a sample.

Most MCDs have evidence of analytical validity in the form of proof of concept or preliminary retrospective studies.





# What evidence does the test need to show?

## Analytical Validity

Measure of how well a test can detect the biomarker in a sample.

## Clinical Validity

Measure of how well a test can predict a clinical outcome.



### **Sensitivity and specificity:**

How well a test identifies people with a specific condition.



### **Positive and negative prediction value:**

How well a test predicts the presence or absence of a condition.

# What are the evidence requirements?

## Analytical Validity

Measure of how well a test can detect the biomarker in a sample.

## Clinical Validity

Measure of how well a test can predict a clinical outcome.

Some have clinical validity evidence from retrospective or prospective studies



# What evidence does the test need to show?

## Analytical Validity

Measure of how well a test can detect the biomarker in a sample.

## Clinical Validity

Measure of how well a test can predict a clinical outcome.

## Clinical Utility

Measure of whether a test can be implemented and improves patient outcomes.

Assessed by:

- Clinical outcomes
- Cost-effectiveness
- Data richness
- Practical concerns
- Ethical and social implications

# What are the evidence requirements?

## Analytical Validity

Measure of how well a test can detect the biomarker in a sample.

## Clinical Validity

Measure of how well a test can predict a clinical outcome.

## Clinical Utility

Measure of whether a test can be implemented and improves patient outcomes.



# Preferred MCD characteristics?



## High Specificity

To avoid high burden and cost of diagnostic follow-ups caused by false positives.



## Sensitivity

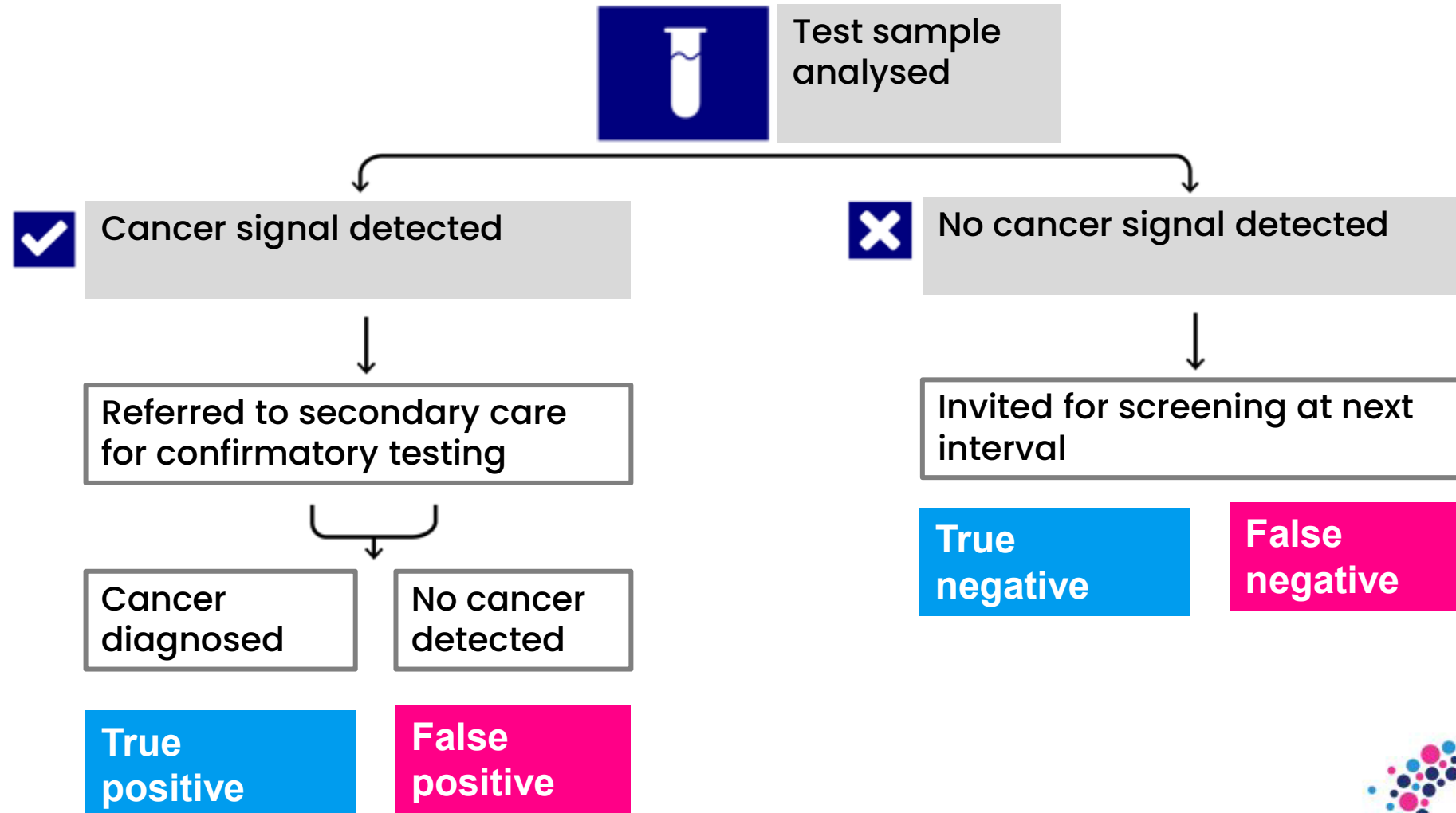
To detect early-stage disease



## Accuracy for CSO

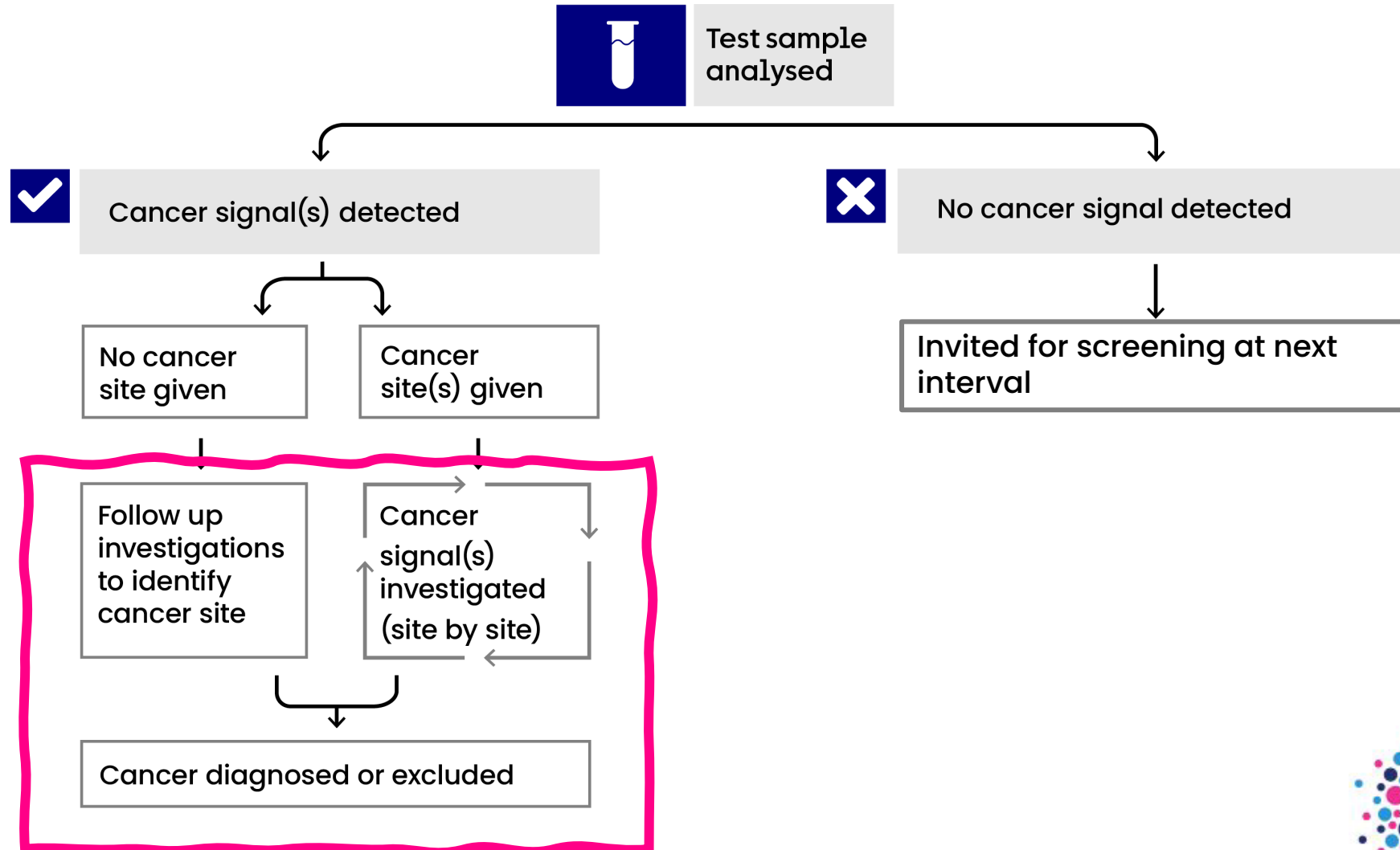
So investigations can be targeted to find the cancer quickly.

# Conventional screening test outcomes



# Multi-cancer test outcomes

Multiple investigations are required to resolve outcome



# MCT Trials

## In the NHS:

- NHS-Galleri Trial
  - Prospective RCT of 140,000 people healthy people [9].
  - The trial aims to demonstrate a statistically significant stage shift and will also look at longer term endpoints, i.e., mortality. Interim results received 2024 with further results to follow in 2026.
- SYMPLIFY
  - Observational retrospective sample analysis of people aged 40+ who have been referred with an urgent suspicion of cancer.
  - Demonstrate sufficient performance to proceed to next phase [10].

## Globally:

- PATHFINDER2 - prospective, multi-center interventional study of 35,500 participants healthy people in North America [11].
- Vanguard Study – aims to assess the feasibility of using multiple MCD tests in future RCT by enrolling up to 24,000 people [12].

There are also other global trials for MCDs that are NOT screening related





# Current levels of evidence for MCDs



## Different cancers

Detect from 3 to 50+ different types of cancer.



## Specificity

High specificity (> 96%).



## Sensitivity

Sensitivity is lower for detecting earlier vs later-stage cancer.



## Accuracy

Diagnostic accuracy varies substantially.



## Acceptability

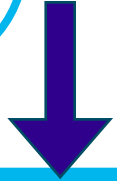
Generally acceptable >95% reporting high satisfaction.



Phase 1



Phase 2



Phase 3



Phase 4



Phase 5



Proof of concept in clinical samples

Proof of concept in intended setting (prospective clinical trials)

Performance in intended setting (real world data)

Health economic impact

Implementation and post-market monitoring

MCDs are still at an early stage of development



# Evidence gaps?



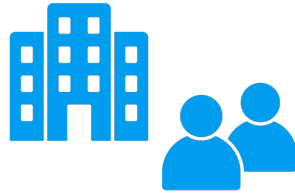
## Performance

Across all cancer sites and stages in a large study, or in a real-world population cohort



## Tumour natural history

Fundamental biology of early cancers and how they release biomarkers



## System & behavioural impact

Impact on existing screening programmes, the wider health system and screened-individuals



## Patient-reported outcomes

Patient-relevant outcomes other than mortality - HRQoL



## Clinical outcomes

Trials with long-term follow-up to give evidence of reducing mortality

# Pillars of evidence to support implementation?

Performance

*e.g., equitable performance, real-world setting*

Patients  
/Public

*e.g., patient behaviour, benefits vs. harms*

Evaluation

*e.g., evidence requirements, cost-effectiveness*

Implementation

*e.g., workforce impact, equitable implementation*

# Considerations for a multi-cancer screening programme

# Unanswered questions?

Is the tumour natural history understood?

Which individuals are at highest risk?

Who would be eligible?

Which cancers should be included?

How to evaluate MCEDs?

How to set performance parameters to not overwhelm diagnostic capacity?

Which test to use?

How can we get timely information?

Will there be available treatment leading to ED benefit?

How to design referral pathways and limit disruption?

Is it acceptable?

Is it feasible to implement?

What will be the impact on health inequalities?

What will be the impact on overdiagnosis?

How will be continually evaluated post-implementation?

Will it be cost-effective?

# In summary...



## **Opportunity**

Many different ways MCDs could impact cancer screening.



## **Evidence gaps**

Many evidence gaps and unanswered questions.



## **Rapidly evolving technology**

New evidence is being generated all the time.



## **Careful evaluation**

Of which, if any, MCD should be used for multi-cancer screening.



## **Consensus**

Convene the community to reach consensus.

# Get in touch

For any questions, please reach out to:

Strategic Evidence Team ([Seinbox@cancer.org.uk](mailto:Seinbox@cancer.org.uk))

Jessica Lloyd ([Jessica.Lloyd@cancer.org.uk](mailto:Jessica.Lloyd@cancer.org.uk))





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