# Multi Cancer Early Detection Testing

## Ready for Primetime?

Paul Kunnath MD FACP
Assistant Professor of Medicine
Saint Louis University School of Medicine

# Disclosures

- I have no relevant financial disclosures

# Objectives

- Review the principles of screening
- Consider success of different cancer screening strategies
- Evaluate tradeoffs for blood based cancer screening tests

# Wilson and Junger's Screening Criteria

- Important health problem
- Acceptable treatments for recognized disease
- Facilities for diagnosis and treatment should be available
- Recognized latent or early symptomatic stage
- Suitable test or examination
- Test should be acceptable to the population
- Natural history of the condition, including development from latent to declared disease, should be adequately understood
- Agreed policy on whom to treat as patients
- Cost of case-finding should be economically balanced in relation to expenditure of medical care as a whole
- Case finding should be a continuing process and not a "once and for all" project

Wilson JMG, Jungner G. Principles and practice of screening for disease. Geneva: WHO; 1968

## Wilson and Junger's Screening Criteria

"Screening works by reducing the risk of death and morbidity through the detection of well defined and clinically important precancerous or early invasive lesions which are more amenable to curative treatments than when detected from clinical presentation."

Doubeni CA, Castle PE. Multicancer Early Detection: A Promise Yet to Be Proven. *American family physician*. 2023;107(3):224-225A.

# Screening - is it always worth it?

- **Important health problem**
- **Acceptable treatments** for recognized disease
- **Natural history** of the condition, including development from latent to declared disease, **should be adequately understood**
  - “Does treatment at the pre-symptomatic stage of a disease affect its course and prognosis?”
  - “Does treatment of the developed clinical condition at an earlier stage than normal affect its course and prognosis?”

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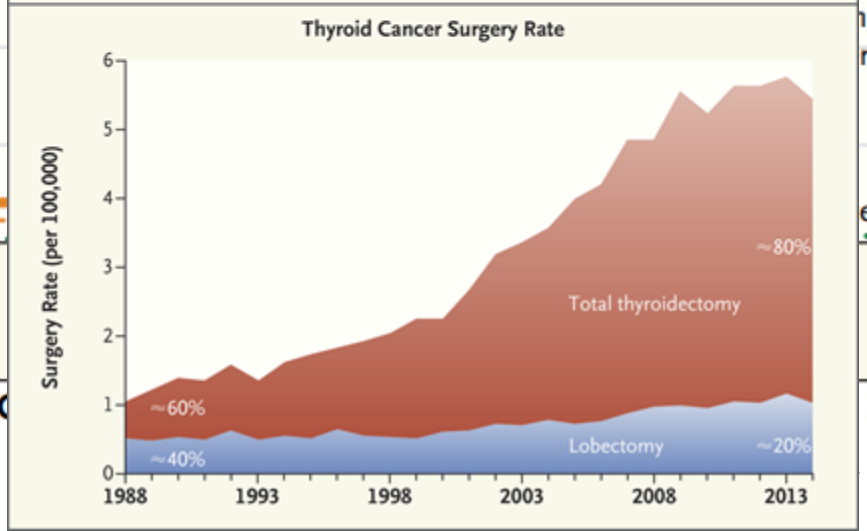
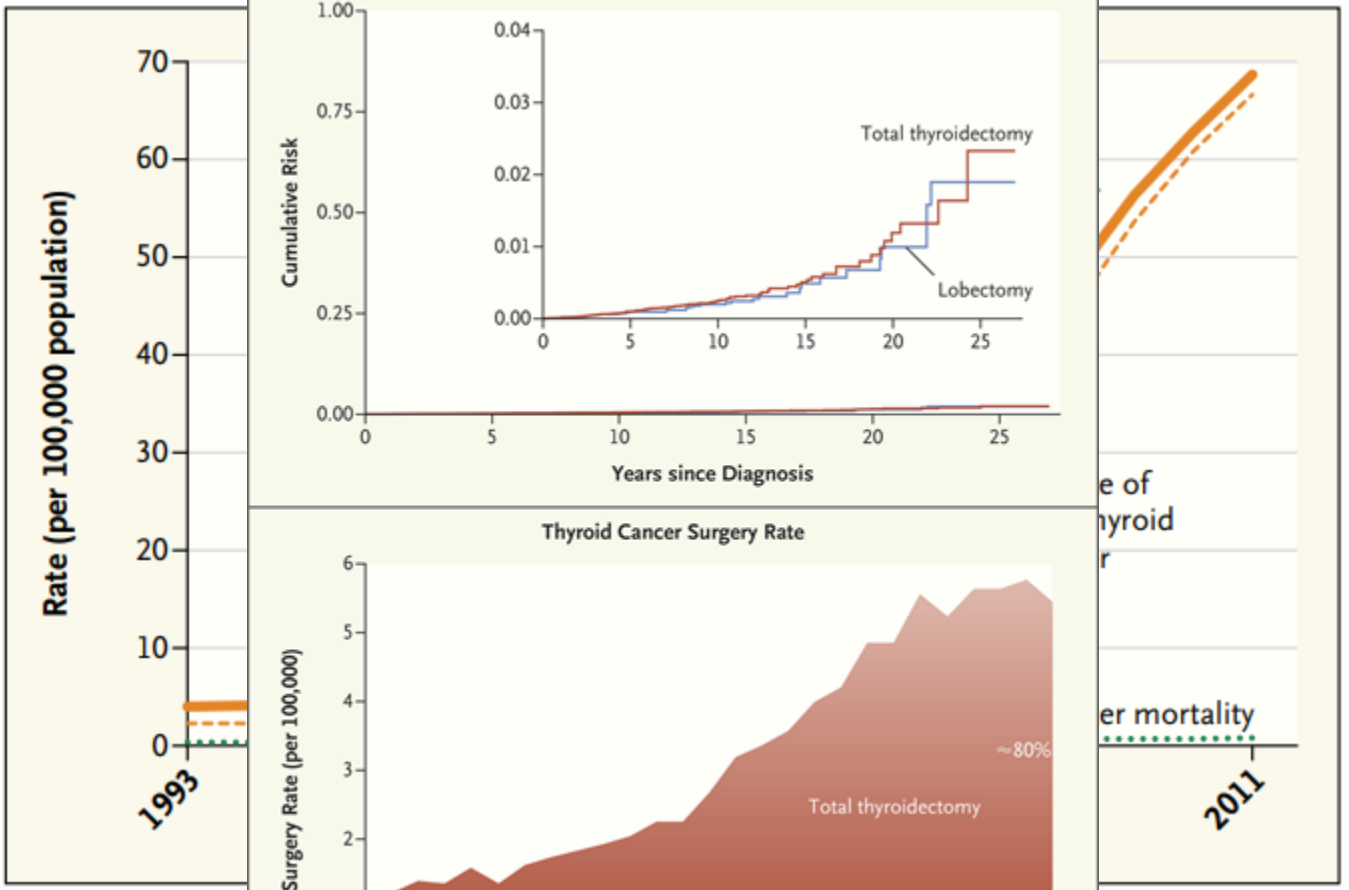
Screen




Thyroid-C

1993–2011.

"epidemic"--screening and overdiagnosis.

# Screening - is it w

- Important health prob
- [illegible]

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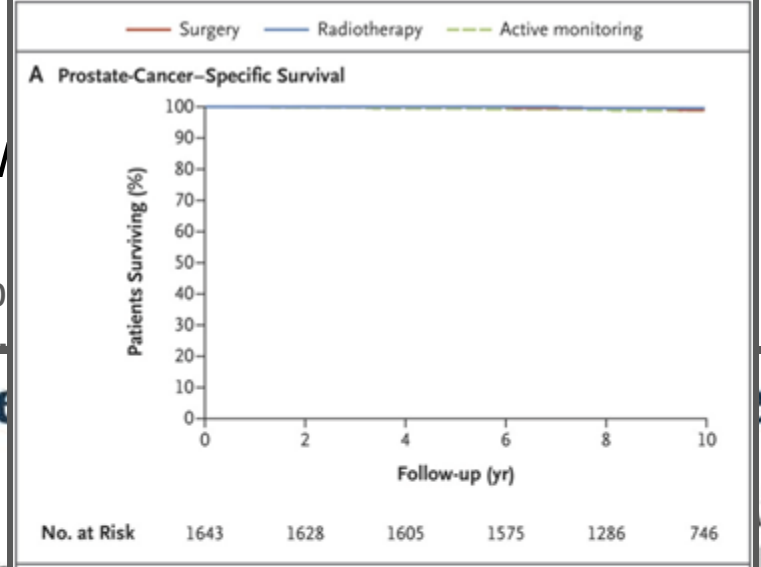


(2011-2017)

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Hamdy FC et al, ProtecT Study Group. 10-Year Outcomes after Monitoring, Surgery, or Radiotherapy for Localized Prostate Cancer. N Engl J Med. 2016 Oct 13;375(15):1415-1424.

w.seer.cancer.gov) SEER*Stat Database: Incidence
isiana Cases, Nov2020 Sub (2000-2018

# Screening - is it worth it?

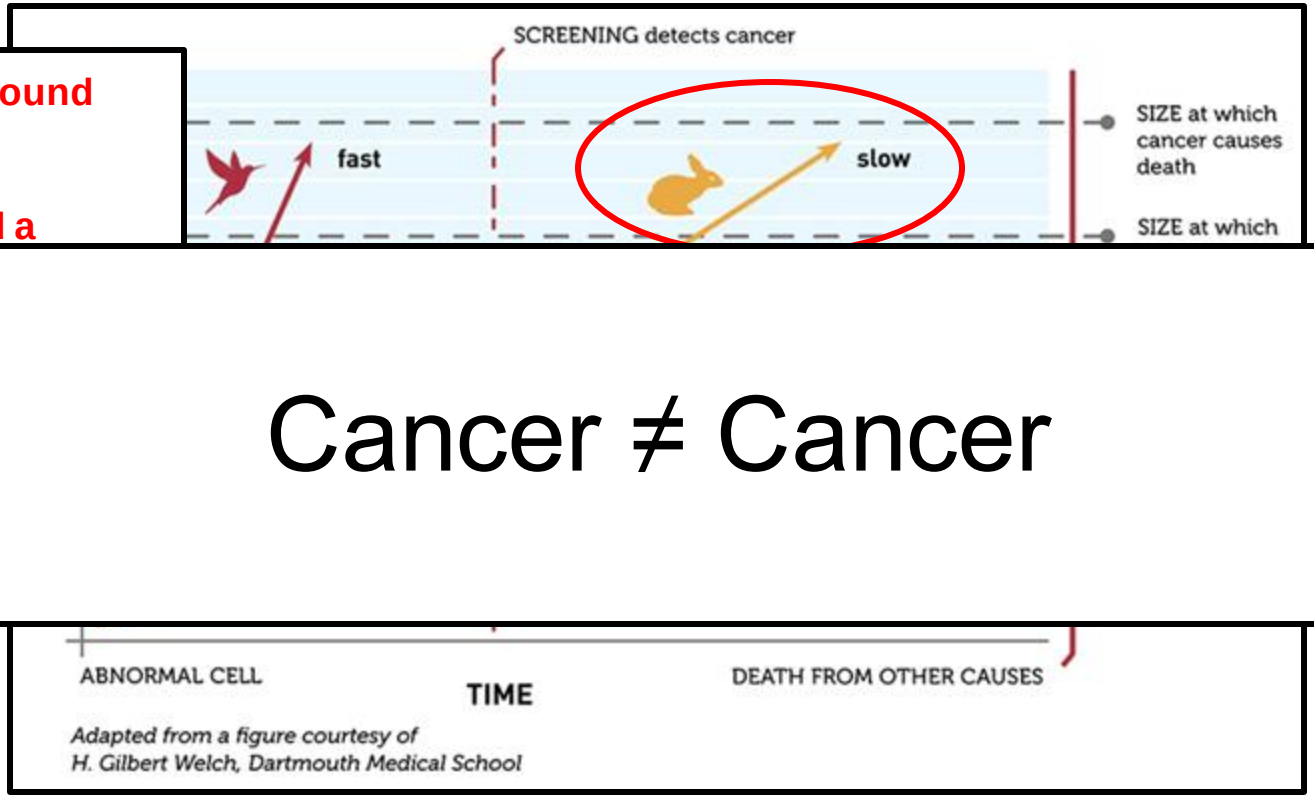
"This corresponds to a 2% reduction in all-cause mortality with screening compared with usual care
MRR, 0.98 [CI, 0.95 to 1.00]; p = 0.016"

Juul FE et al. 15-Year Benefits of Sigmoidoscopy Screening on Colorectal Cancer Incidence and Mortality : A Pooled Analysis of Randomized Trials. *Annals of internal medicine*. 2022.

# Screening - does early detection always save lives?

**May benefit if found early**

**Unlikely to find a rea inte**




## Cancer ≠ Cancer

**to**

https://prevention.cancer.gov/news-and-events/infographics/what-cancer-overdiagnosis

# Objectives

- Review the principles of screening
- Consider success of different cancer screening strategies
- **Evaluate tradeoffs for current blood based cancer screening tests**

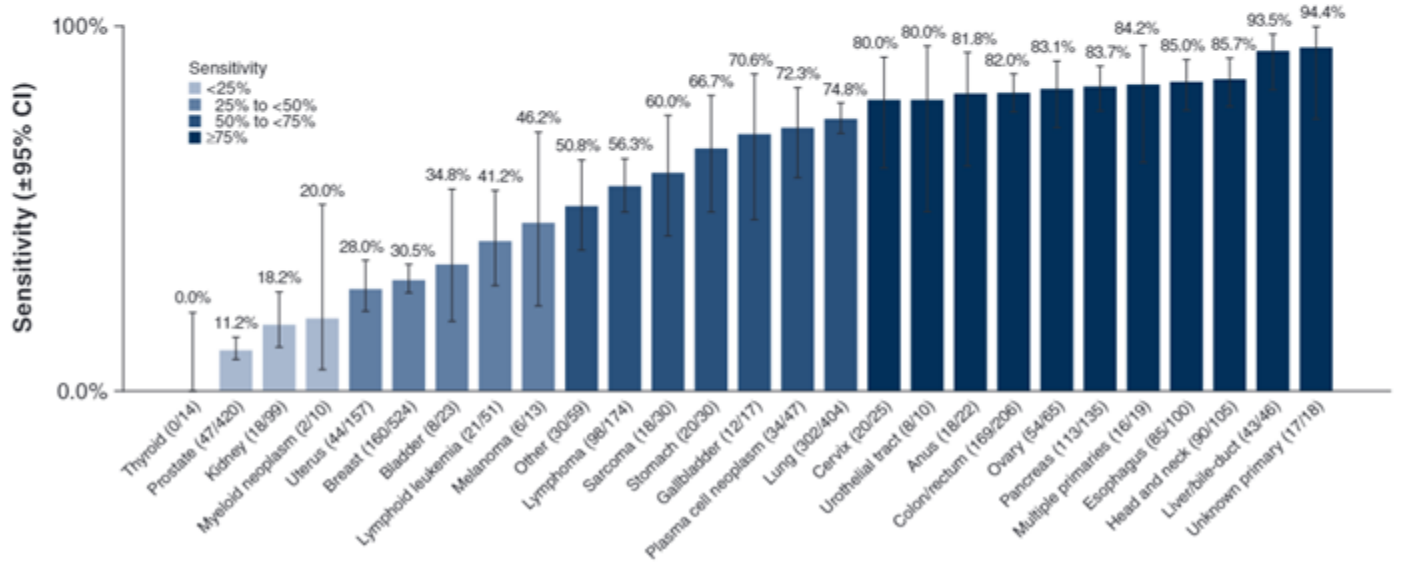
MCEI

A

| | Cancer | Non-cancer | Total |
|---|---|---|---|
| | 2823 | 1254 | 4077 |
| Test positive | 1453 | 6 | 1459 |
| Test negative | 1370 | 1248 | 2618 |
| | Sensitivity = 1453/2823<br>51.5% (49.6%-53.3%) | Specificity = 1248/1254<br>99.5% (99.0%-99.8%) | |

Two-sided 95% Wilson confidence intervals were calculated.

B




+LR 103
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arly detection test

# MCED Testable Cancers

**eTABLE A**

**Multicancer Detection Tests in Development or Being Marketed in the United States**

| Assay | Technology | Target cancers for detection by assay: Lung | Colon/rectum | Breast | Pancreas | Liver | Esophagus | Stomach | Ovary | Prostate | Bladder | Kidney | Uterus | Head/neck | Lymphoma | Leukemia | Plasma cell | Brain | Company/developer |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Galleri | CpG-cfDNA NGS | ■ | ■ | | ■ | ■ | ■ | ■ | ■ | | ■ | | | ■ | ■ | | ■ | | Grail |

- Exclude routinely screened cancers (lung/colorectal)
- Prevalence of remaining: 1.3%

Doubeni CA, Castle PE. Multicancer Early Detection: A Promise Yet to Be Proven. *American family physician*. 2023;107(3):224-225A.
National Cancer Institute, SEER Database

# MCED - PPV

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| Galleri | CpG-cfDNA NGS | ■ | ■ | | ■ | ■ | ■ | ■ | ■ | | ■ | | | ■ | ■ | | ■ | | Grail |

- Exclude routinely screened cancers (lung/colorectal)
- Prevalence of remaining: 1.3%
- PPV for positive test: ~57%

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| Galleri | CpG-cfDNA NGS | ■ | ■ | | ■ | ■ | ■ | ■ | ■ | | ■ | | | ■ | ■ | | ■ | | Grail |

- Criticisms
  - Spectrum bias: tested in previously diagnosed cancers, applicable in screening?
  - Verification bias: reference standard tests only done in diseased group

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# MCED - Better evidence?

- STRIVE: observational registry study, May 2025
- SUMMIT: prospective observational cohort for validation study, August 2023
- PATHFINDER 2: single arm safety and performance, February 2024

clinicaltrials.gov

# MCED - Better evidence?

## Study Overview

**Brief Summary:**
The Galleri test is a new test that looks for potential signs of cancer in a blood sample. The test can find many different types of cancer but cannot find all cancers. The trial aims to see if using the Galleri test alongside standard cancer testing in the NHS can help to find cancers at an early stage when they are easier to treat.

The trial has enrolled approximately 140,000 participants who will be actively followed for approximately three years from the date of enrollment.

**Detailed Description:**
This is a prospective, randomized, controlled trial to assess the performance and clinical utility of a multi-cancer early detection test for population screening in the UK when added to standard of care. Participants and the study teams remain blinded throughout the study with the exception of the study nurses returning the results and a small number of staff to enable them to perform administrative duties. Blinding is maintained for participants with the exception of those participants who test positive. Those who test positive will be informed by designated trial staff and will be referred for standard of care investigations and treatment. Trial sponsor employees, the CIs and site staff (unless identified different...

+ Show more

OFFICIAL TITLE

A Randomized, Controlled Trial to Assess the Clinical Utility of a Multi-cancer Early Detection (MCED) Test for Population Screening in the United Kingdom (UK) When Added to Standard of Care

STUDY START (ACTUAL)
2021-08-31

PRIMARY COMPLETION (ESTIMATED)
2024-07-15

STUDY COMPLETION (ESTIMATED)
2026-02-28

ENROLLMENT (ACTUAL)
140000

STUDY TYPE
Interventional

clinicaltrials.gov

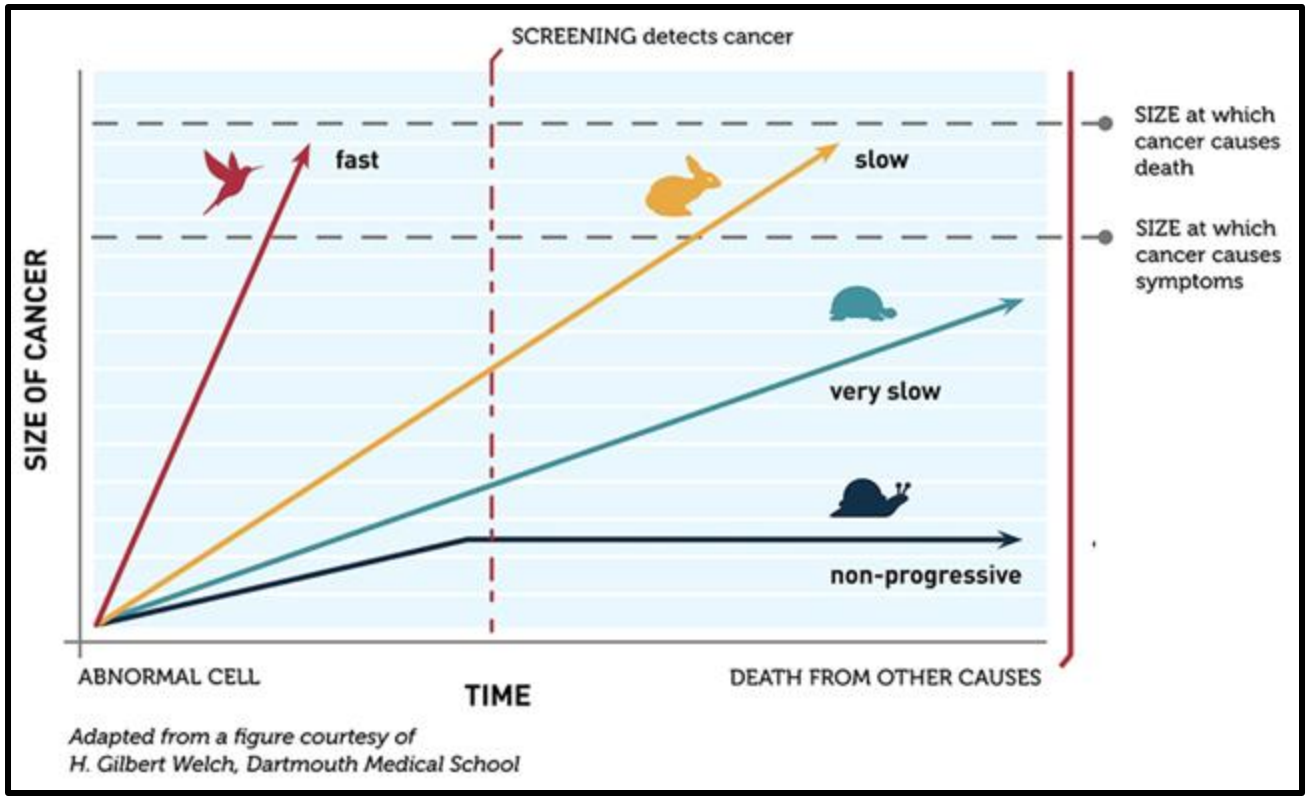
# MCED - Downsides?

- Estimated cost of workup for positive screening test
  - +Lung/liver: CT chest/abdomen/pelvis ~ $481
  - +Lymphoma/myeloma: CT chest/abdomen/pelvis + bone marrow biopsy ~ $793
  - +Esophagus/stomach: EGD ~ $1940
  - +Ovarian: pelvic ultrasound + laparoscopy? ~ $11,165
- False positives
  - 99.5% specificity: out of 1000 screened, 5 false positives
  - Out of 100M adults screened, 500K false positives
  - ~$500M in downstream workup of false positives
- Opportunity cost?
  - Better ways to reduce the risk of cancer mortality with $500M?
  - Childhood education, smoking cessation, diet/exercise, psychosocial support etc.

# MCED - Tradeoffs

- Benefits
  - Better test characteristics than current screening tests
  - Easier to obtain than most current screening tests
- Harms
  - Monetary cost of screening + downstream testing
  - Opportunity cost of resources
  - Insurance cost?
- Unknowns
  - Balance of harms/benefits in a screening population
  - Which cancers are most likely to be found?
  - **Will it go the way of thyroid (turtles) or colorectal (rabbit) screening?**

# Questions?




https://prevention.cancer.gov/news-and-events/infographics/what-cancer-overdiagnosis