ANNUAL

Advances and Innovations in Endoscopic Oncology and Multidisciplinary Gastrointestinal Cancer Care

Beyond Boundaries: Bringing Advanced Cancer Detection to the World's Most Vulnerable Corners

Jordan Iannuzzi, MD

Clinical Assistant Professor, Department of Medicine and Division of Gastroenterology and Hepatology

Clinical Lead, Hereditary Polyposis Program

University of Calgary

Disclosures

- I do not have any relevant financial relationships.

This presentation and/or comments will provide a balanced, non-promotional, and evidence-based approach to all diagnostic, therapeutic and/or research related content

Cultural Linguistic Competency (CLC) & Implicit Bias (IB)

STATE LAW:

The California legislature has passed Assembly Bill (AB) 1195, which states that as of July 1, 2006, all Category 1 CME activities that relate to patient care must include a cultural diversity/linguistics component. It has also passed AB 241, which states that as of January 1, 2022, all continuing education courses for a physician and surgeon **must** contain curriculum that includes specified instruction in the understanding of implicit bias in medical treatment.

The cultural and linguistic competency (CLC) and implicit bias (IB) definitions reiterate how patients' diverse backgrounds may impact their access to care.

EXEMPTION:

Business and Professions Code 2190.1 exempts activities which are dedicated solely to research or other issues that do not contain a direct patient care component.

This presentation is dedicated solely to research or other issues that do not contain a direct patient care component.

From the previous talks this morning

- Examples of what MCED technology is and descriptions of test performance.
- How AI can be used to enhance MCED.
- How MCED technology can be integrated with interventional endoscopy techniques.

Objectives

1. Cost-effectiveness of early cancer detection
2. Assess the financial feasibility of MCED in various settings
3. Discuss implementation of AI, genomics, and MCD in resource-limited environments including socialized health systems and HMO's
4. Explore the ethical implications of early cancer detection technology potentially becoming exclusive to affluent populations

Objectives

1. Cost-effectiv
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4. Explore the eth detection technology potentially becoming exclusive to affluent populations

Are these screening technologies:

- **Affordable**
- **Feasible (micro and macro-level)**
- **Ethical**

"All screening programs do harm; some do good as well, and, of these, some do more good than harm at a reasonable cost"

- Sir Muir Gray

Gray et al. (2008). Maximising benefit and minimising harm of screening. *BMJ*

MCED	COMPANY	*Sensitivity (95%CI)	*Specificity (95% CI)	COST	Study examples
Galleri	GRAIL (Menlo Park, CA, USA)	**20.8%** (14 – 29)	**98.4** (98.1 - 98.8)	**~1000 USD**	PATHFINDER, SYMPLIFY, CCGA sub-study
CancerSEEK / Cancerguard	Exact Sciences (Madison, WI, USA)	**27.1%** (18.5 - 37.1)	**98.9%** (98.7 - 99.1)	**~500 USD**	DETECT-A, proof of concept study
SPOT-MAS	Gene Solutions (Ho Chi Minh City, Vietnam)	**72.4%** (66.3 - 78)	**97%** (95.1 - 98.4)	**??**	K-DETEK, earlier case control study
Trucheck	Datar Cancer Genetics (Bayreuth, Germany)	**90%** (55.5 - 99.7)	**96.4%** (95.9 - 96.8)	**~ 1500 Euro**	RESOLUTE, TrueBlood
Cancer Differentiation Analysis (CDA)	AnPac Bio (Shanghai, China)	**40%** (12.2 - 73.8)	**97.6** (96.8 - 98.2)	**??**	PPCS

Wade et al. (2025). Multi-cancer early detection tests for general population screening: a Systematic literature review. *Health technol Assess.*

Do we have concrete real-world data on cost-effectiveness?

Not yet

- The initial studies are either dedicated to test performance / refinement or preliminary modelling studies.

Does modelling suggest that MCED is cost-efficient?

Hackshaw et al. 2021

Goal

- Provide National estimates (USA and UK) for screening performance measures and financial costs of diagnostic investigations currently implemented (over the span of 1 year) and then modelled with addition of MCED testing.

Population

- 2020 Census Data on adults between 50-79 for both scenarios
    - USA: 107,000,000 / UK: 21,834,470

Hackshaw et al (2021). Estimating the population health impact of a multi-cancer early detection genomic blood test to complement existing screening in the US and UK. *Br J Cancer*.

Does modelling suggest that MCED is cost-efficient?

Hackshaw et al. 2021

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  - USA: 107,000,000 / UK: 21,834,470

*NB: Assumption of 100% compliance with screening tests and all downstream diagnostic investigations.

**NB: Diagnostic cost estimates only based on "one test to diagnose".

Hackshaw et al (2021). Estimating the population health impact of a multi-cancer early detection genomic blood test to complement existing screening in the US and UK. *Br J Cancer*.

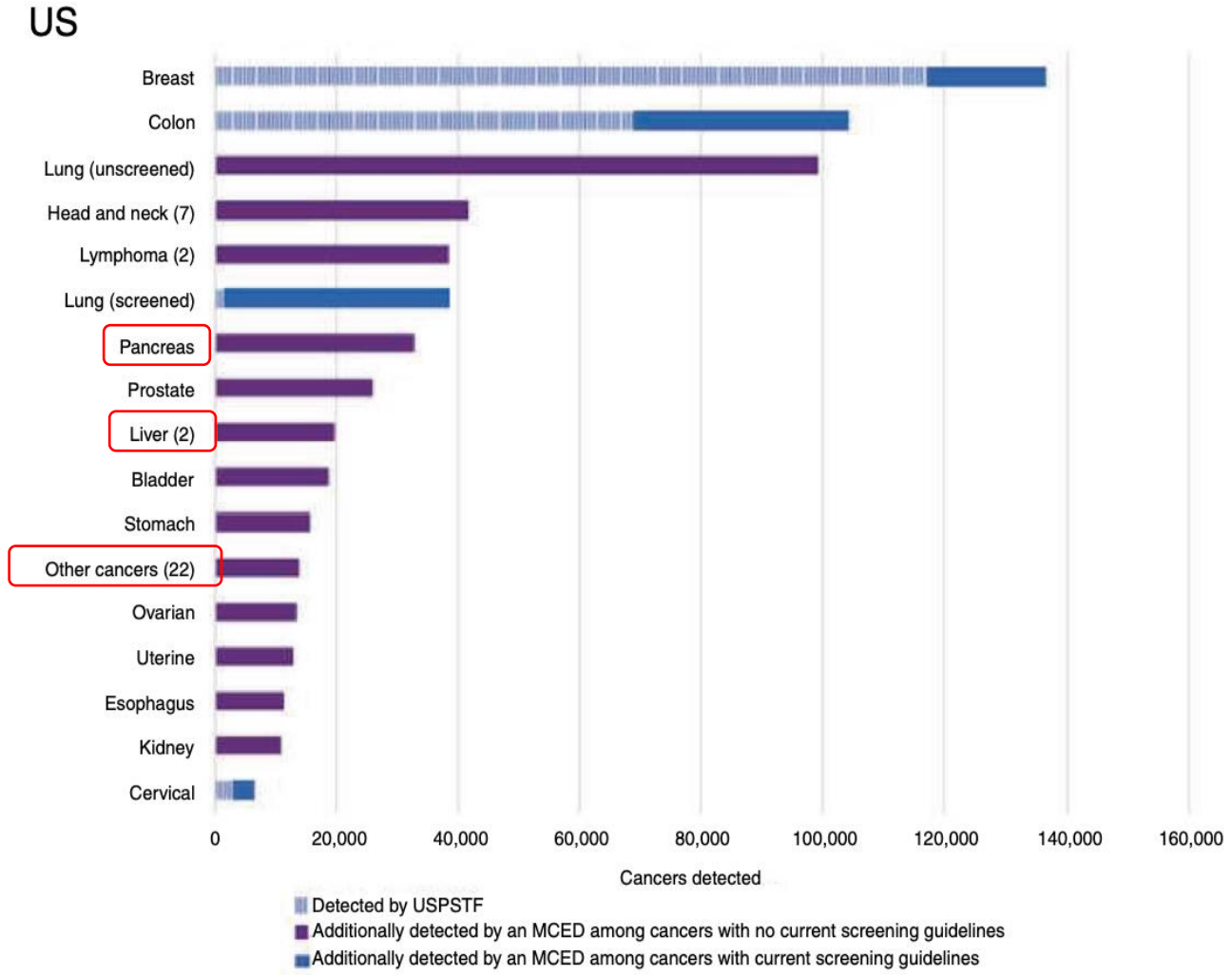
Does modelling suggest that MCED is cost-efficient? USA

Screening Programs (no MCED)

- 189,498 breast / lung / colorectal / cervical cancers found.
- **Screening Efficacy: 1:43**
- **CDR: 15%**
- **Dx cost/cancer: $89,042**
- **Dx Cost overall/year: ~16.9 Billion**

Screening Programs (with MCED)

- 422,105 additional cancers diagnosed
- **Screening Efficacy: 1:1.8**
- **CDR: 34%**
- **Dx cost/cancer: $7060**
- **Dx Cost overall/year: ~20 billion**



Hackshaw et al (2021). Estimating the population health impact of a multi-cancer early detection genomic blood test to complement existing screening in the US and UK. *Br J Cancer*.

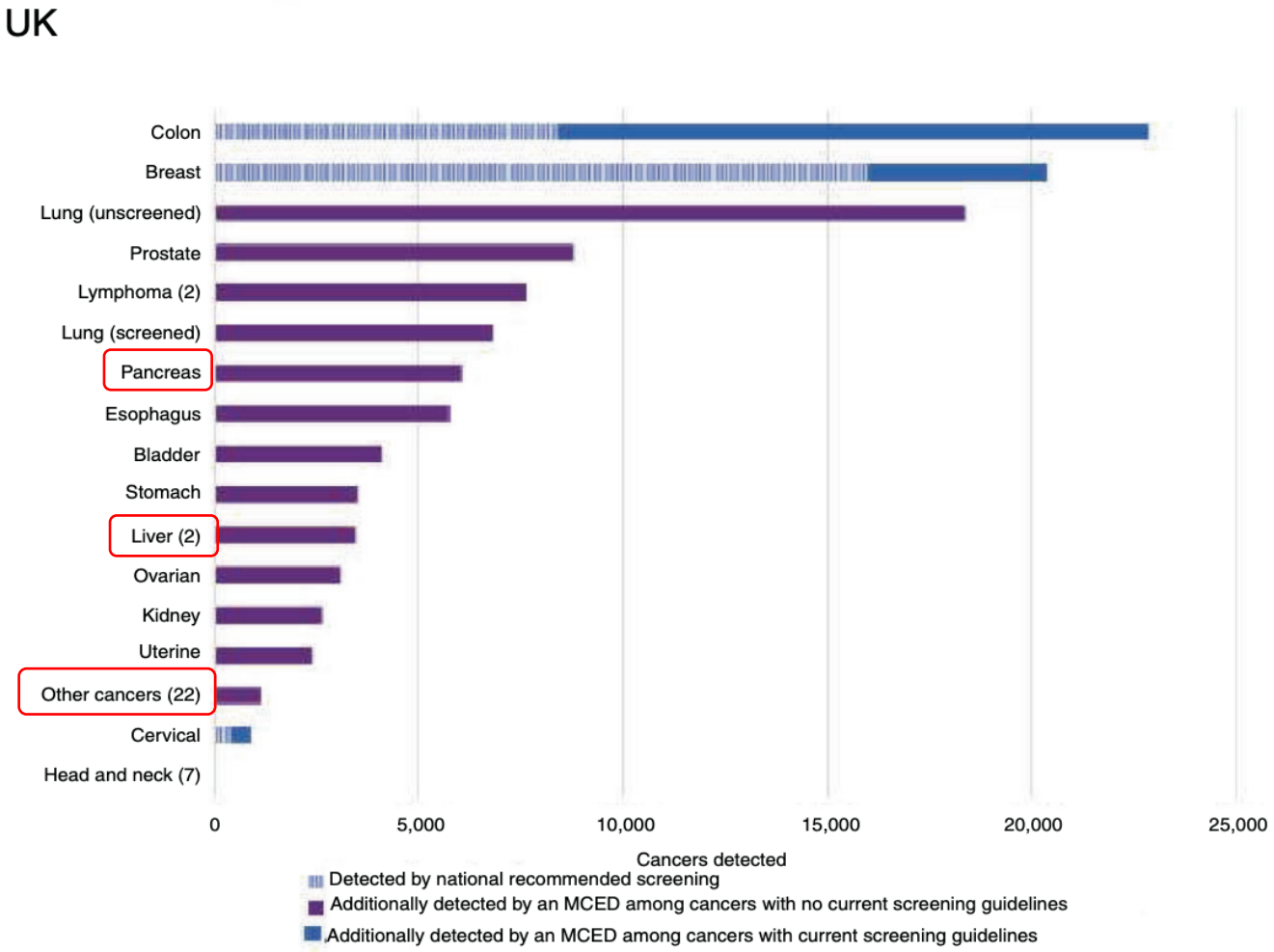
Does modelling suggest that MCED is cost-efficient? UK

Screening Programs (no MCED)

- 24,888 breast / lung / colorectal / cervical cancers found.
- **Screening Efficacy: 1:18**
- **CDR: 12%**
- **Dx cost/cancer: $10,452 (euro)**
- **Dx Cost overall/year: ~260 million (euro)**

Screening Programs (with MCED)

- 92,817 additional cancers diagnosed
- **Screening Efficacy: 1:1.6**
- **CDR: 43%**
- **Dx cost/cancer: $2175 (euro)**
- **Dx Cost overall/year: ~462 million (euro)**



Hackshaw et al (2021). Estimating the population health impact of a multi-cancer early detection genomic blood test to complement existing screening in the US and UK. *Br J Cancer*.

Affordability

Does modelling suggest that MCED is cost-efficient?

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Affordability

Does modelling suggest that MCED is cost-efficient?

Some limitations of this study

Potentially

- Only provided estimates of screening over a single year
- Unable to estimate reduction in cancer mortality / stage shift
- Over-estimation of cost savings
- Exclusion of pre-cancerous lesions (ex. Cervical or colon polyps)
- Used current test performance estimates which may change as the technology develops, thus changing the findings.

Hackshaw et al (2021). Estimating the population health impact of a multi-cancer early detection genomic blood test to complement existing screening in the US and UK. *Br J Cancer*.

Health System feasibility example

Assumption:

- ~50% of people over age 50 are appropriate for asymptomatic screening and will follow through with a screening test.

For a single round of MCED tests on a population level (without additional downstream costs):

COUNTRY	~ Number of people ≥ 50	~ Number screened (Assumption)	~Cost per test (ex. Galleri)	Total $$
USA	120 Million	60 Million	1000 USD	60 Billion USD
Canada	16 Million	8 Million	1440 CAD	11.52 Billion CAD
UK	27 Million	13.5 Million	777.20 GBP	10.49 Billion GBP

Population numbers based on 2024 census data and information collected through Statista, CIHI (Canadian Institute for Health Information), population pyramid.net. , and health.org.uk

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UK	27 Million	13.5 Million	777.20 GBP	10.49 Billion GBP

By cost alone (ignoring other implementation barriers), population level screening with MCED unlikely to be a feasible option given the current financial climate.

Population numbers based on 2024 census data and information collected through Statista, CIHI (Canadian Institute for Health Information), population pyramid.net. , and health.org.uk

Feasibility (micro)

Feasibility for the individual – do they want it?

Testing available as an *a-al-carte* option ordered through MD , paid for by patients

- Surveys
  - **70-85% of participants would accept** a blood-based MCED test if offered in addition to currently recommended cancer screening.
- Qualitative Interviews
  - **Enthusiastic** about blood-based testing ("ease", "more cancers screened", "peace of mind worth the cost")
  - Preference to be offered through **primary care**.
  - **Endorsed concerns** around "cost", "risk of false positives" (ie. Test performance), "need for additional screening / diagnostic testing", and "MCED equity".
    - Felt that a price of $20 - $500 would be more accessible...

Crossnohere et al. (2024). Public Perspectives on Multi-Cancer Early Detection: A qualitative study
Gelhorn et al. (2023). Patient preferences for multi-cancer early detection (MCED) screening tests.
Myers et al. (2023). Primary care patient interest in multi-cancer early detection for cancer screening.

Feasibility for the individual – would they pay for it?

Testing available as an *a-al-carte* option ordered through MD , paid for by patients

- **Willingness to pay (WTP)** = maximum amount of money an individual / consumer is willing to pay for a specified health intervention.

- Systematic Review [Ben-Aharon et al. (2023)]: 103 WTP studies between 1997 - 2020
  - USA (25 studies) / Canada (11 studies) / UK (6 studies)
  - Heterogeneity in methodology and size
  - Factors noted to influence WTP values include SES, sex, ethnicity, family history, and personal history of cancer.

Ben-Aharon et al. (2023) Willingness to pay for cancer prevention, screening, diagnosis, and treatment: a systematic review.
Crossnohere et al. (2024). Public Perspectives on Multi-Cancer Early Detection: A qualitative study

Feasibility (micro)

Feasibility for the individual – would they pay for it?

Testing available as an *a-al-carte* option ordered through MD , paid for by patients

- Systematic Review [Ben-Aharon et al. (2023)]: 103 WTP studies between 1997 - 2020
  - Mean WTP values for cancer-related technology [63 studies] - MOST COMMON was **< $500**

COUNTRY	SCREENING ($)
USA	Breast Ca (101-500) CRC (101-500) Cervix (101-500)
CANADA	Cervical Ca (0-100)
UK	Cervical Ca (0-100) Breast Ca (101 – 500)

Ben-Aharon et al. (2023) Willingness to pay for cancer prevention, screening, diagnosis, and treatment: a systematic review.
Crossnohere et al. (2024). Public Perspectives on Multi-Cancer Early Detection: A qualitative study

Implementation in resource-limited environments.

Outside of financial feasibility, what are barriers we need to consider before implementation?

Implementation Barriers

- **Ensuring Clinical Utility**
  - **Does test performance remain the same in real-world (outside validation studies)?**
  - **Do MCED test results change patient management? Improve outcomes?**
  - **If beneficial – individual and/or population-level?**

Putcha G et al. (2021). Mulicancer Screening: One Size Does Note Fit All. *JCO Precis Oncol*

Implementation Barriers

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- **Positioning of MCED**
    - **Screening replacement test or adjunct to current screening?**

Putcha G et al. (2021). Mulicancer Screening: One Size Does Note Fit All. *JCO Precis Oncol*

Implementation Barriers

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- Positioning of MCED
    - Screening replacement test or adjunct to current screening?
- **Choosing the right population**
    - **Average risk vs. High risk?**
    - **Different test & performance characteristics for different cancers?**

Putcha G et al. (2021). Mulicancer Screening: One Size Does Note Fit All. *JCO Precis Oncol*

Implementation

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- Choosing the right population
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Future Study Outcomes?

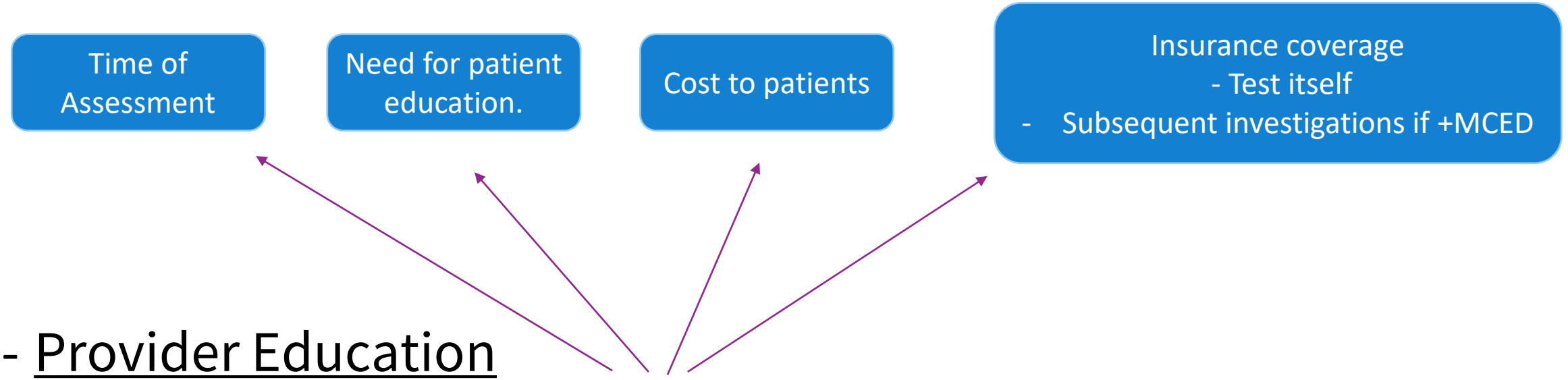
Putcha G et al. (2021). Mulicancer Screening: One Size Does Note Fit All. *JCO Precis Oncol*

Implementation Barriers cont.

- <u>Patient Education / Access</u>
  - Multi-pronged approach.
  - Incorporation into employee benefits.
- <u>Provider Education</u>
  - PCPs are generally receptive to the idea of incorporation of MCED into screening programs
    - Different from other forms of genetics-based testing studies

Cance et al. (2023). Employer-based Implementation of Galleri® Multi-cancer Early Detection Testing to Address Socioeconomic Disparities in Receipt of Screening
Putcha G et al. (2021). Mulicancer Screening: One Size Does Note Fit All. *JCO Precis Oncol*
Chambers et al. (2023). Primary Care Provider Receptivity to Multi-Cancer Early Detection Test Use in Cancer Screening. *J Pers Med*.

Implementation Barriers cont.



- Provider Education
  - However, their main concerns were within the following areas:

Putcha G et al. (2021). Mulicancer Screening: One Size Does Note Fit All. *JCO Precis Oncol*
Chambers et al. (2023). Primary Care Provider Receptivity to Multi-Cancer Early Detection Test Use in Cancer Screening. *J Pers Med*.

Implementation Barriers cont.

- **Regulatory Structures**
  - **Pre-market controls + Post-market commitment vs. requirements?**
  - **Post-market regulation of test QA / QI / data-legacy**
  - **Health Equity Assurance**

Putcha G et al. (2021). Mulicancer Screening: One Size Does Note Fit All. *JCO Precis Oncol*

Implementation Barriers cont.

- Regulatory Structures
  - Pre-market controls + Post-market commitment vs. requirements?
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  - Health Equity Assurance

- **Reimbursement Frameworks**
  - **Will coverage be introduced into certain insurance plans / HMOs?**
  - **Will socialized health systems see net $$$ saved to offset high test cost?**

Putcha G et al. (2021). Mulicancer Screening: One Size Does Note Fit All. *JCO Precis Oncol*

Implementation Barriers cont.

- Socialized Healthcare (publicly funded > private)
  - 2022 CADTH (Canadian Agency for Drugs and Technologies in Health) statement
    - Need for real-world measures of test performance.
    - Address specifics around complex benefits and harms of screening.
    - Disruptiveness to the Healthcare System

https://www.cda-amc.ca/emerging-multi-cancer-early-detection-technologies

Hackshaw et al (2021). Estimating the population health impact of a multi-cancer early detection genomic blood test to complement existing screening in the US and UK. *Br J Cancer*.

Upcoming implementation studies

- Neal et al. (2022) Cell-free DNA-based multi-cancer early detection test in an asymptomatic screening population (NHS-Galleri): design of a pragmatic, prospective RCT.

- Nadauld (2021) THE PATHFINDER Study: assessment of the implementation of an investigational multi-cancer early detection test into clinical practice (USA-CancerSEEK)

Ethical considerations of MCED as a population screening technology

- GOAL = A test that can find cancer at early stage, in average risk populations, and with sufficient accuracy.
- BALANCED WITH the need for the test to be both acceptable (including the harms), accessible, and sustainable to the individuals or healthcare system funding the test.

Dondorp and de Wert (2022) Towards responsible ctDNA-based multi-cancer screening: a preliminary exploration and discussion of ethically relevant aspects. *Extracell Vesicles Circ Nucl Acids.*

Possible Harms of MCED screening

PHYSICAL	Complications of downstream investigations (whether TP or FP)
	Complications of subsequent cancer therapies
PSYCHOLOGICAL (Cancer-Signal Negative)	False reassurance and reduced uptake of other proven cancer screening programs
PSYCHOLOGICAL (Cancer-Signal Positive)	Unable to identify clear origin site for detected ctDNA
	Identification of indolent cancer (over-diagnosis)
	Identification of tumor without good / effective treatment options
FINANCIAL	Personal (already discussed)
	Healthcare System (already discussed)

Dondorp and de Wert (2022) Towards responsible ctDNA-based multi-cancer screening: a preliminary exploration and discussion of ethically relevant aspects. *Extracell Vesicles Circ Nucl Acids.*
Hackshaw et al. (2022). New genomic technologies for multi-cancer early detection: rethinking the scope of cancer screening. *Cancer Cell*.

Issues of access to MCED screening: Health Equity

- Recruitment to clinical trials
- Need for an ordering physician
- Need for financial security
  - Over 8% of Americans do not have health insurance
  - If individuals insured, unclear if MCED will eventually be covered
  - Does the test meet an individual's WTP threshold?

Dondorp and de Wert (2022) Towards responsible ctDNA-based multi-cancer screening: a preliminary exploration and discussion of ethically relevant aspects. *Extracell Vesicles Circ Nucl Acids.*
Kessler et al. (2023) The modeling of multicancer early detection (MCED) tests' residual risk and the challenges of MCED evaluation and implementation. Cancer

Revised WHO Screening Program Criteria	MCED testing has achieved
Screening program should respond to recognized need	Yes
The objectives of screening should be defined at the outset	Not Clear yet
- There should be a defined target population	Not Clear yet
- There should be scientific evidence of screening program effectiveness	No
- The program should integrate education, testing, clinical services, and ongoing program management	Yes
There should be quality assurance, with mechanisms to minimize potential risks of screening	No
- The program should ensure informed choice, confidentiality, and respect for autonomy	Yes
- The program should promote equity and access to screening for the entire target population	No
Program evaluation should be planned from the outset	Not Clear Yet
The overall benefits of screening should outweigh the harm	Not Clear Yet

Andermann (2008). Revisiting Wilson and Jungner in the genomic age: a review of screening criteria over the past 40 years. *Bull World Health Organ*

Revised WHO Screening Program Criteria	MCED testing has achieved
Screening program should respond to recognized need	Yes
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- The progr	
- The progra population	
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The overall benefits of screening should outweigh the harm	Not Clear Yet

MCED Consortium Statement

1. **Insufficient evidence for the widespread use in the population screening context outside of clinical trials.**

2. **Should MCED tests prove to have benefits that exceed harms at an acceptable cost, systems to ensure fair and equitable use *must* be established.**

Kessler et al. (2023) The modeling of multicancer early detection (MCED) tests' residual risk and the challenges of MCED evaluation and implementation. Cancer

https://healthsperien.com/mced-position-paper/

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Health Organ

Thank you!

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