City of Hope

ANNUAL

Advances and Innovations in Endoscopic Oncology and Multidisciplinary Gastrointestinal Cancer Care

High-Risk Patients and Health Disparities: Unresolved Issues in Multi-Cancer Early Detection Screening

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City of Hope

Disclosures

- Adela – Research Support

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.

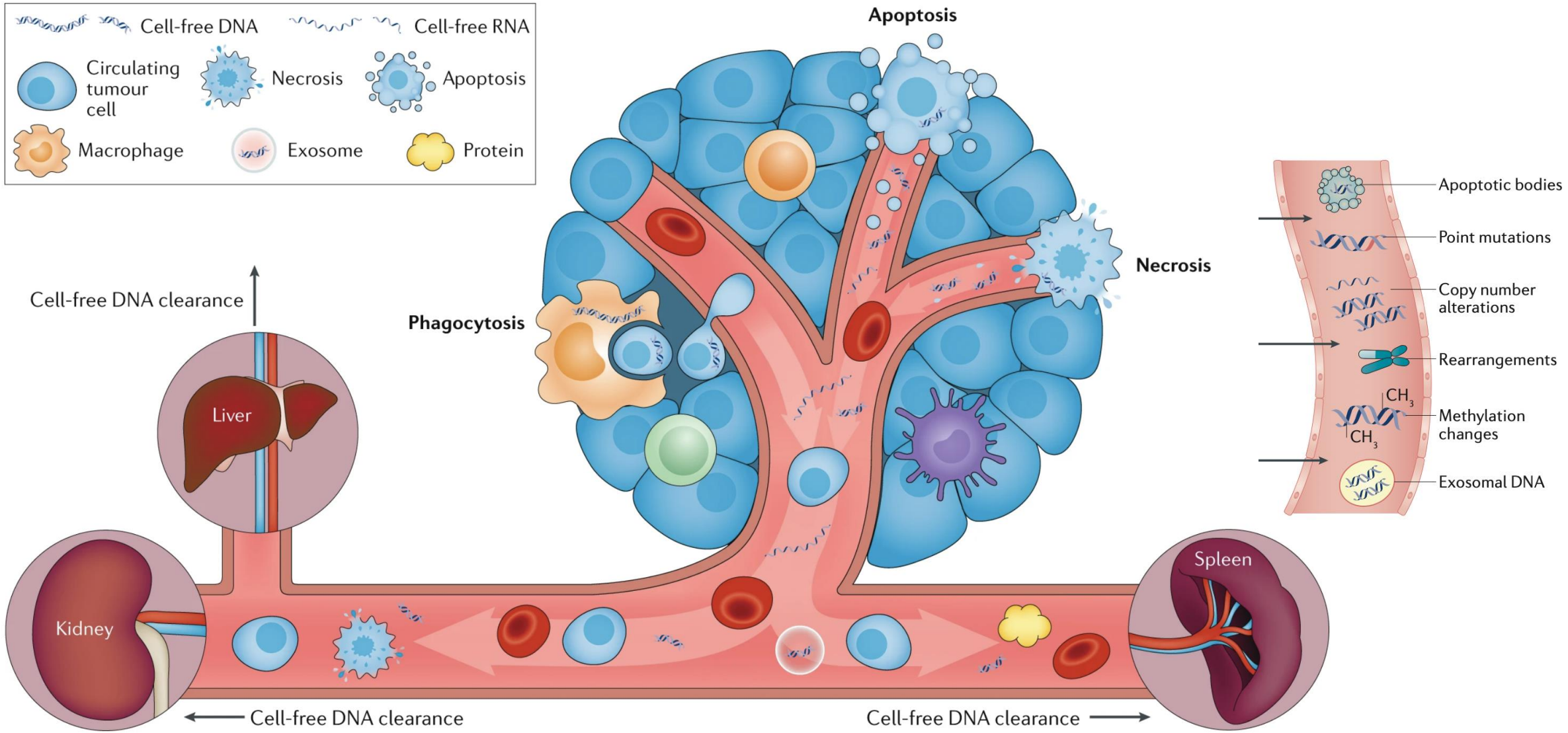
The cultural and linguistic competency (CLC) and implicit bias (IB) definitions reiterate how patients' diverse backgrounds may impact their access to care.

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.

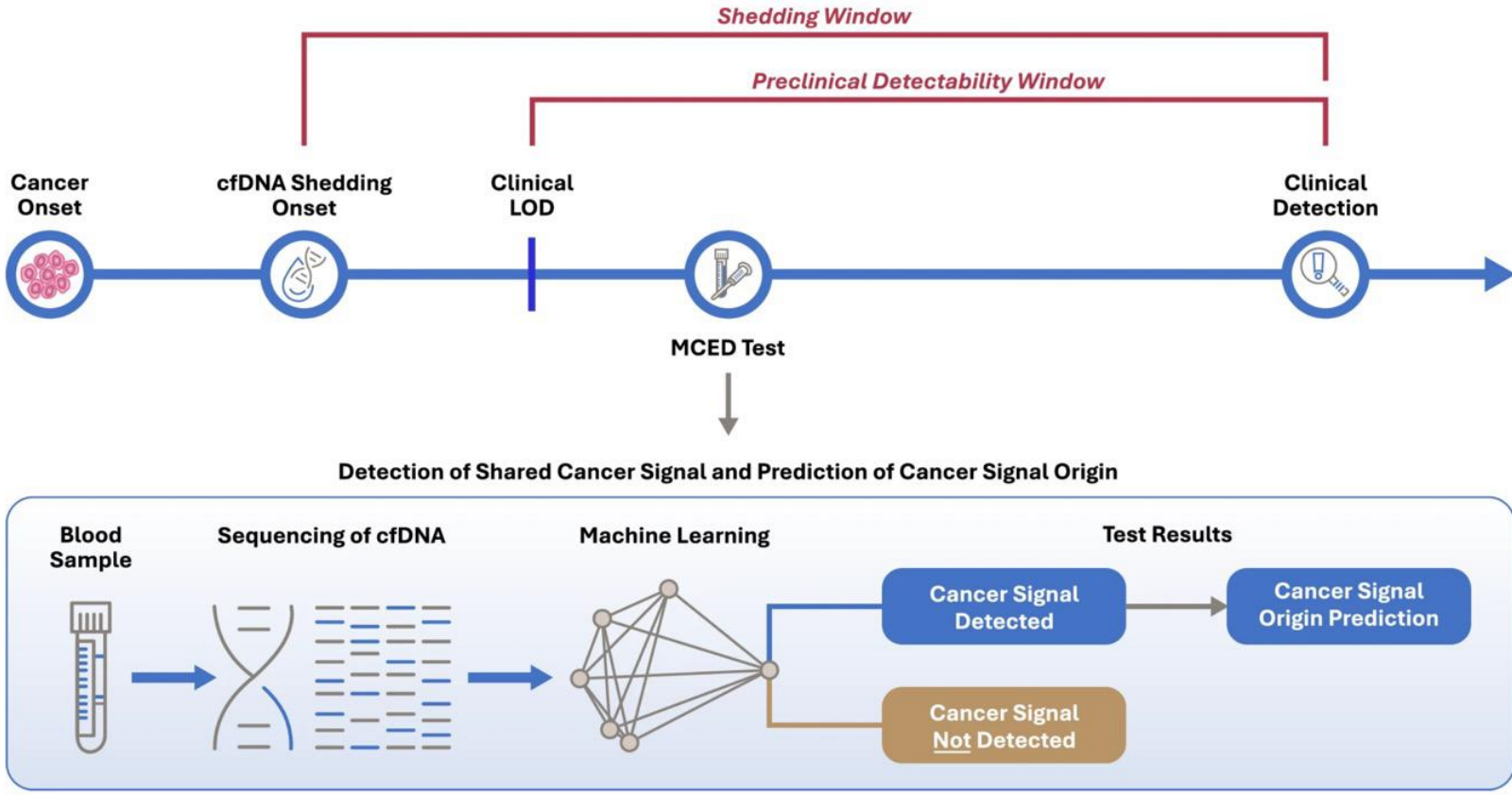
Multi-Cancer Early Detection (MCED) and Liquid Biopsy



Wan et al Nature Reviews April 2017
Maia et al Nature Reviews Urology March 2020

Liquid Biopsy in Cancer Screening: Blood-based MCED Tests

- USPSTF screening recommendations only exist for 5 cancers—breast, colorectal, lung, cervical, and prostate.
- Malignancies that lack population screening account for ~50% of new cancer diagnoses.
- MCEDs positioned as an adjunct to ‘evidence-based’ cancer screening to screen for these ‘other’ cancers.



cfDNA cell-free DNA, LOD limit of detection, MCED multi-cancer early detection.

Personal Genome Diagnostics
Foundation Medicine
Burning Rock
Biological Dynamics
Precision Epigenomics
20/20 GeneSystems
EarlyDiagnostics
Epic Sciences
Singlera Genomics
Biocept
QIAGEN
Exact Sciences
Guardant Health
GRAIL
Natera
Bluestar Genomics
Oncocyte
Delfi Diagnostics
Freenome
StageZero
Cardiff Oncology
LungLife AI
Resolution Bioscience
Elypta
Exosome Diagnostics
Adela
Caris Life Sciences

I think I'd like to have an MCED test, Doc, but which one?

MEDICAL OFFICE

NCI Division of Cancer Prevention
https://prevention.cancer.gov/mced

Blood-based MCED Tests

- 6 MCEDs evaluated
- >15 in development
- Completed Studies: 13 cohort, 17 case-control
- Ongoing Studies: 1 RCT, 5 cohort or case-control
- 4 to 50 cancers screened
- Assess individual or combinations of ct-DNA (methylation, sequencing), RNA, proteins

		Completed prospective studies			Ongoing prospective studies			
Manufacturer	**Test name**	**RCT**	**Cohort**	**Case-control**	**RCT**	**Cohort**	**Case-control**	**Number of cancers[a]**
Available MCED tests								
GRAIL	Galleri (refined MCED test)	–	PATHFINDER[31] SYMPLIFY[40] Cance, 2023[41]	CCGA substudy 3[32]	NHS-Galleri[42]	PATHFINDER2[43] REFLECTION[44] SUMMIT[45]	–	50[b,5]
Exact Sciences	CancerSEEK	–	DETECT-A[6]	Cohen, 2018[34]	–	–	–	15
Gene Solutions	SPOT-MAS	–	K-DETEK[8]	Nguyen, 2023[46]	–	–	–	5
Datar Cancer Genetics	Trucheck	–	RESOLUTE[9] TrueBlood[9]	–	–	–	–	4[c]
AnPac Bio	CDA	–	PPCS[d,10]	–	–	–	–	26[e]
Ajinomoto Group	AICS	–	Mikami, 2019[11] AICS follow-up study[47] Suzuki, 2014[f,48]	–	–	–	–	6[g]

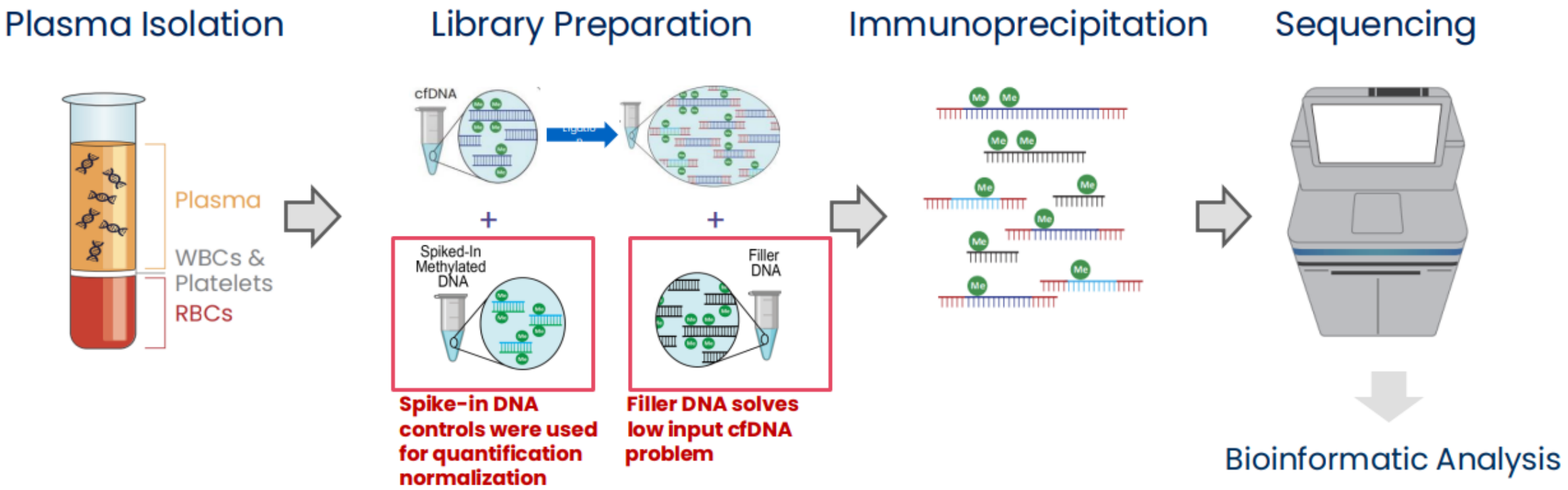
- Overall low quality data (high risk of bias)
  - No RCT
  - Limited follow-up duration and variable gold standard
  - Limited data in asymptomatic screening population > 50 years
  - Limited outcomes: Mortality, PROs, Harms.

Wade et al Health Technol Assess 2025;29(2)

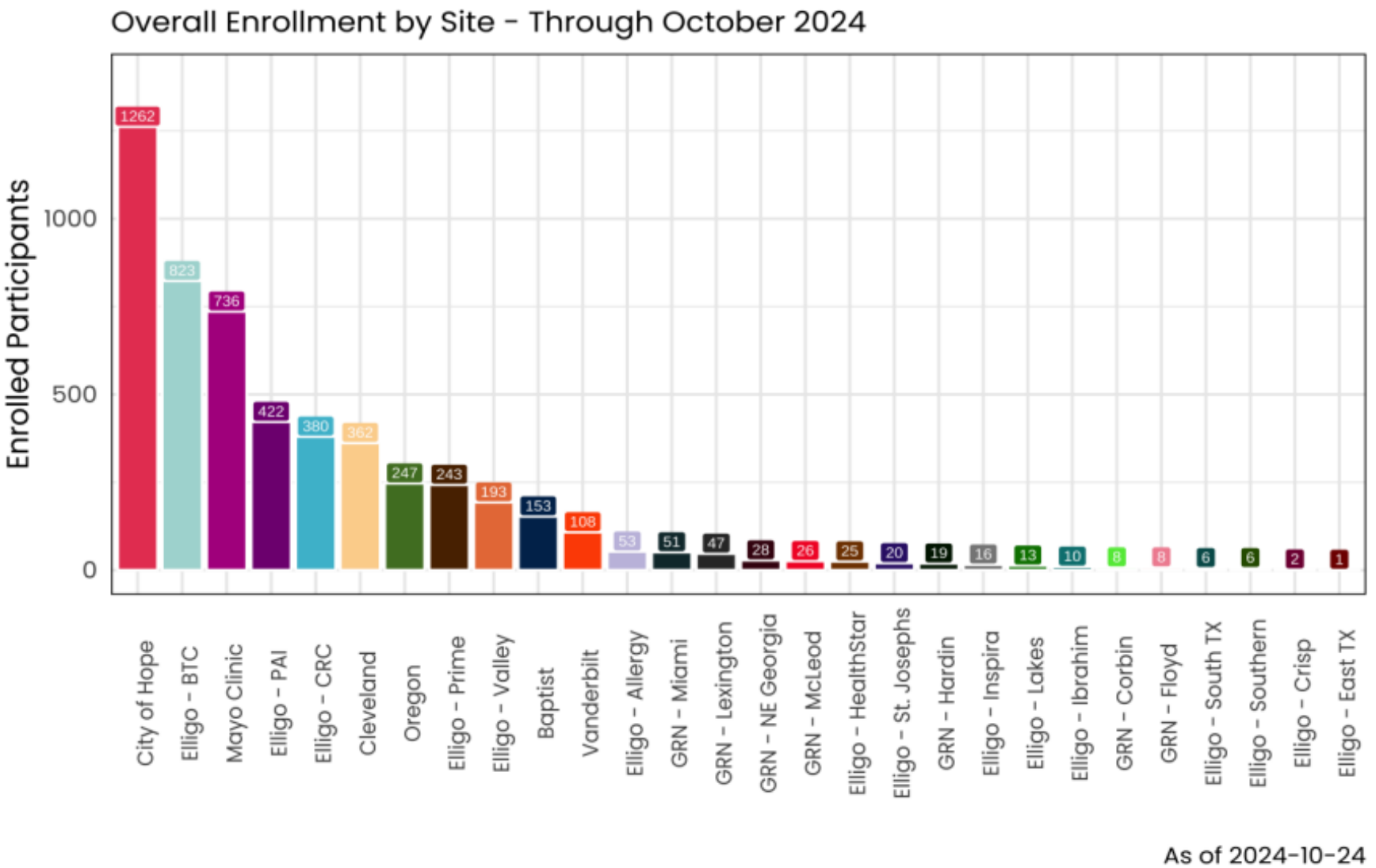
Adela Multi-Cancer Early Detection Blood Test (CAMPERR)

Genome-Wide Methylome Enrichment Platform Enables High Specificity for Recovery of Methylated cfDNA

Utilizes cfMeDIP-seq platform



CAMPERR Enrollment by Site



As of 2024-10-24

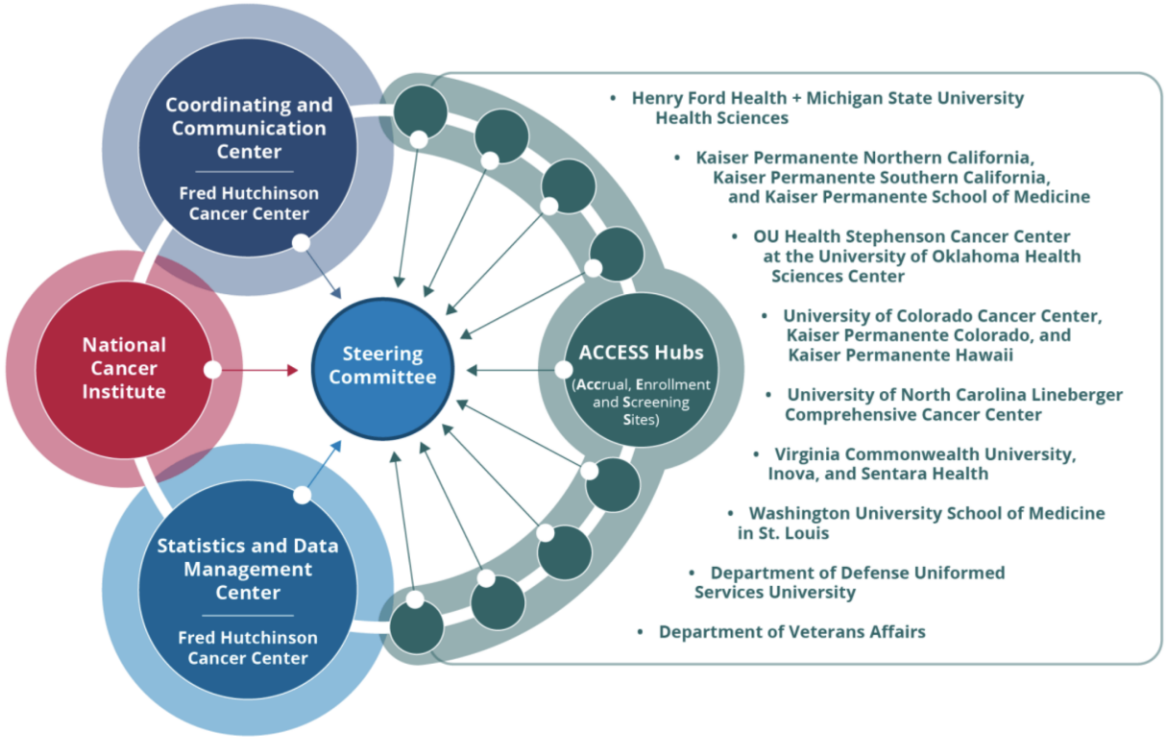
Cumulative Enrollment

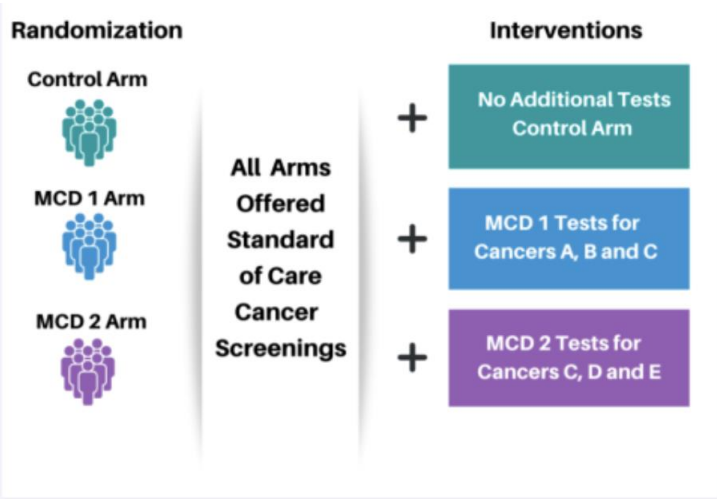
Month	Total
May - Dec 2022	2214
2023	4571
January 2024	4665
February 2024	4761
March 2024	4830
April 2024	4896
May 2024	4946
June 2024	5003
July 2024	5081
August 2024	5144
September 2024	5205
October 2024	**5264***

*Enrollment as of 24Oct2024

MCED Tests in Average Risk Populations

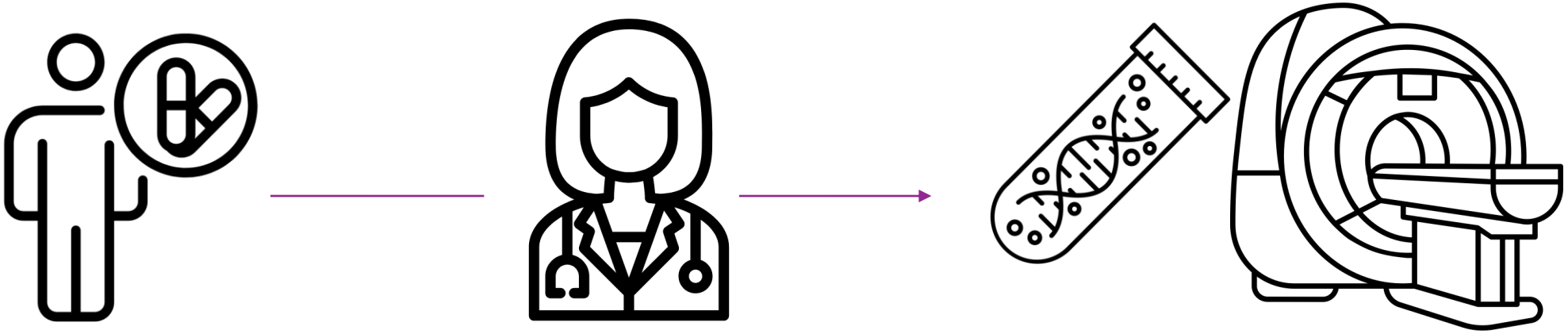
- NCI Cancer Screening Research Network Vanguard RCT
  - Goal 24,000 participants
  - 2 MCED Tests:
    - Guardant Health Shield Platform
    - Clear Note Health Avantect
  - 10 Cancer Types: Lung, breast, colorectal, prostate, bladder, ovarian, pancreatic, esophageal, liver and gastric.
  - Outcomes: Feasibility, Adherence, Cancer Incidence and Stage





Changing Care Delivery Paradigm in Medicine

Traditional



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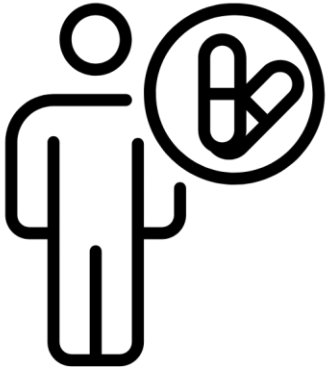

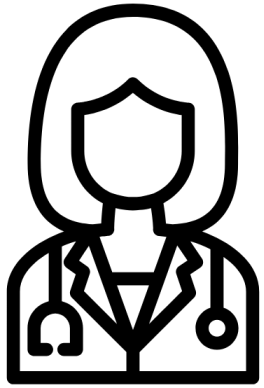

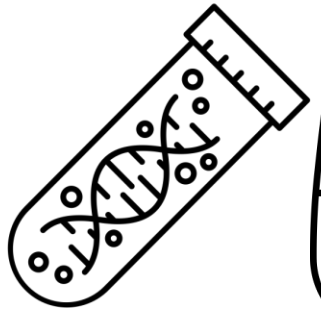

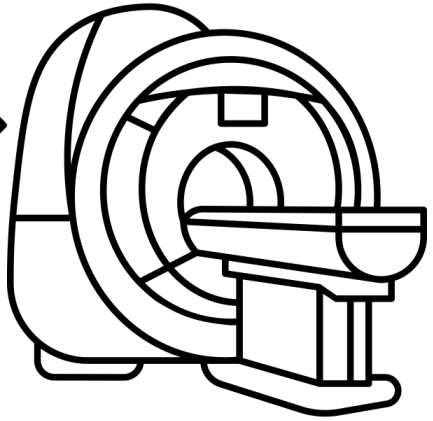

MCED Testing

(WB)MRI

How do patients and healthcare system navigate these two realms?

- ↓Tolerance for "Medical Paternalism"
- ↓ Faith in Public Health

Direct-to-Consumer

(testing may not have clear evidence-base nor indication)

Bottom Line

- Should MCEDs be used as an adjunct for evidence-based cancer screening?
  - Not yet at the population-level.
  - Can be considered on a per-patient basis.
- Core Issues:
  - No MCEDs are FDA-approved nor insurance covered.
  - No RCT data.
  - Lower sensitivity for early-stage disease.
  - False Positives and overall costs.
- Several Remaining Questions:
  - Overdiagnosis?
  - Lead-Time Bias?
  - Gold standard for diagnostic resolution after + screen? Insurance coverage?
  - Frequency of MCED administration?
  - 1° efficacy outcome: Late-stage cancer vs mortality (cancer-related vs all-cause)
  - Relevance in a hereditary cancer population?

MCED Tests in Hereditary Cancer Syndromes

- Do MCED Tests work in Hereditary Cancer?
  - Not clear: Different mechanisms of carcinogenesis between BRCA 1/2, Lynch, LFS etc
  - Prelim Evidence: LFS (Wong Cancer Discov 2024), NF1 (MPNST) (Cortes-Ciriano Cancer Discov 2023)

- CHARM Consortium (cfDNA in Hereditary and High-Risk Malignancies)
  - 8 genetics centers across Canada (Farncombe Am J Hum Genet 2023)
  - Patient acceptability: Benefits > Harms (Adi-Wauran Eur J Hum Genet 2023)
  - Provider acceptability: Optimists and Pessimists (Schick Oncologist. 2022)

- Dana Farber Experience
  - The INFORM Study – Prospective trial of 1,000 participants
    - Age ≥ 22 for patients with TP53 germline pathogenic variants, age ≥ 35 for all other variants in cancer predisposing genes (BRCA, ATM, NF1)
    - Age >45 for patients with family history of cancer
    - Test Performance (i.e. sensitivity, specificity) and Patient Experience

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MCED Testing and Inherited Susceptibility to Cancer

- Feasibility trial of patients undergoing MCED and Whole Body MRI (Raz DJ et al. Cancer. 2025 Jan 1;131(1).)
  - 33% with a germline pathogenic variant, 73% with at least two first degree relatives with cancer
  - Four patients found to have malignancy (Lung Adenocarcinoma (Stage T1BN0), Prostate Cancer (Stage T3aN0), Neuroendocrine Carcinoma of Duodenum (Stage T2bN1), Ovarian Mass (Brenner Tumor)
  - 98% of participants were satisfied with the research study

Stephen Gruber, MD

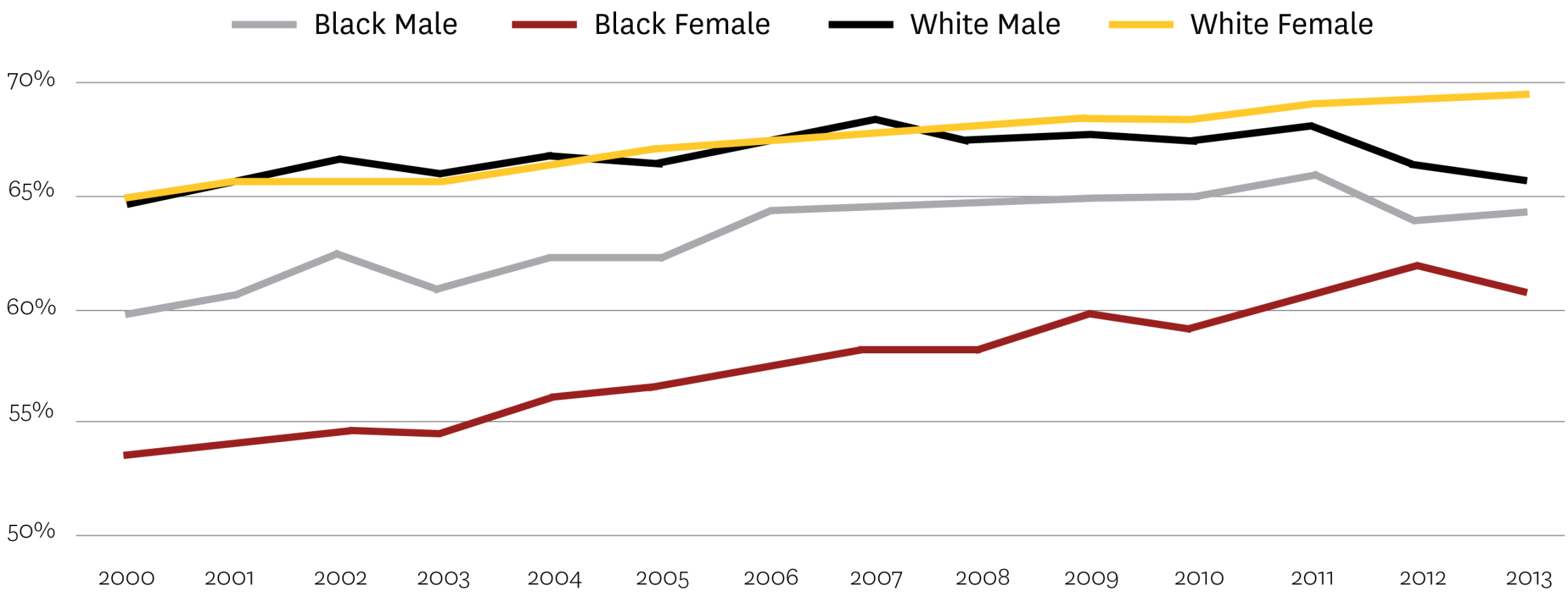
City of Hope just awarded new National Cancer Institute grant for Multi-Cancer Early Detection in those at high genetic risk

- Results are *not* returned to patients
- Purpose is to validate tests in high-risk individuals

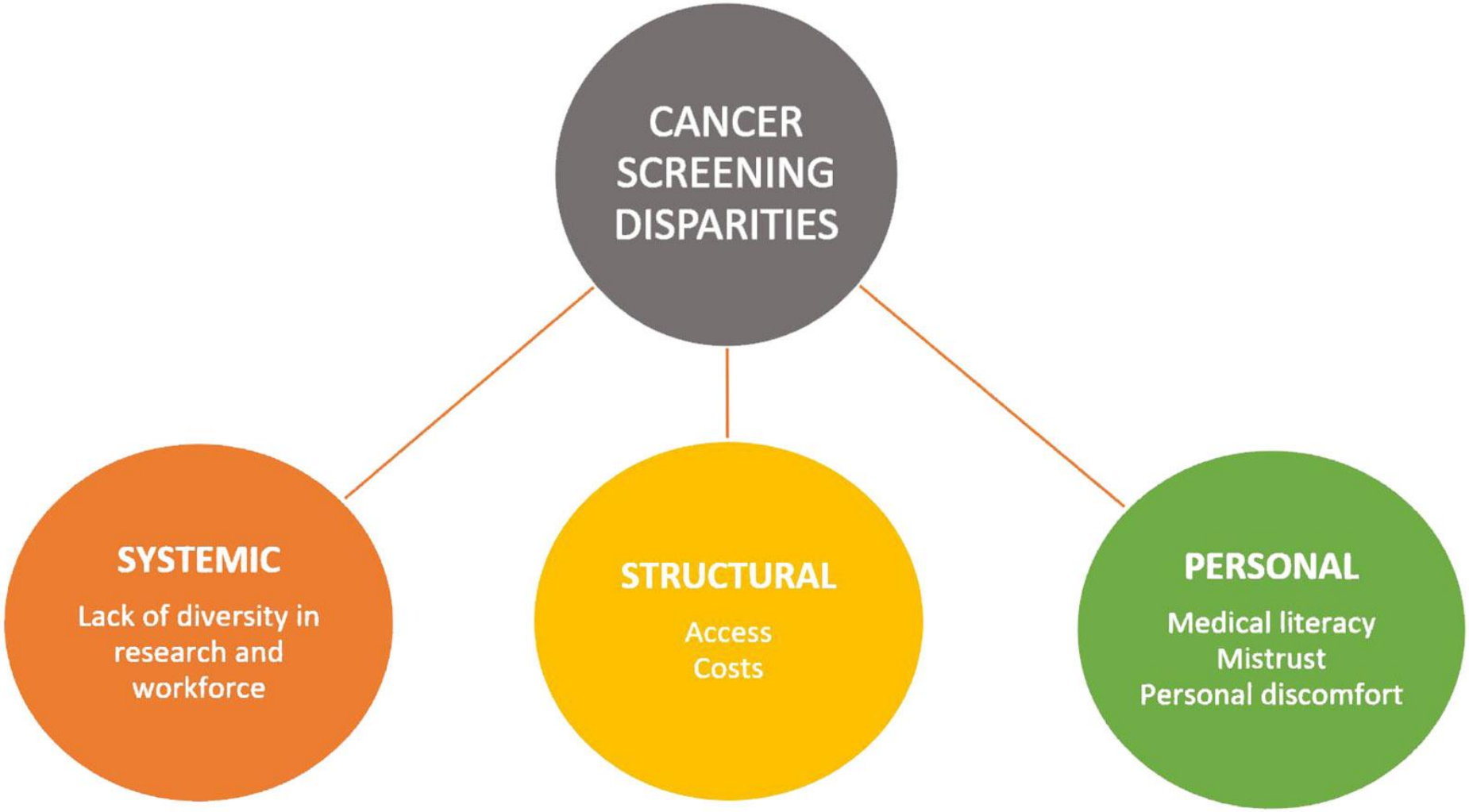
Health Disparities in Cancer Diagnosis

- Underserved groups (e.g., Black, Hispanic, and Indigenous populations) often experience later-stage cancer diagnoses due to barriers in access to screening and healthcare
- Lower screening prevalence of breast, cervical, and colorectal cancers was noted among individuals with low household income. (Benavidez GA et al. Prev Chronic Dis. 2021 18:E37)
- Colorectal cancer screening rates are significantly lower among Hispanic and other racial/ethnic minority groups. (May FP et al. Clin Gastroenterol Hepatol 2020 18:1796-804)
    - Implementation of the Affordable Care Act did not substantially change these disparities.
- Racial minorities and socioeconomically disadvantaged individuals are much less likely to obtain lung cancer screening. (Sosa E. et al. CA Cancer J Clin 2021 71:299-314)

Figure 1. Relative 5-Year Survival for all Cancer Sites (%) 2000-2013



Source: SEER*Explorer: An interactive website for SEER cancer statistics [Internet]. Surveillance Research Program, National Cancer Institute. [Cited 2021 April 15]. Available from https://seer.cancer.gov/explorer/.



Design Considerations

- Increase diversity of research participants
- Build trust with a diverse, culturally competent workforce and community engagement

Design Considerations

- Affordability of testing
- High test specificity

Design Considerations

- Navigation to follow-up testing and treatment, if positive result
- Build trust with diverse, culturally competent workforce and community engagement

Potential Impact of MCED Tests on Underserved and High Cancer Risk Populations

- How do MCED tests have the potential to address health disparities, particularly in underserved communities?
- What are the specific challenges in implementing MCED tests across different racial and socioeconomic groups?
- What is potential impact of MCED tests on those with an inherited susceptibility to cancer?
- What are the potential advantages of using MCED tests in high-risk populations compared to current standard screening methods for hereditary cancers?

Thank you!