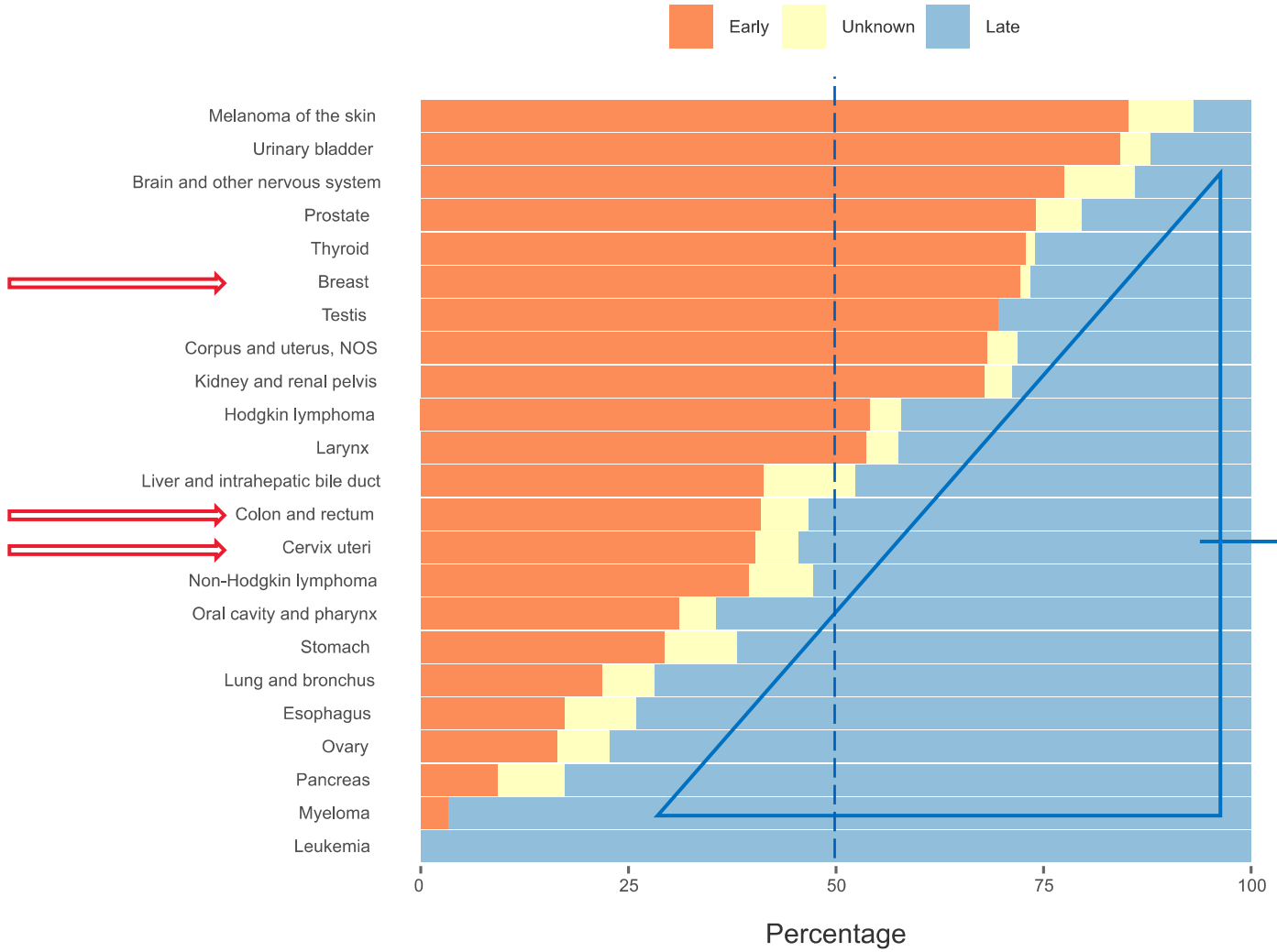
Guardant Health Approach to MCD Clinical Development

Craig Eagle, MD – Global Chief Medical Officer

28th October 2024

Percentage Distribution of Stage at Diagnosis by Primary Site among Pennsylvanians



Can these patients be shifted into early stage by enhancing current cancer detection methods (screening technology)?

Current screening program

Source: Pennsylvania Cancer Registry, 2018
For lymphomas, early is defined as stages I and II, and late is defined as stages II and IV.
Based on 2015 diagnoses

Source: Pennsylvania Cancer Registry, 2018 : https://www.health.pa.gov/topics/HealthStatistics/CancerStatistics/net-survival/Documents/2018/Documents/stage.aspx Accessed 01062022

MCD Development consideration

1. Complexity of “cancer”	Assess “cancer” or assess cancer-type
2. Test Accuracy	“Test validity” – Analytic / Clinical
3. Outcome	“Gold Standard” test & clinical outcome
4. Health resource impact	Current state versus future state
5. Public acceptance	Adherence/Acceptance to testing
6. Time	Data generation timing
7. Scalability	Infra-structure: MCED order to timely individual results
8. Resources	Sustainability/viability

ASSAY PERFORMANCE

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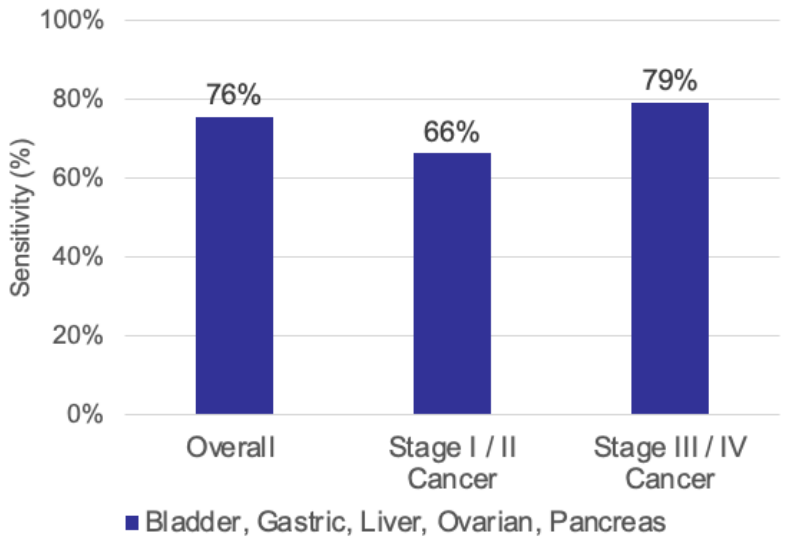
Guardant Health Approach

- Development of targeted MCD test Multi-cancer detection test development focused on analytical validity and clinical validity
  - Goal: Detect clinically relevant cancers with high accuracy while reduces the risk of false positives
- Partner with key stakeholders to understand implementation (e.g. downstream evaluations following a positive test, education on continued SOC screening in those with a negative test)
- Given the significant impact of detection of late-stage cancers, leverage surrogate endpoints like cancer detection rate and stage shift
  - Detecting cancer at any stage, prior to symptoms, will bring clinical benefit
- Leverage real-world evidence and data to address clinical trial execution gaps
  - e.g. LTFU, transfer of care

In the study cohort, this integrated, single device, multi-cancer test yielded overall sensitivity in bladder, gastric, liver, ovarian, and pancreas cancers was 75% (stage I/II: 66%) at 98% overall specificity.

Figure 3: Test Performance for non-Screening Cancers at 98% Specificity



He, AACR 2023 Annual Meeting

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PUBLIC IMPACT
PERFORMANCE

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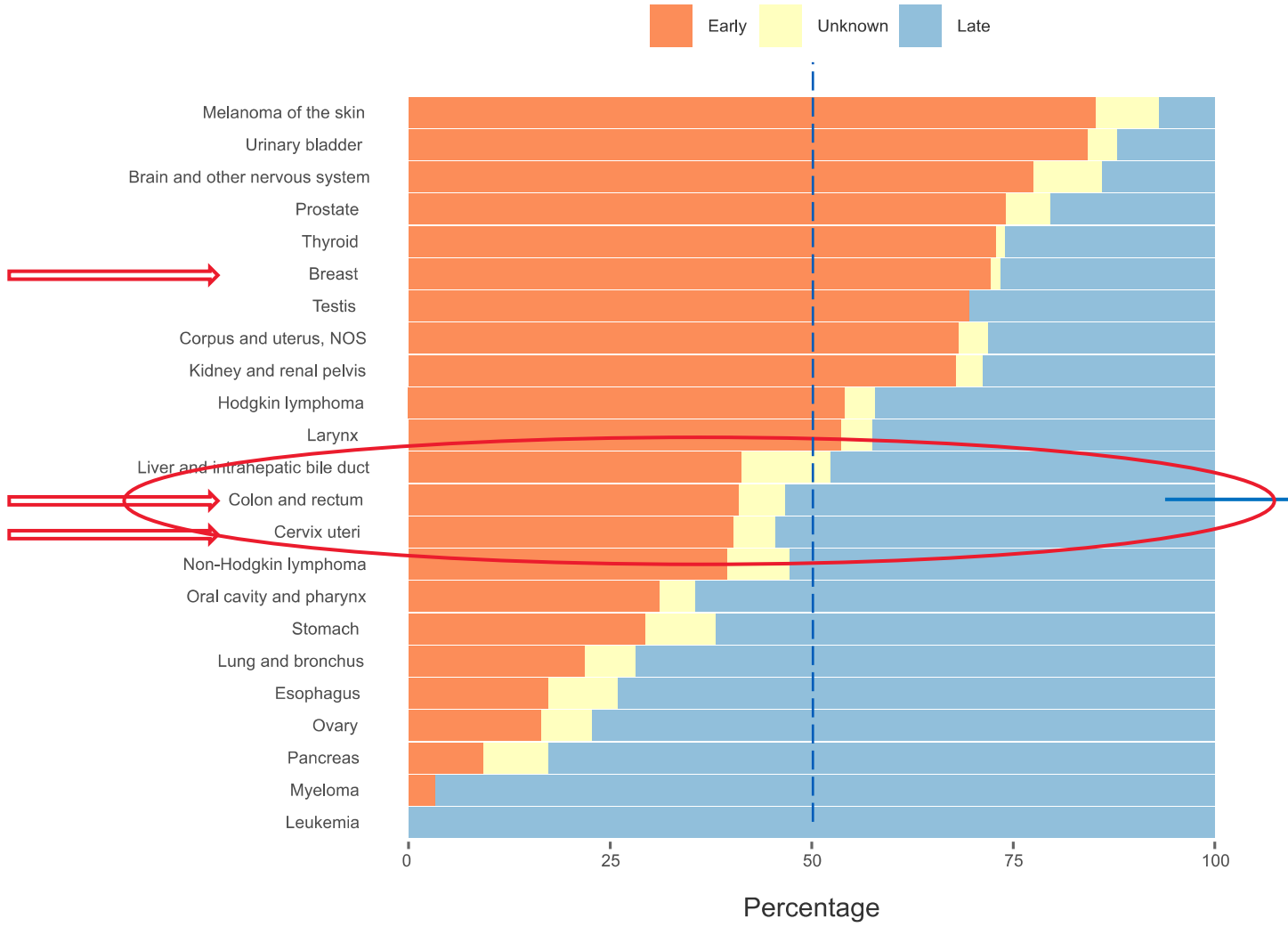

- 2nd leading cause of cancer deaths nationally[1]
- 50 million US Adults 45 – 75 Years Old Not Up To Date with CRC Screening[2]
- 75% of deaths in people not up-to-date[3]

Current screening program

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1. Siegel, 2024 ;
2. https://www.census.gov/library/visualizations/interactive/how-has-our-nations-population-changed.html
3. Doubeni 2019

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DATA & TEST EXECUTION

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Re-thinking approach to developing “clinical utility”

- Important to evaluate an MCD test in the intended use population (e.g. case-control of individuals with known diagnosis of cancer is informative in early test development, but not for final clinical validation)
  - Overall cancer specific mortality considered the “gold standard” for evaluation
- How to generate this data knowing:
  - For a population undergoing MCD testing, vast majority will have negative tests, similar to all cancer screening interventions, so cancer cases will be few
  - Approaches:
    - Enroll hundreds of thousands of participants and follow for several decads – Infeasible, long, expensive
    - Enrich population based on specific demographics (e.g. age, exposures, etc) – which demographics? How to execute?
    - Leverage real world data and evidence approaches – new and scary
    - Consider surrogate endpoints (e.g. cancer stage shift) – is this enough?

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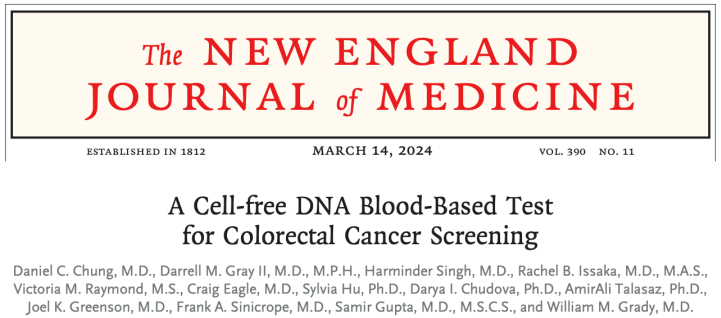
Multiple Data Requirements in Real World Setting

~2500/100, 000 cancer incidence[1]

Shield™ CRC Screening



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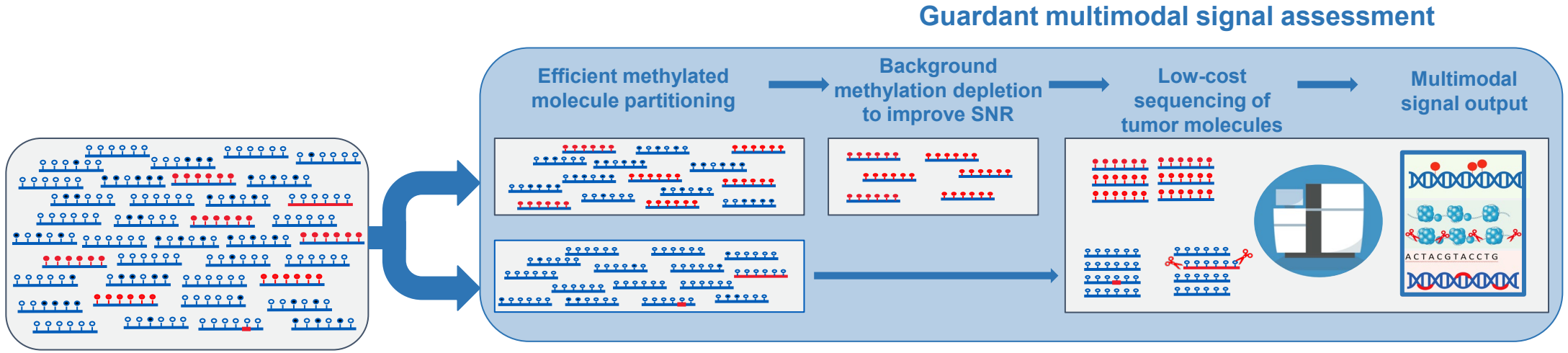
A Cell-free DNA Blood-Based Test for Colorectal Cancer Screening

Daniel C. Chung, M.D., Darrell M. Gray II, M.D., M.P.H., Harminder Singh, M.D., Rachel B. Issaka, M.D., M.A.S., Victoria M. Raymond, M.S., Craig Eagle, M.D., Sylvia Hu, Ph.D., Darya I. Chudova, Ph.D., AmirAli Talasaz, Ph.D., Joel K. Greenson, M.D., Frank A. Sinicrope, M.D., Samir Gupta, M.D., M.S.C.S., and William M. Grady, M.D.

De-identified and Linked to Available outcome databases



1. SEER*Explorer: An interactive website for SEER cancer statistics [Internet]. Surveillance Research Program, National Cancer Institute; 2024 Apr 17. [updated: 2024 Jun 27; cited 2024 Oct 28]. Available from: https://seer.cancer.gov/statistics-network/explorer/. Data source(s): SEER Incidence Data, November 2023 Submission (1975-2021), SEER 22 registries.

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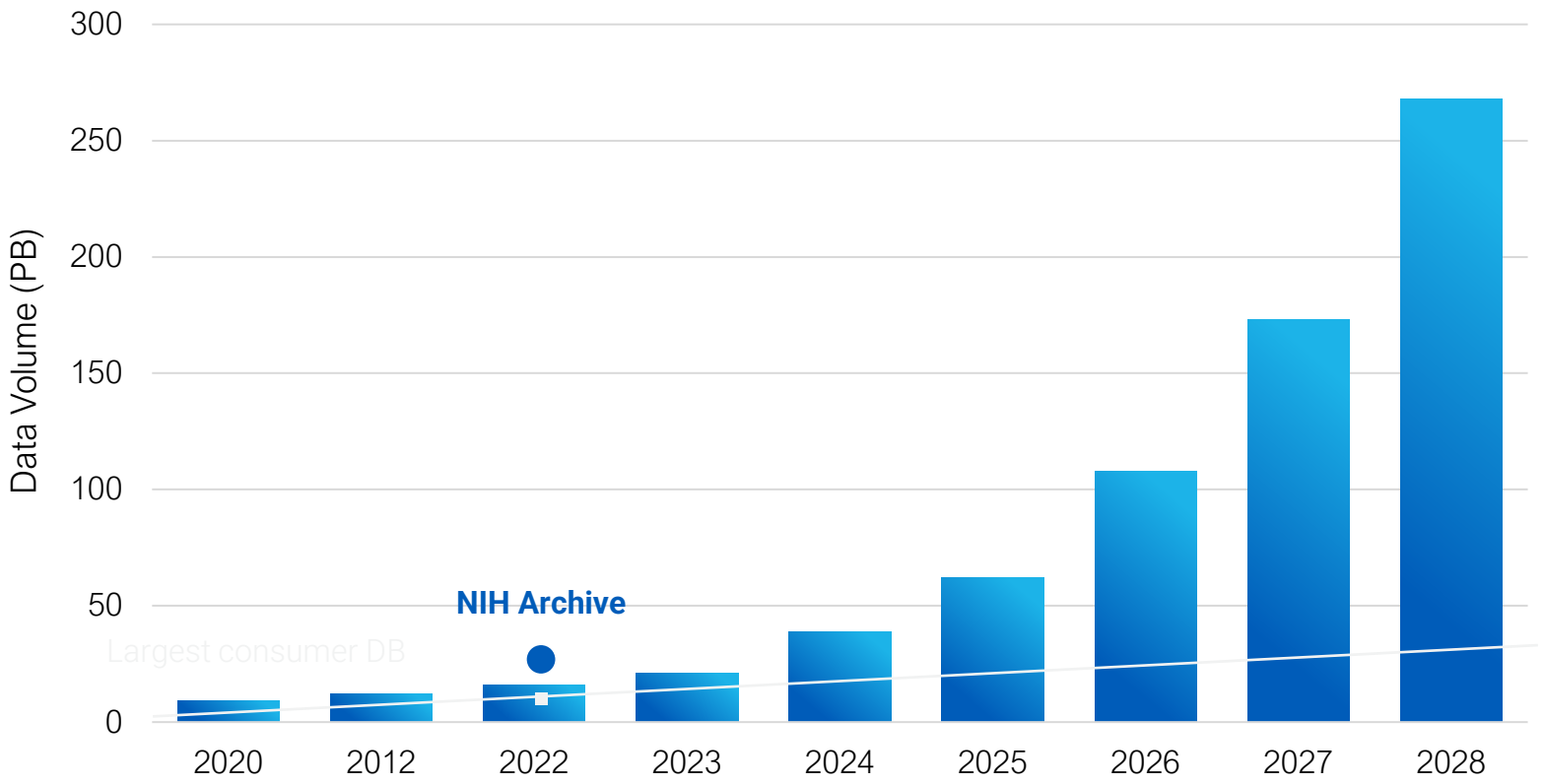
Data generation at scale

- Single Platform
- Scalable
- Cost-Efficient
- Configurable

Expecting to sequence millions of clinical samples per year across **average risk population** and **patients impacted by cancer**

Data growth powering research



18-month doubling rate

Guardant data growth is comparable to that of the largest NIH archive of genomic data

Source: NIH Archive and Guardant Health data on file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