P0463

Blood-based MCED Testing During Routine Colonoscopies to Enhance Early Detection of High-Mortality Gastrointestinal Cancers

Harbinger Health

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BACKGROUND

Colonoscopy is the gold standard for colorectal cancer screening in U.S. adults aged 45–75, driving over 15 million procedures annually.[1] However, non-colorectal gastrointestinal (GI) malignancies, such as gastric, pancreatic, and biliary cancers, lack population-based screening protocols despite stage-dependent survival benefits. Missed opportunities also arise from suboptimal adherence to guidelines in other cancers, including lung.

Blood-based multi-cancer early detection (MCED) tests offer the potential to expand cancer interception by detecting malignancies other than colorectal cancer at the time of colonoscopy. Embedding MCED testing into routine colonoscopy workflows leverages an established healthcare touchpoint to enhance early detection across a broader spectrum of GI and other high-mortality cancers.[2]

OBJECTIVES

The Cancer Origin Epigenetics-Harbinger Health (CORE-HH) study (NCT05435066) is a multi-cancer, prospectively enrolled case-control study that evaluated a blood-based multi-cancer early detection (MCED) test.

Using this study, we aimed to assess MCED performance that could be integrated into routine colonoscopy workflows to expand cancer interception beyond colorectal cancer to include hepatobiliary (liver, biliary tract), pancreatobiliary (pancreas, gallbladder), upper GI (esophagus, stomach, esophagogastric junction), head and neck, and lung cancers.

METHODS & MATERIALS

Peripheral blood samples (NCT05435066) were used to train predictive models on over 5,000 specimens, with blinded validation conducted in a mutually exclusive cohort of adults aged 45–75 (412 treatment-naïve cancer patients and 946 non-cancer controls).

A two-step testing workflow was applied: an initial low-cost assay optimized for sensitivity to identify cancer signal, followed by reflex testing with a broader biomarker panel for high-specificity and tissue-of-origin (TOO) classification.

We established the specificity (true negative rate), conventional sensitivity (probability of detecting a cancer signal regardless of tissue of origin), and intrinsic accuracy (probability of detecting the correct tissue of origin) of the MCED test across individual cancer types. Methods used are described in DiRienzo et al.[3] We used SEER22 data to model the distribution of test outcomes at the population level.[4]

RESULTS

Characteristics	Cancer (N=412)	Non-Cancer (N=946)
Sex		
Female	172 (41.7%)	520 (55.0%)
Male	240 (58.3%)	426 (45.0%)
Age (Years)		
Mean (SD)	65.5 (6.6)	62.0 (8.0)
(Min, Max)	45, 75	45, 75
Race		
White	334 (81.1%)	670 (70.8%)
Black or African American	27 (6.6%)	101 (10.7%)
Asian	6 (1.5%)	11 (1.2%)
American Indian or Alaska Native	3 (0.7%)	4 (0.4%)
Native Hawaiian or other Pacific Islander	4 (1.0%)	2 (0.2%)
Other Race	12 (2.9%)	10 (1.1%)
Unknown/Missing/Not reported	26 (6.3%)	148 (15.6%)
Ethnicity		
Not Hispanic/Latino	342 (83.0%)	751 (79.4%)
Hispanic/Latino	34 (8.3%)	49 (5.2%)
Unknown/Missing/Not reported	36 (8.7%)	146 (15.4%)

Table 1. Cohort demographics summary.

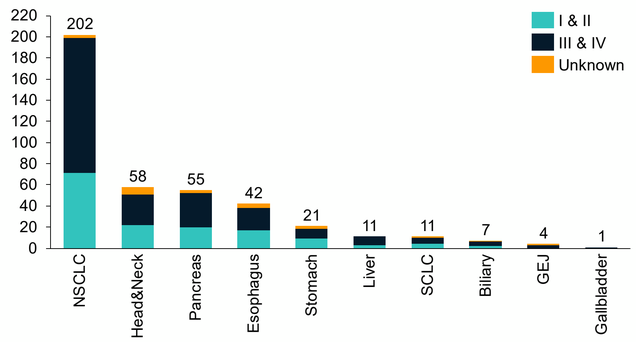

Figure 1. Distribution of cancer types and stages in the study. Vertical axis representing the total number of cases for each cancer type, stratified by stage

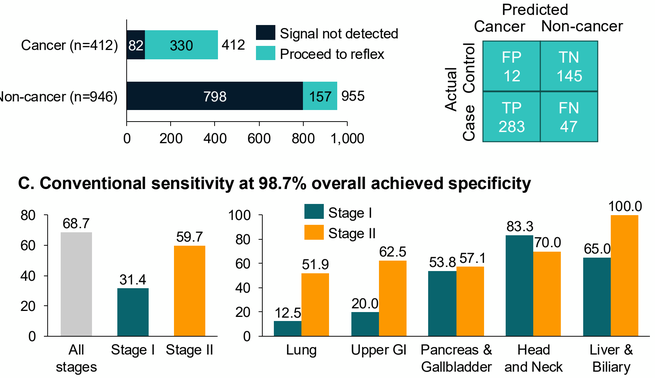

Figure 2. Performance of a sequencing liquid biopsy testing strategy for cancer detection. A. testing among 1,358 samples. B. Reflex test confusion matrix. C. The test achieved an overall sensitivity of 68.7% (283/412) and a specificity of 98.7% (934/946). Abbreviations: TP, true positive; FP, false positive; FN, false negative; TN, true negative.

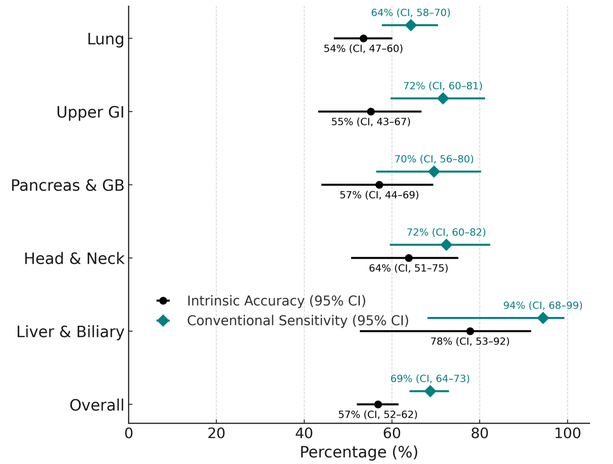

Figure 3. Conventional Sensitivity and intrinsic accuracy across cancer types with 95% confidence intervals (CI). Diamonds represent sensitivity (probability of cancer signal detection irrespective of TOO) and circles represent intrinsic accuracy (probability of correct TOO classification). Lines represent 95%CI. Results are shown for lung, upper GI, pancreas & gallbladder (GB), head & neck, liver & biliary, and overall performance, highlighting variability in test performance across cancer types in the context of gastrointestinal and related cancers.

DISCUSSION

- The 98.7% specificity achieved in this validation establishes a critical benchmark for population-scale screening, reducing the likelihood of false positives that drive unnecessary diagnostic workup, patient anxiety, and health system burden.
- The overall conventional sensitivity of 68.7%, with early-stage detection rates of 31.4% for stage I and 59.7% for stage II disease, underscores the potential of this blood-based MCED approach to intercept cancers at stages where outcomes are meaningfully improved. While early-stage sensitivities varied across cancer types, the ability to identify a measurable proportion of stage I–II hepatobiliary and pancreaticobiliary cancers, which are historically diagnosed late, represents an important advance for clinical gastroenterology practice. (Figure.2C)
- Intrinsic accuracy for TOO classification further highlights opportunities for clinical integration. High classification rates for hepatobiliary cancers (77.8%) and moderate accuracies across other GI and thoracic cancers provide meaningful information to guide diagnostic workup.
- In settings with low adherence to existing screening protocols, such as lung cancer, a blood-based signal even at somewhat lower sensitivity than LDCT may still provide meaningful clinical value if it increases uptake and ensures that more at-risk individuals receive follow-up.
- A modeled cohort of 100,000 tested individuals using SEER22 would detect the correct TOO for 28/49 pancreaticobiliary, 24/31 hepatobiliary, and 20/36 upper GI cancers, including 3/7, 11/14, and 2/10 stage I–II cases, respectively. The ability to correctly identify dozens of pancreaticobiliary, hepatobiliary, and upper GI cancers, including early-stage cases, illustrates the meaningful contribution this test could make when deployed alongside colonoscopy. By leveraging an established and widely utilized care setting, this approach provides a scalable pathway to expand interception beyond colorectal cancer, potentially improving survival outcomes and advancing health equity.

CONCLUSIONS

Opportunistic integration of this MCED into colonoscopy workflows extends the impact of established screening infrastructure to high-mortality cancers without routine surveillance. The sequential reflex strategy achieves high specificity and clinically meaningful early-stage detection, particularly for GI cancers and by augmenting lung screening in relevant populations. These findings highlight the promise of embedding this blood-based MCED into standard endoscopic care pathways, offering a scalable framework for earlier diagnosis, improved patient outcomes, and broader health equity.

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DISCLOSURES

This study was sponsored by Harbinger Health. Cambridge, MA

ACKNOWLEDGEMENTS

Editorial support was provided by Sean Husick (Harbinger Health, Cambridge, MA)
We gratefully acknowledge all participants for their contributions, without whom this research would not have been possible.

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