Erasmus School of Health Policy & Management

# Multi-Cancer Early Detection Tests: The Holy GRAIL or a Mirage in Future Cancer Control?

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## Background

- Cancer mortality in selected tumors can be improved by early detection at earlier stages of disease
- Multi-Cancer Early Detection (MCED) tests are developed, all based on single blood draws
- MCEDs (table 1) can detect 3-8 tumors, with one MCED (Galleri by GRAIL) testing for >50 cancers

In addition to clinical validation and utility, the objective of this qualitative study was to identify:

- For which cancers could MCEDs be relevant in four settings?
- What health system factors would be implementation?

| Test name (first author) | CancerSEEK (Cohen et al., 2018) | Pantum/EDIM (Grimm et al., 2013) | PanSeer (Chen et al., 2020) | Galleri (Klein et al., 2021) |
|---|---|---|---|---|
| Company name (country) | Exact Science (USA) | RMDM Diagnostics/ Zyagnum AG (Germany) | Singlera Genomics (USA) | GRAIL (USA) |
| Biological signal | Mutations and protein markers | Apo10 and TKTL1 in monocytes | DNA methylation | cfDNA methylation |
| Age range, years | 17-93 | 19-85 | 35-85 | >20 |
| % women | 51% | 46% | 34% | 55% |
| Number of cancer types | 8 | 3 | 5 | >50 |
| Sensitivity (number with cancer)* | 62% (1,005) | 97% (213) | 95% (98) | 52% (2823) |
| Tumor of origin accuracy | 83% | - | - | 89% |
| FPR* | 0.9% (812) | 4.0% (74) | 3.9% (207) | 0.5% (1,254) |

*Note.* Reprinted from "New genomic technologies for multi-cancer early detection: Rethinking the scope of cancer screening", by Hackshaw et al., 2022, Cancer Cell, 40(2), 109-113.
*For any cancer

**Table 1** I Examples of MCED tests being developed and validated

## Methods

*Approach*

- Four scenarios of MCED use were considered:


- Using cancer registries to determine population prevalence and positive predictive value
- 13 semi-structured interviews were conducted:
  - Selection using expert sampling, aiming for a broad representative group of individuals from different professional backgrounds.

*Interview and analysis*

- Identify determinants influencing viability and critical system factors of MCED use in these settings;
- Identifying key uncertainties related to the implementation of MCEDs in the Dutch healthcare system;
- Interviews were transcribed verbatim and analyzed using grounded theory and a thematic analysis approach (Gibbs, 2007);
- Findings were structured using a thematic networks approach (Attride-Stirling, 2001).

## Results

*Qualitative exploration of MCED use scenarios*

1. *Over-the-counter*:
   - Considered undesirable by all stakeholders as free availability to a low-risk, asymptomatic population will strain healthcare capacity.
2. *Population screening:*

❖ *As a primary screening test:*
- A broad MCED was questioned by most stakeholders due to low asymptomatic disease risk for many cancer types. A limited MCED is proposed potentially feasible.

❖ *As a complementary test to current population screening:*
- Considered by most stakeholders as a means to enhance screening specificity, reducing healthcare system strain by eliminating false positives.

3. *Primary care:*
   - No added value expected in this symptomatic population by many stakeholders due to the need for diagnostic imaging and pathology in cancer diagnosis
4. *Hospital diagnosis*

- Limited value in initial diagnostics foreseen by many stakeholders. Potential value in differentiating indolent and aggressive cancers, reducing patient burden, healthcare capacity strain, and costs

*The association between disease prevalence, sensitivity and predictive value*

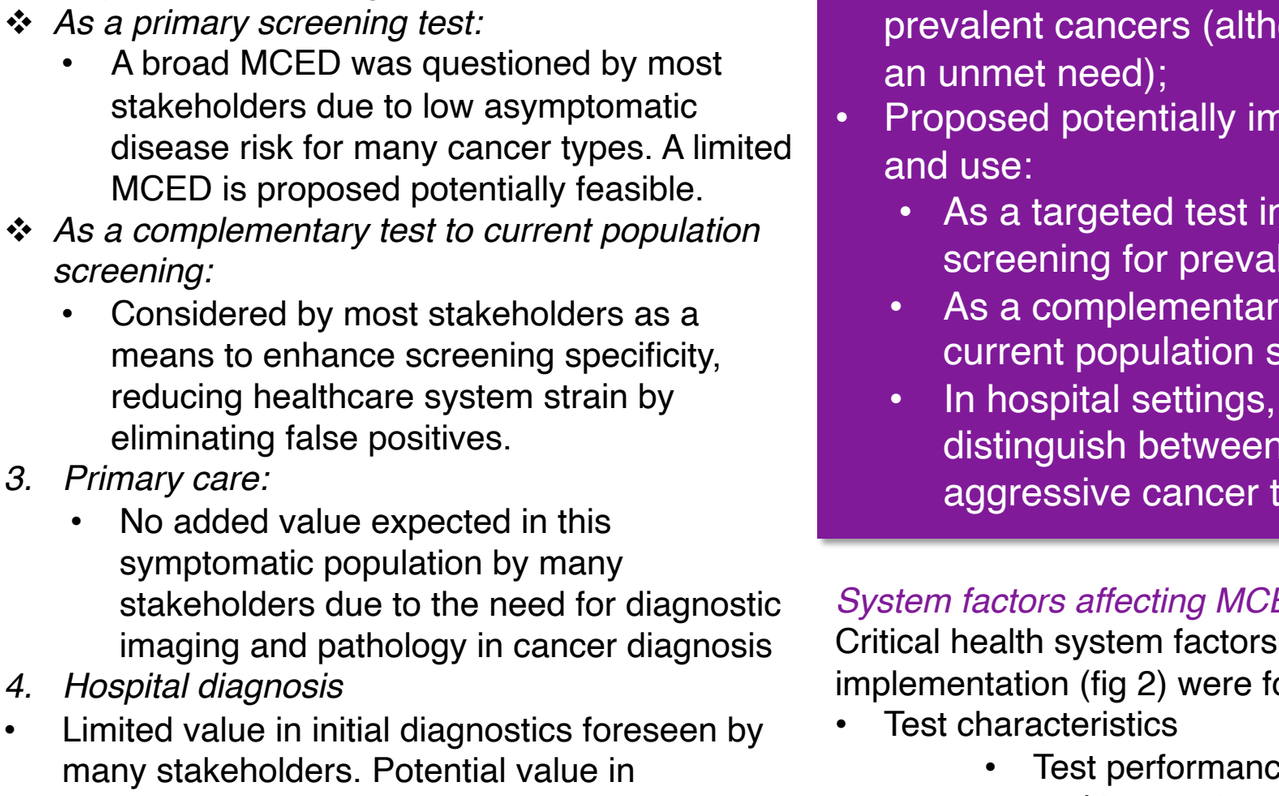


**Fig 1** I The association between disease prevalence and predictive value for MCEDs

## Conclusions

- Distinguish tumor informative from tumor agnostic assays as they may have different uses and stage dependent test performance;
- Cancer prevalence excludes feasibility of screening in low prevalent cancers (although there is an unmet need);
- Proposed potentially implementation and use:
  - As a targeted test in population screening for prevalent cancers,
  - As a complementary test in current population screening,
  - In hospital settings, to distinguish between indolent and aggressive cancer types.

*System factors affecting MCED feasibility*

Critical health system factors regarding MCED implementation (fig 2) were found to be:

- Test characteristics
  - Test performance (cancer type and tumor stage-specific)
  - Tumor informative properties
  - Ability to distinguish indolent cancers
- Cost-effectiveness
- Healthcare system capacity

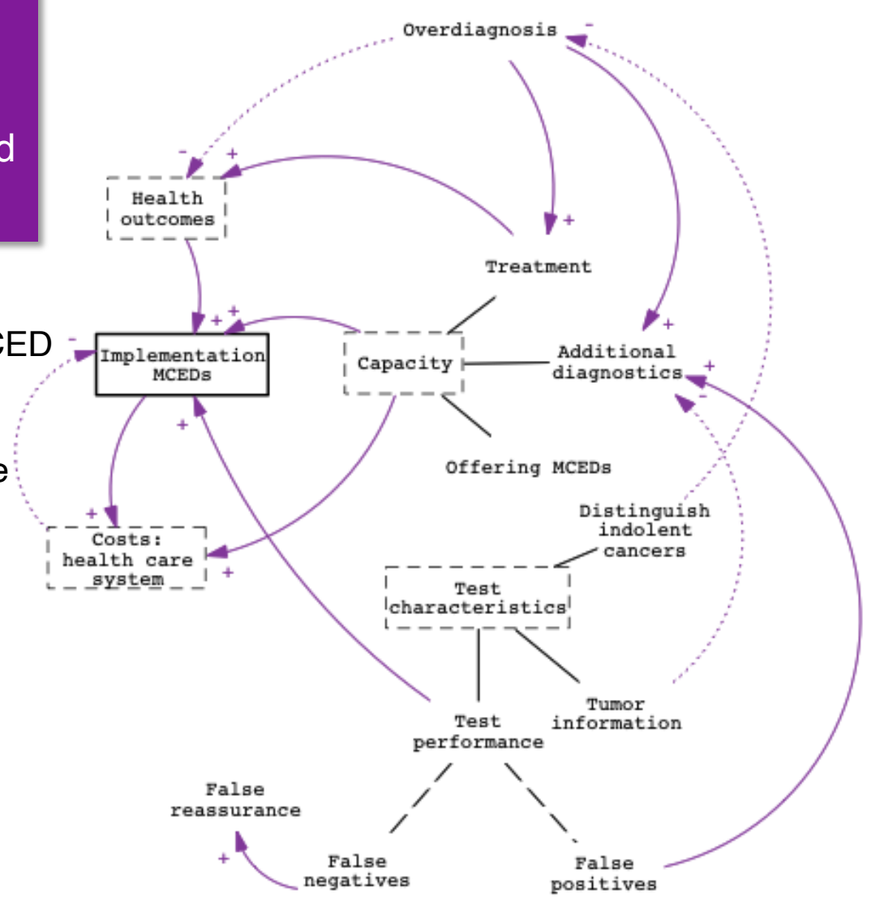


**Fig 2** I System map of factors affecting MCED feasibility across all scenarios

## References

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