Erasmus School of
Health Policy
& Management

Multi-cancer early detection:
A health systems perspective

Maarten J. IJzerman, PhD
University of Melbourne, Melbourne, Australia
Erasmus University Rotterdam, the Netherlands

Acknowledgments: Mussab Fagery, Hadi Khorshidi, Stephen Wong, Özge Karanfil, Lotte de With

Erasmus University Rotterdam

1

Conflicts of interest

- I do not receive an honorarium nor compensation of other expenses for participating in this panel

- I do not have any other conflicts of interest to declare

THE UNIVERSITY OF
MELBOURNE

2

Multi-Cancer Early Detection (MCED)

- MCEDs analysing methylations and mutations in cfDNA, miRNA and/or cancer proteins
  - Ability to identify Tissue of Origin (TOO)
- Designed with fixed false-positive rate to avoid cumulative false-positives
- Improved outcomes through stage shift, i.e. earlier detection a-symptomatic
  - Alternatively, TOO in CUPs

- **Where to use MCEDs and add value?** (de With *et al*, 2023)
  - Over the counter ⛔
  - Population screening ✅, but unlikely for all cancers due low prevalence
  - Primary care ✅, possible for ruling out, yet symptomatic in advanced stage
  - Hospital ⛔

THE UNIVERSITY OF MELBOURNE

3

MCEDs

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)

Adapted from: Hackshaw *et al*, 2021

4

Initial validation results (Galleri™)
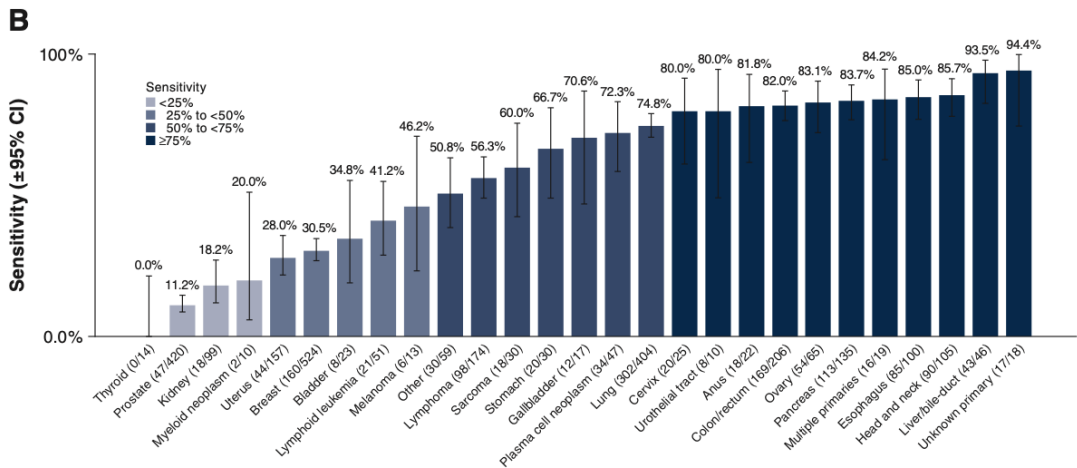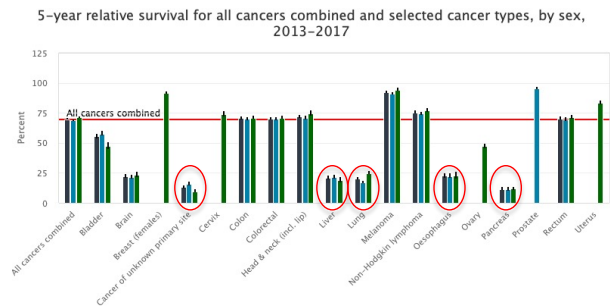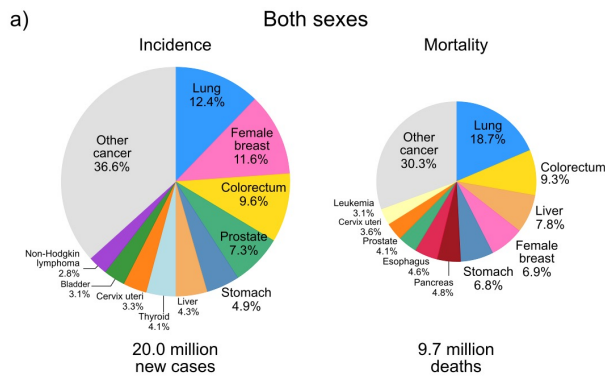

Klein *et al*. Annals Oncology, 2021
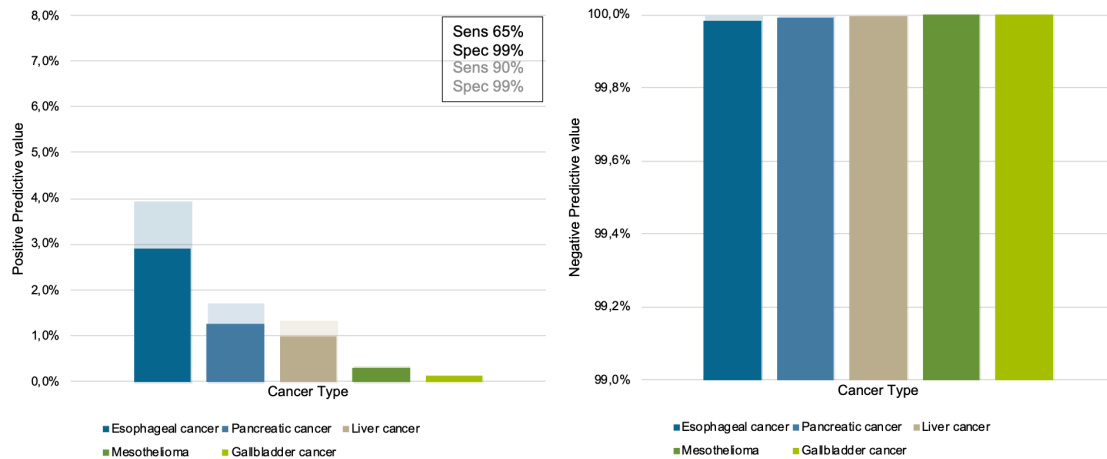
5

Deadly cancers (mortality vs. 5-year survival)

Bray et al, 2024

Source: Cancer Australia

6

A needle in a haystack?

Sens 65%
Spec 99%
Sens 90%
Spec 99%

Positive Predictive value — Cancer Type
Esophageal cancer · Pancreatic cancer · Liver cancer
Mesothelioma · Gallbladder cancer

Negative Predictive value — Cancer Type
Esophageal cancer · Pancreatic cancer · Liver cancer
Mesothelioma · Gallbladder cancer

7

Utility of screening multiple diseases?

- Low-dose CT screening for LC, COPD, CVD (Behr *et al*, Eur Radiology, 2022)
  - Population sharing the same risk factors
  - Probability of concurrent presence of diseases (e.g. probability CVD+LC)
  - Clinical utility of detection is different for LC, CVD, COPD

Table 2 Headroom analysis outcomes for a screening population of current and former smokers between 50 and 75 years old

Diseases screened*	Patients with disease	Incremental disease management costs (€ per screened individual)	Effectiveness gap (incremental QALY per screened individual)	Incremental MAC (€ per screened individual) WTP: €20 k/QALY	WTP: €80 k/QALY
LC+CVD+COPD	155,966	−14	0.048	971	3,844
LC+CVD	136,752	−12	0.044	895	3,546
LC+COPD	43,666	−37	0.009	230	809
LC	13,262	−37	0.004	113	341

8

4

Cancer screening and participation rates

Tumor	Eligible population	A$ per screen	Policy	Participation rates
Breast cancer	3,590,050	A$ 59	50-74, once in 2 years	
Colorectal cancer	6,090,980	A$ 65	50-74, once in 2 years	
Cervical Cancer	6,859,061	A$ 35	25-74, once in 5 years	
Lung Cancer	580,000	A$ 299	To commence 2025	

1 A$ = 0.65 US$

MCED test approximately A$1,500 (US$ 949)
Lung cancer screening for people aged 50-70, no symptoms and at least 30 pack-years

BreastScreen AUSTRALIA
A joint Australian, State and Territory Government Program

NATIONAL BOWELCANCER SCREENING PROGRAM

NATIONAL CERVICAL SCREENING PROGRAM
A joint Australian, State and Territory Government Program

9

Cancer screening and participation rates

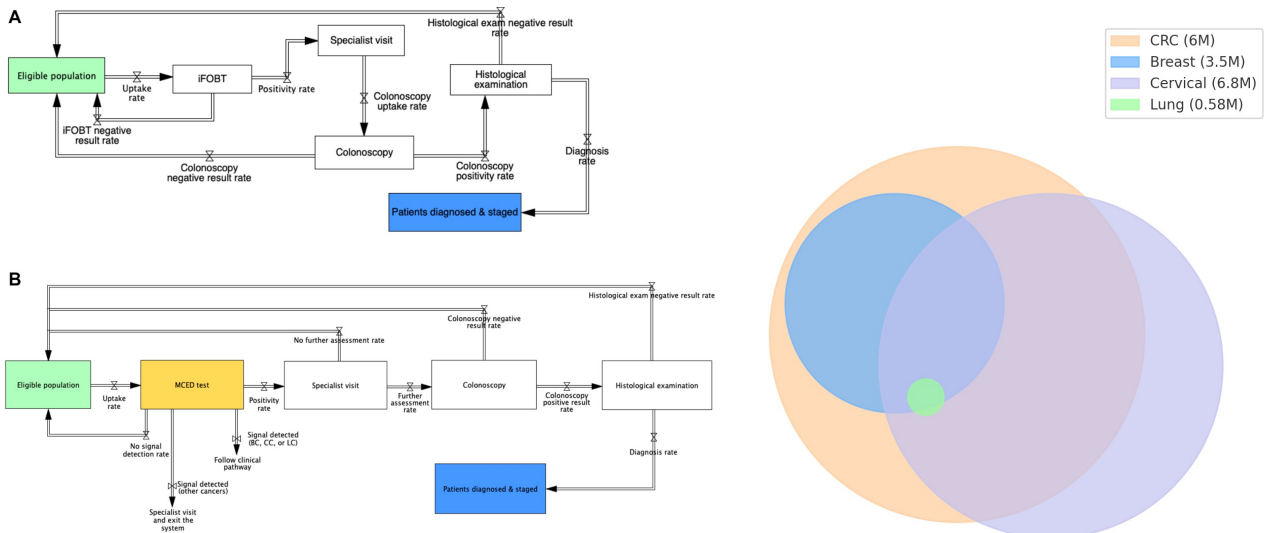| Tumor	Eligible population	A$ per screen	Policy	Participation rates
Breast cancer	3,590,050	A$ 59	50-74, once in 2 years	47.5%
Colorectal cancer	6,090,980	A$ 65	50-74, once in 2 years	40.9%
Cervical Cancer	6,859,061	A$ 35	25-74, once in 5 years	62.4%
Lung Cancer	580,000	A$ 299	To commence 2025	60%

1 A$ = 0.65 US$

MCED test approximately A$1,500 (US$ 949)
Lung cancer screening for people aged 50-70, no symptoms and at least 30 pack-years

BreastScreen AUSTRALIA
A joint Australian, State and Territory Government Program

NATIONAL BOWELCANCER SCREENING PROGRAM

NATIONAL CERVICAL SCREENING PROGRAM
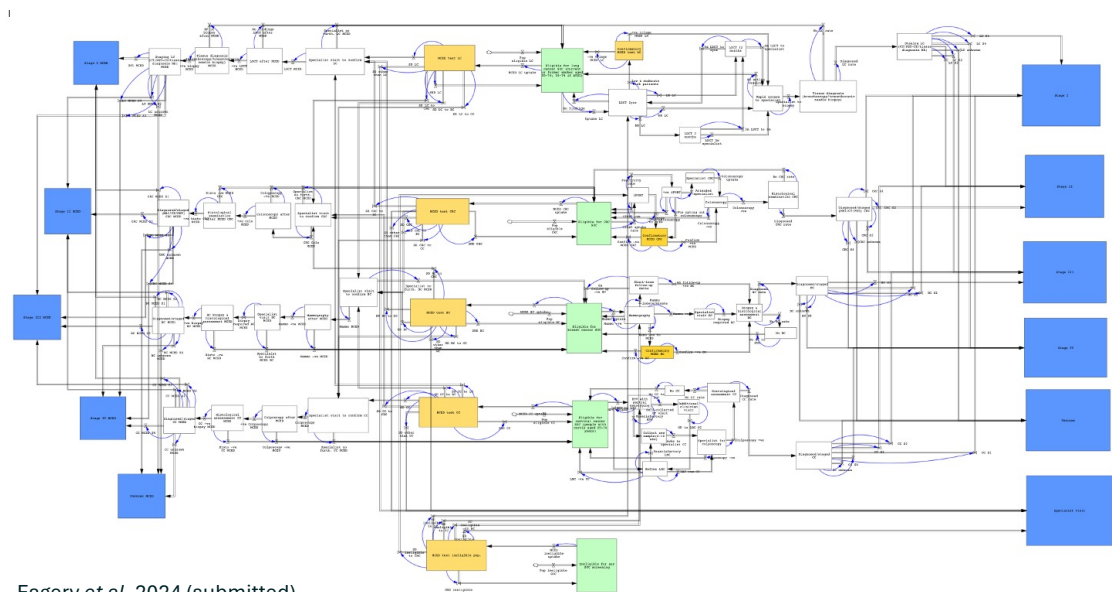A joint Australian, State and Territory Government Program

10

Complementing SoC screening
non-participants and overlapping target populations

Fagery *et al*, Pharmacoeconomics Open, 2024

11

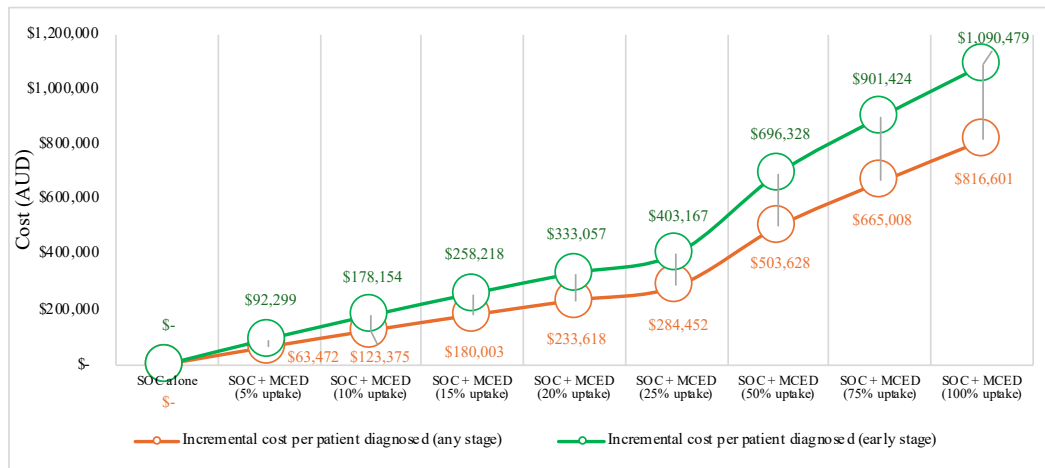# A systems dynamics approach

Fagery *et al*, 2024 (submitted)

12

Results for varying uptake rates

1 A$ = 0.65 US$

13

Conclusions

- MCED targeting non-participants, assuming 25% uptake of MCED
  - Aggregate detection rate increases from 18.5% to 21.3% (+729 patients)
  - 400k A$ / early detected case
  - Population budget impact is 2,9 billion A$
    - Total cost of cancer care approximately 10 billion A$

Points for discussion
- Utility and improved outcomes in high volume cancers only?
- SOC participation rates are low, why not increase participation?
- Is offering MCED testing an incentive for SoC screening non-participation?
- Will non-participants adhere to MCED if not opting for SOC screening?
- Overdiagnosis (non-lethal cancers); value of knowing remains controversial

14

Literature

- De With, L de, Multi-Cancer Early Detection Tests: The Holy GRAIL or a Mirage in Future Cancer Control? Presented European Cancer Summit, November 2023, Brussels, Belgium
- Fagery M, et al Integrating Multi-Cancer Early Detection (MCED) Tests with Standard Cancer Screening: System Dynamics Model Development and Feasibility Testing. Pharmacoeconomics Open, October 2024 (online)
- Hubbell, E., et al., Modeled Reductions in Late-stage Cancer with a Multi-Cancer Early Detection Test. Cancer Epidemiol Biomarkers Prev, 2021. 30(3): p. 460-468.
- Tafazzoli, A., et al., The Potential Value-Based Price of a Multi-Cancer Early Detection Genomic Blood Test to Complement Current Single Cancer Screening in the USA. Pharmacoeconomics, 2022. 40(11): p. 1107-1117.
- Neal, R.D., et al., Cell-Free DNA-Based Multi-Cancer Early Detection Test in an Asymptomatic Screening Population (NHS-Galleri): Design of a Pragmatic, Prospective Randomised Controlled Trial. Cancers (Basel), 2022. 14(19)
- Klein, E.A., et al., Clinical validation of a targeted methylation-based multi-cancer early detection test using an independent validation set. Ann Oncol, 2021. 32(9): p. 1167-1177
- Cohen, J.D., et al., *Detection and localization of surgically resectable cancers with a multi-analyte blood test*. Science, 2018. 359(6378): p. 926-930
- Hackshaw, A., et al., 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, 2021. 125(10): p. 1432-1442
- Lavaze, P et al., Combined population genomic screening for three high-risk conditions in Australia: a modelling study. eLancet, December 2023
- Behr CM et al., Can we increase efficiency of CT lung cancer screening by combining with CVD and COPD screening? Results of an early economic evaluation. European Radiology, 2022, May;32(5):3067-3075