Multi-cancer detection tests for population-wide screening of asymptomatic individuals

A systematic review of prospective evidence

MCD SPOTLIGHT
EVALUATING THE POTENTIAL OF MULTI-CANCER DETECTION TESTS IN AUSTRALIA

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KEY TAKE-AWAYS

Our **comprehensive systematic review** of international evidence on MCD tests for screening of asymptomatic populations found that MCD tests can detect some cancers, but also miss many, especially early-stage cancers. False-positive results commonly outnumber detected cancers and can trigger prolonged diagnostic journeys.

Whether MCD testing improves population health will depend not only on test performance, but on who is tested, how results are acted upon, and the local healthcare context.

Full paper here

WHO ARE WE?

MCD Spotlight | 2025–2030

A collaborative transdisciplinary research program asking:

What is the potential of MCD tests for screening people without cancer symptoms in Australia?

Our work:
- Consolidates international evidence
- Maps potential healthcare pathways
- Evaluates benefits, harms and costs
- Creates a Roadmap for future policy and practice

WHAT DID WE DO?

Define research questions
Evidence on performance of MCD tests for cancer screening, including diagnostic pathways, acceptability, and potential harms.

Search global databases
Medline, Embase, and Cochrane Library to 1 Feb 2026

Identify relevant studies
Cohort studies, fully-paired cohort studies, and RCTs, with focus on blood-based MCD tests and studies in primarily asymptomatic adults.

Extract relevant data
Pre-specified outcomes, considered separately for "interventional" and "observational" cohort studies.

Assess critically
Risk of bias assessment using QADAS-2 tool

Synthesize & Report

EVIDENCE LANDSCAPE

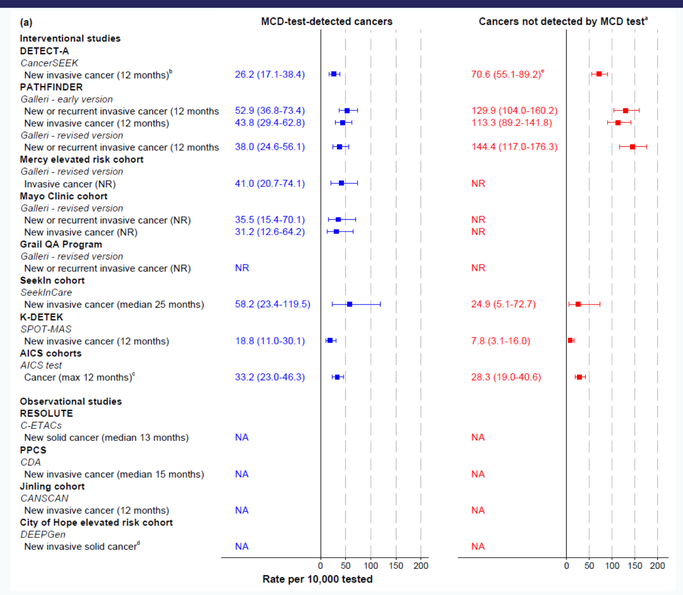
2723 screened titles/abstracts → 132 screened full-text articles → 18 articles included *12 not in previous reviews*

18 articles on 12 unique studies, 9 MCD tests

5 countries:
- USA
  - CancerSEEK
  - DEEPGen
  - Galleri
- China
  - CANSCAN
  - CDA
  - SeekIn
- Japan
  - AICS
- India
  - C-ETACs
- Vietnam
  - SPOT-MAS



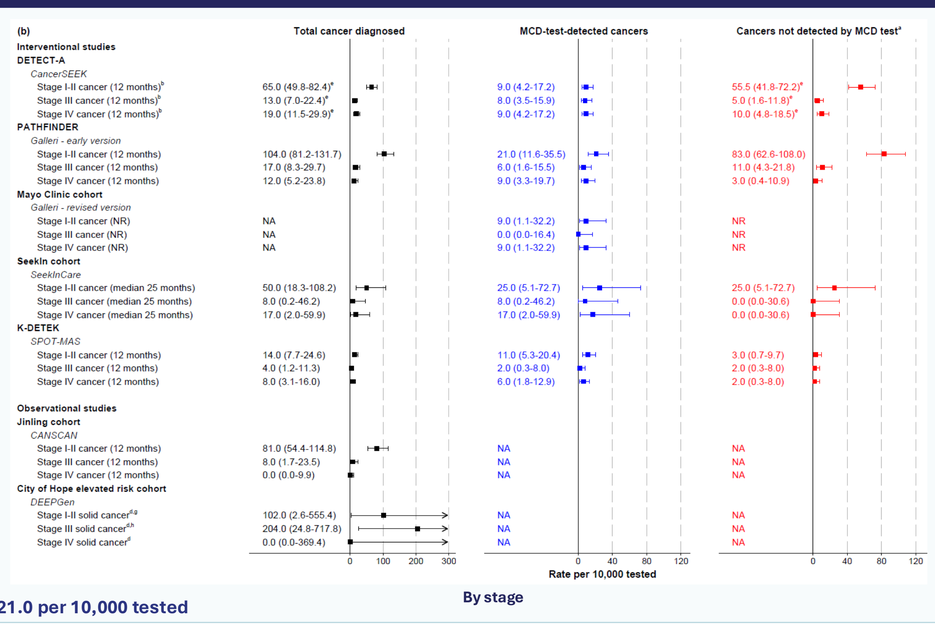
KEY RESULT 1 | CANCER YIELD VARIED MARKEDLY ACROSS STUDIES



All stages

Results – Cancer Detection Rates

The number of cancers detected per 10,000 people varied greatly, likely reflecting heterogeneity from different MCD tests, investigation processes, and study populations (e.g. different ages, risk levels, background standard-of-care-screening)



By stage

MCD-detected new invasive cancers (12 months): 18.8–43.8 per 10,000 tested | Stage I–II (12 months): 9.0–21.0 per 10,000 tested

KEY RESULT 2 | FALSE-POSITIVES OUTNUMBER CANCERS DETECTED

Study	MCD test	PPV (95% CI)	CSO prediction correct: Most likely site	CSO prediction correct: 1st or 2nd mostly likely site
DETECT-A	CancerSEEK (early)	19.4% (13.1-27.1%)	NA	NA
PATHFINDER	Galleri (early)	38% (28.8-48.3%)	85% (69.9-93.6%)	97% (85.1-99.8%)
	Galleri (refined)	43.1% (31.2-55.9%)	84% (65.3-93.6%)	88% (70.0-95.8%)
Mercy (high-risk)	Galleri (refined)	NR	NR	NR
Mayo Clinic	Galleri (refined)	NR	88%	88%
GRAIL QA Program^	Galleri (refined)	49.4% (43.2-55.7%)	NR	NR
K-DETEK	SPOT-MAS	39.5% (26.4-54.4%)	NR	53% (31.0-73.8%)
SeekIn	SeekInCare	10.9% (4.5-21.2%)	NR	43% (NR)
AICS	AICS	NR	NA	NA
RESOLUTE	C-ETACs	3.5% (1.6-6.5%)^^	NA	NA
PPCS	CDA	7.8% (2.2-18.9%)^^	NA	NA
Jinling	CANSCAN	20.7% (12.9-30.4%)^^	47%#	68%#
City of Hope (high-risk)	DEEPGen	0^^	NA	NA

^PPV based on 211 participants with positive MCD test, diagnostic investigations completed, and asymptomatic at MCD test
^^ calculated by review team using data reported in included articles. CSO: Cancer Signal Origin. #of all test-positive invasive cancers

KEY RESULT 3 | DIAGNOSTIC JOURNEYS

Study	DETECT-A	PATHFINDER	Mercy (high-risk)	GRAIL QA Program^	K-DETEK
Time to diagnostic resolution (median months [IQR])					
All people with positive MCD test (N)	NR	**2.6 [1.2-7.3]** (N=90)	NR	NR	**0.4 [<0.1-6.2]** (N=43)
Positive MCD test & cancer detected (N)	**4 [2-7]** (N=15)	**1.9 [1.1-4.8]** (N=33)	**0.9 [0.1-6.8]** (N=11)	**1.4 [0.7-3.1]** (N=115)	**<0.1 [<0.1-6.2]** (N=17)
Positive MCD test, no cancer detected (N)	NR	**5.4 [1.5-8.3]** (N=57)	NR	NR	**0.4 [<0.1-1.5]** (N=26)

^ only reported for subset of participants with positive MCD test who were asymptomatic, had complete investigations and diagnosis available (n=115); noting no follow-up information was available for 552/1,011 participants with positive MCD test.

Median time to diagnostic resolution short in several studies, but 75th percentile often higher – means some participants can experience prolonged diagnostic journeys.
Only 4 of 8 interventional studies detailed pre-specified or suggested diagnostic pathways (consolidated in this review to support future research).

NO STUDY HAD OVERALL LOW RISK OF BIAS

Study type and outcomes	Study and MCD test (articles)	Risk of bias (QUADAS-2): Participant selection[a]	Index test[b]	Procedures (as relevant to outcome)[c]	Flow and timing[d]	Overall[e]
Interventional studies, outcomes of i) rates of cancers detected by MCD test, ii) MCD test positive predictive value (PPV), and iii) MCD test false-positive rates.	DETECT-A - CancerSEEK (Lennon 2020 & 2024)	Low	Low	Low	Unclear	Unclear
	PATHFINDER - Galleri (Schrag 2023)	Low	Low	Low	Unclear	Unclear
	Mercy elevated risk - Galleri (Semenkovich 2024)	Low	Low	Unclear	High	High
	Mayo Clinic - Galleri (Hurt 2025)	Low	Low	Low	High	High
	Grail QA Program - Galleri (Matrana 2025)[f]	Low	Low	Unclear	Unclear	Unclear
	K-DETEK - SPOT-MAS (Nguyen 2025)	Low	Low	Low	Unclear	Unclear
	SeekInCare (Li 2025)	Low	Low	Unclear	Unclear	Unclear
	AICS (Mikami 2019)	Low	Low	Unclear	High	High
Interventional studies, outcomes of i) rates of cancers not detected by MCD test and ii) MCD test negative predictive value (NPV).	DETECT-A - CancerSEEK (Lennon 2020 & 2024)	Low	Low	High	Low	High
	PATHFINDER - Galleri (Schrag 2023)	Low	Low	High	Low	High
	Mercy elevated risk - Galleri (Semenkovich 2024)	NA	NA	NA	NA	NA
	Mayo Clinic - Galleri (Hurt 2025)	NA	NA	NA	NA	NA
	Grail QA Program – Galleri (Matrana 2025)	NA	NA	NA	NA	NA
	K-DETEK - SPOT-MAS (Nguyen 2025)	Low	Low	High	Low	High
	SeekInCare (Li 2025)	Low	Low	High	Unclear	High
	AICS (Mikami 2019)	Low	Low	High	Unclear	High
Observational studies	RESOLUTE - C-ETACs (Ranade 2021)	Low	Low	High	High	High
	PPCS - CDA (Xie 2022)	Low	Low	High	Unclear	High
	Jinling - CANSCAN (Bao 2025)	Low	Low	Moderate	Low	Moderate
	City of Hope - DEEPGen (Raz 2025)	Low	Unclear	Unclear	Low	Unclear

% participants with positive MCD test not undergoing diagnostic investigations not reported or >10%; or limited details on diagnostic investigations

cancers diagnosed through screening or symptoms under-estimate total cancers present

CONCLUSIONS

WHAT WE KNOW
✓ MCD tests can detect some cancers
✓ Miss many cancers (especially early-stage)
✓ False-positive results would create substantial burden of diagnostic investigations

WHAT WE DON'T KNOW
? Impact on cancer progression and mortality
? Equity of access and outcomes
? Optimal implementation pathways

WHAT WE NEED
Randomised trial outcomes • long-term follow-up • paired test comparisons • research on equity, implementation, health economic impacts

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Learn more

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The Daffodil Centre
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