P184

Modelled Impact of a Multi-Cancer Early Detection Screening Programme on the Demand for Diagnostic Endoscopy in England

British Society of Gastroenterology Conference 2025, 23–26 June 2025 Glasgow

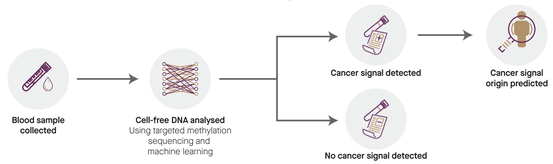
Andrew Millar[1,*], Ewan Gray[2,†], Katharine Halliday[3], Willie Hamilton[4], Sara Hiom[2], David A. Jones[2], Joanne Martin[5], Sean McPhail[6], Libby Ellis[2]

[1]Royal Free London NHS Foundation Trust; [2]GRAIL Bio UK, Ltd.; [3]Nottingham University Hospitals NHS Trust; [4]University of Exeter; [5]Queen Mary University of London; [6]National Disease Registration Service, NHS England. *Presenting author. †Affiliation at time of writing.

INTRODUCTION

- Multi-cancer early detection (MCED) tests screen simultaneously for two or more cancer types using a biological specimen, e.g., blood, to detect cancer signals before symptomatic presentation and diagnosis in usual care.[1–3]
- The clinical utility of one blood-based MCED test (Galleri®; GRAIL, Inc., Menlo Park, CA, USA) for population screening in asymptomatic individuals aged 50–79 years in England is being assessed in the NHS-Galleri trial (NCT05611632).[1]
  - Detection of a methylation pattern associated with cancer by this MCED test is returned as a cancer signal detected (CSD; 'positive') test result (**Figure 1**).
  - Further analysis is performed to predict the tissue type or organ associated with the cancer signal (cancer signal origin; CSO).

Figure 1. Mechanism Of The Galleri Multi-Cancer Early Detection (MCED) Test.



- Modelling has predicted that an MCED screening programme could reduce late-stage (stage III and IV) cancer incidence by 201 (40%) in every 100,000 persons, and cancer mortality by 74 (17%) in every 100,000 persons.[4]
  - For example, net survival for gastrointestinal cancers decreases with increasing stage, particularly between stages III and IV;[5,6] thus, detection of gastrointestinal cancers at an earlier stage could have substantial survival benefits.
- To realise these benefits, people for whom a cancer signal is found need timely, appropriate diagnostic investigation and subsequent treatment and care.

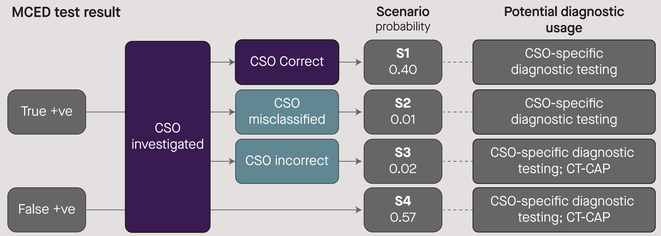
OBJECTIVE

- To model the likely demand for diagnostic modalities, including endoscopy, relative to current national usage in England if screening using the Galleri MCED test was offered alongside current screening.

METHODS

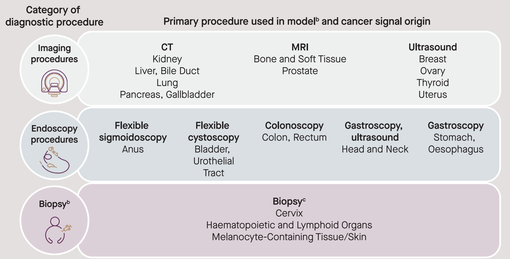
- We used a decision tree model (**Figure 2**) to predict diagnostic use by modality, with the following inputs:
  1. estimates of the volume of people who would be referred for diagnostic investigation due to a CSD test result if an MCED screening programme was introduced in England, based on performance data for the Galleri MCED test[7];
     - The predicted proportion of CSD test results when using the MCED test for asymptomatic screening was 1.4%.[7]
     - The distribution of true and false positives was based on the positive predictive value of the MCED test (43.1%).[7]
  2. estimates of the distribution of CSOs in the screened population, based on the inferred distribution and accuracy of the predicted CSO reported by the MCED test.
- The primary diagnostic modality used to investigate any given CSD result was determined by the predicted CSO.
  - To identify the primary diagnostic investigation(s) that would likely be undertaken for each CSD result, we mapped each of the 18 possible CSOs to standard-of-care diagnostic procedures in England, using existing clinical guidance and expert clinical input (**Figure 3**).
- Diagnostic use was estimated for two scenarios:
  1. an initial (prevalent) screening round following the addition of MCED screening to current screening programmes, representing a population aged between 50 and 79 years attending their first screen;
  2. an established (steady-state) annual screening programme, representing a population in which individuals enter an MCED screening programme at 50 years of age and participate in annual MCED screening until 79 years of age.
- We compared predicted diagnostic usage with current total annual usage using routine NHS datasets, including the NHS Monthly Diagnostic Waiting Times and Activity data set for 2023–24.
- Predicted diagnostic usage associated with MCED screening is reported for every 1 million people screened, as a scalable metric.

Figure 2. Decision Tree Model Showing Potential Diagnostic Resource Use Following Cancer Signal Detected Multi-Cancer Early Detection (MCED) Test Results.



'CSO misclassified' means that the predicted CSO was incorrect but the diagnostic test led to detection of a different cancer type. CSO: cancer signal origin; CT-CAP: computed tomography of the chest, abdomen and pelvis.

Figure 3. Map of Multi-Cancer Early Detection (MCED) Test Cancer Signal Origins (CSOs) To Diagnostic Procedures Used In This Study[a].



[a]Standard of care investigation would also likely include a blood test for all suspected cancer types, with the possible exception of bone.
[b]One primary procedure was included in the model for all CSOs except head and neck, which has two; this is due to the diverse anatomical locations included in this CSO.
[c]Biopsy results not reported. CT: computed tomography; MRI: magnetic resonance

KEY RESULTS: INTRODUCTION OF MCED SCREENING IS LIKELY TO RESULT IN A SMALL INCREMENTAL INCREASE IN ENDOSCOPY PROCEDURES

- For every 1 million persons screened, there would be an estimated 14,000 CSD results referred for diagnostic investigation (at a 1.4% CSD rate).
- Following the initial introduction of MCED screening, the greatest relative increases in diagnostic usage for every million persons screened were for colonoscopy (0.49%, ~3000 additional procedures compared to current annual usage) and gastroscopy (0.28%, ~2000 additional procedures; **Table 1**).
- In a steady-state MCED screening programme, the increases in usage for colonoscopy and gastroscopy were attenuated to 0.16% (~1000 additional procedures) and 0.10% (~700 additional procedures), respectively.
- The greatest absolute increase in diagnostic usage for every million screened was in CT (0.16%, ~13,000 additional procedures following initial introduction of MCED screening; 0.06%, ~5000 in a steady-state MCED screening programme).
- The more substantial relative increases in the use of colonoscopy and gastroscopy compared with other diagnostic modalities are due in part to the greater prevalence of and relatively high sensitivity of the MCED test for gastrointestinal cancers.
  - For example, 23% of all CSD results in the initial screening round had a colorectal CSO.

Table 1. Predicted Change In Diagnostic Activity For Every One Million Screened Following Initial Introduction Of A Multi-Cancer Early Detection (MCED) Screening Programme And In A Steady-State MCED Screening Programme In England.

Diagnostic modality	Total activity (n) in England (2023-24)[a]	Initial introduction of an MCED screening programme		Steady-state MCED screening programme	
		Annual activity (n) with MCED screening[b]	Percentage change (%) in total annual activity[c]	Annual activity (n) with MCED screening[b]	Percentage change (%) in total annual activity[c]
Colonoscopy	656,100	3180	0.49	1040	0.16
Gastroscopy	723,200	2010	0.28	700	0.10
CT	8,221,600	13,180	0.16	4720	0.06
Cystoscopy	344,600	300	0.09	99	0.03
Flexible sigmoidoscopy	200,900	87	0.04	35	0.02
Ultrasound	8,267,800	2880	0.03	1070	0.01
MRI	4,346,300	380	0.01	180	<0.01

[a]Data presented to the nearest hundred. [b]Data presented to the nearest ten (or nearest unit when <100). [c]Data presented to two decimal places. CT: computed tomography; MRI: magnetic resonance imaging.

CONCLUSIONS

- Assuming the modelled parameters are accurate, there is likely to be a small initial increase in diagnostic endoscopy if an MCED screening programme was offered alongside current screening programmes in England in the future; this increase is likely to persist to a lesser extent in the long term.
- Endoscopy services are currently under strain in England, with activity increasing year-on-year (12–15% annual increase in procedures from 2017 to 2019[8]).
  - The estimated increase associated with MCED screening is incremental compared to these increases.
- If MCED screening was introduced, annual testing would likely result in cancers being diagnosed asymptomatically in earlier years rather than diagnosed symptomatically in later years, bringing at least some diagnostic events forward and potentially preventing others. However, our model did not account for future reductions in diagnostic activity in the longer term.
- Other tests, such as the faecal immunochemical test (FIT), may also support diagnostic decision making following a CSD MCED test result; however, it is not yet clear how other diagnostic or triage tests might integrate into diagnostic pathways for MCED screening.
- This study contributes to a small but growing evidence base that will support diagnostic workforce and resource planning for the potential addition of MCED screening to current screening programmes in future.

References

1. Neal, R.D. et al. *Cancers* 2022, 14, 4818.
2. Brito-Rocha, T. et al. *Cells* 2023, 12, 935.
3. Clarke, C.A. et al. *Clin Transl Sci.* 2024, 17, e70016.
4. Sasieni, P. et al. *Br J Cancer* 2023, 129, 72–80.
5. McPhail, S. et al. *Br J Cancer* 2015, 112 (Suppl 1), S108–115.
6. NHS England. Available online: https://digital.nhs.uk/data-and-information/publications/statistical/cancer-survival-in-england/cancers-diagnosed-2016-to-2020-followed-up-to-2021/cancer-survival-by-stage
7. Schrag, D. et al. *Lancet* 2023, 402, 1251–1260.
8. Ravindran, S. et al. *Frontline Gastroenterol.* 2021, 12, 451–460.

Disclosures

L.E., D.A.J., and S.H. are employees of GRAIL Bio UK, Ltd., and hold stock in GRAIL, Inc. E.G. was previously employed by GRAIL Bio UK, Ltd. K.H. is President of the Royal College of Radiologists. J.M. is National Specialty Advisor for Pathology for NHS England. A.M. is an investigator on the Rapid Diagnostic Centre Biomarker Research Study (RDC-Bio), sponsored by the Royal Marsden Hospital NHS Foundation Trust. W.H. and S.M. have nothing to declare.

Acknowledgements

Writing and editorial assistance provided by Emma B. Saxon (London, UK). Graphic assistance provided by PosterDocs (Oakland, CA, USA). This work uses data that has been provided by patients and collected by the NHS as part of their care and support. The data are collated, maintained and quality assured by the National Disease Registration Service, which is part of NHS England.