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NHS-Galleri Trial Design: Equitable Study Recruitment Tactics For Targeted Population-Level Screening With a Multi-Cancer Early Detection (MCED) Test

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INTRODUCTION

- Cancer is the second leading cause of death globally[1,2] with over 10 million deaths attributed to 29 cancer types in 2019.[3]
- In the US and UK, cancer screening, including for breast, cervical and bowel cancer, has been shown to reduce cancer mortality through earlier detection, which allows for more effective treatment.[4,5]
- Yet, many cancers are detected late (stages III and IV), and a limited number of single-cancer screening programmes exist (breast, cervical and bowel/colorectal cancer screening in the UK and US, and lung cancer in high-risk individuals in the US).[4–7]
- Screening attendance is also lower in certain groups, including those with greater socioeconomic deprivation, despite healthcare being free at the point of access in the UK via the National Health Service (NHS).[8–10]
- A blood-based multi-cancer early detection (MCED) test (Galleri®) uses targeted methylation signals from cell-free DNA (cfDNA)[11,12] shown to detect a shared cancer signal from more than 50 different cancer types, and predict a cancer signal of origin to direct diagnostic workup.[13]
- The pragmatic, prospective, partially blinded (see *Study Design Overview*), randomised, controlled NHS-Galleri trial (ISRCTN91431511) is the first of its kind, designed to see if there is a clinical benefit to population screening with this MCED test.
  - It utilises multiple strategies to optimise study recruitment, with the goal of enrolling a diverse and representative sample.

OBJECTIVES

- The primary objective is to demonstrate a significant reduction in the absolute numbers of stage III and IV cancers diagnosed in the intervention arm compared with the control arm.
- Key secondary objectives, including MCED test performance, safety, the impact of MCED test use on healthcare resource utilisation for cancer diagnosis and treatment, the potential impact of overdiagnosis, and cancer-specific mortality will be assessed after trial follow-up.
- Exploratory endpoints include assessing the primary and secondary objectives by participant age, sex, level of social deprivation, and ethnicity.

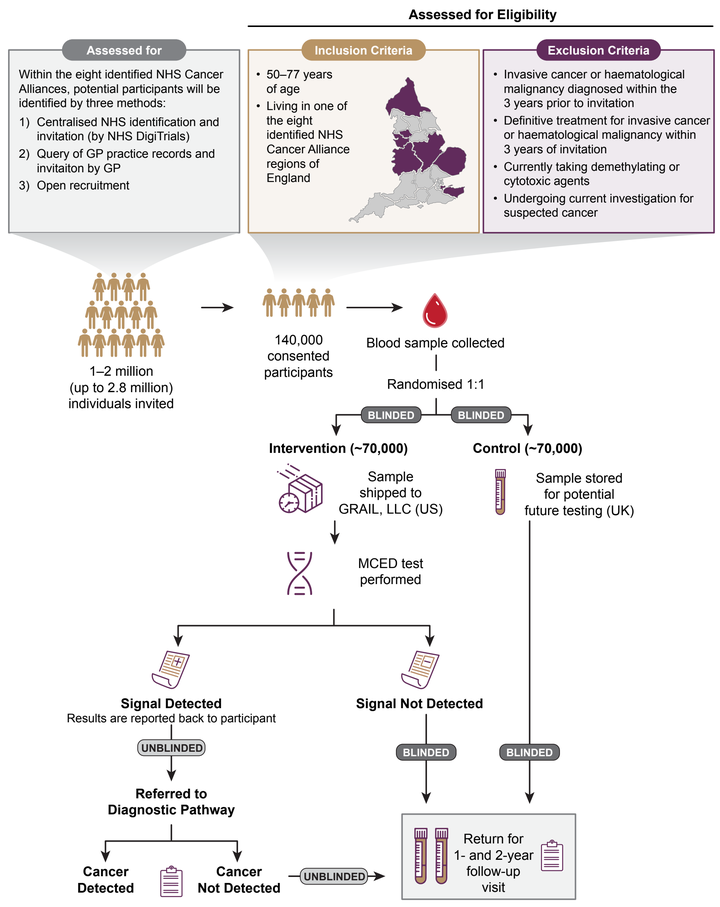
METHODS

The NHS-Galleri trial is utilising multiple strategies to ensure representativeness in study recruitment, with the goal of enrolling a participant population reflective of the general population aged 50–77 years in England.

Study Design Overview

- A little over 1 million people are being invited with a plan to enrol 140,000 asymptomatic participants from the general population of England based on inclusion criteria (Figure 1).
- Following baseline blood sample collection, participants are being randomised 1:1 to the intervention (blood sample analysed by the MCED test) or control arm (blood sample stored for research purposes).
- Only participants in the intervention arm with a 'cancer signal detected' MCED test result have reports returned to them becoming unblinded to arm). This result includes one or two predicted cancer signal origins. These participants are being referred for diagnostic investigations and any necessary treatment.

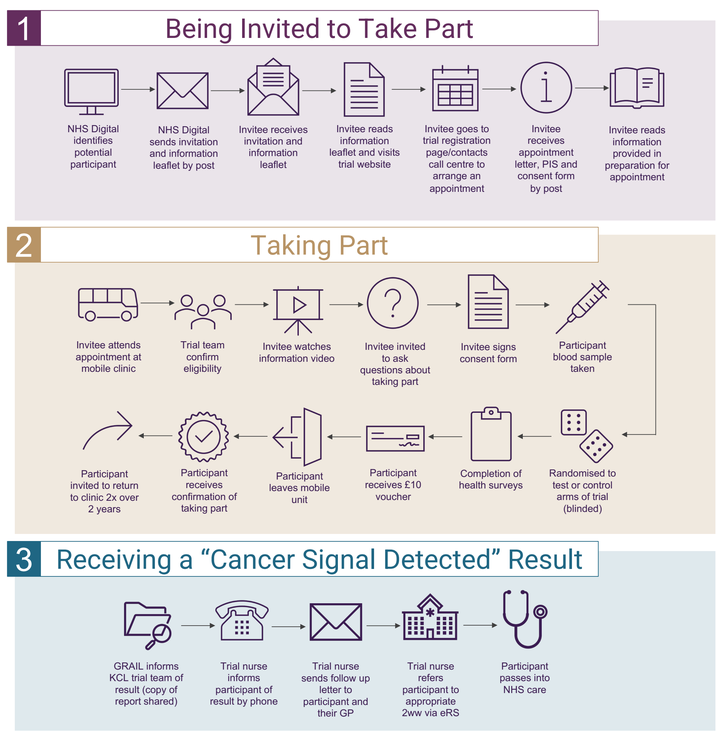
Figure 1. An Overview of the NHS-Galleri Trial Design.



Participant Journey

- Peripheral blood is being collected by routine venipuncture at up to three study visits one year ± six weeks apart, reflecting an annual screening approach (Figure 2).
- All collections are being carried out using specialised mobile clinics that are:
  - Enrolling participants across the eight Cancer Alliance regions;
  - Providing language translation services (at all mobile units);
  - Providing wheelchair accessibility (at all large mobile units).
- Participant follow-up data, including for those diagnosed with invasive cancer, are accrued in routine NHS datasets.

Figure 2. Participant Journey From Invitation, Through Study Participation, and 'Cancer Signal Detected' MCED Result Reporting.



PIS, Participant Information Sheet; KCL, King's College London; 2ww, two week wait; eRS, e-referral system.

Monitoring of Representativeness of Participant Population Enrolment

- The eight Cancer Alliances were selected based on average late stage cancer diagnosis and mortality and having locations with higher deprivation and ethnic diversity (based on data from the Strategic Health Atlas Planning and Evaluation [SHAPE] web tool).[14]
- There is near real-time weekly characterisation and monitoring of the representativeness of enrolled participants to the general population aged 50–77 in target geographic regions, with dynamic adjustment of invitation lists and targeted invitation tactics as indicated (Figure 3).
  - Enrolled participant demographics, such as ethnicity, are collected via participant-reported questionnaires within EDC at the time of their enrollment visit.
  - Enrolled participant demographics can be compared to national-level demographic statistics (Table 1).
  - Adjustments are being made by index of multiple deprivation (IMD) depending on the demographics of participants recruited so far and additional efforts made to target ethnic groups as needed.

Figure 3. Monitoring for Representative Trial Enrolment.

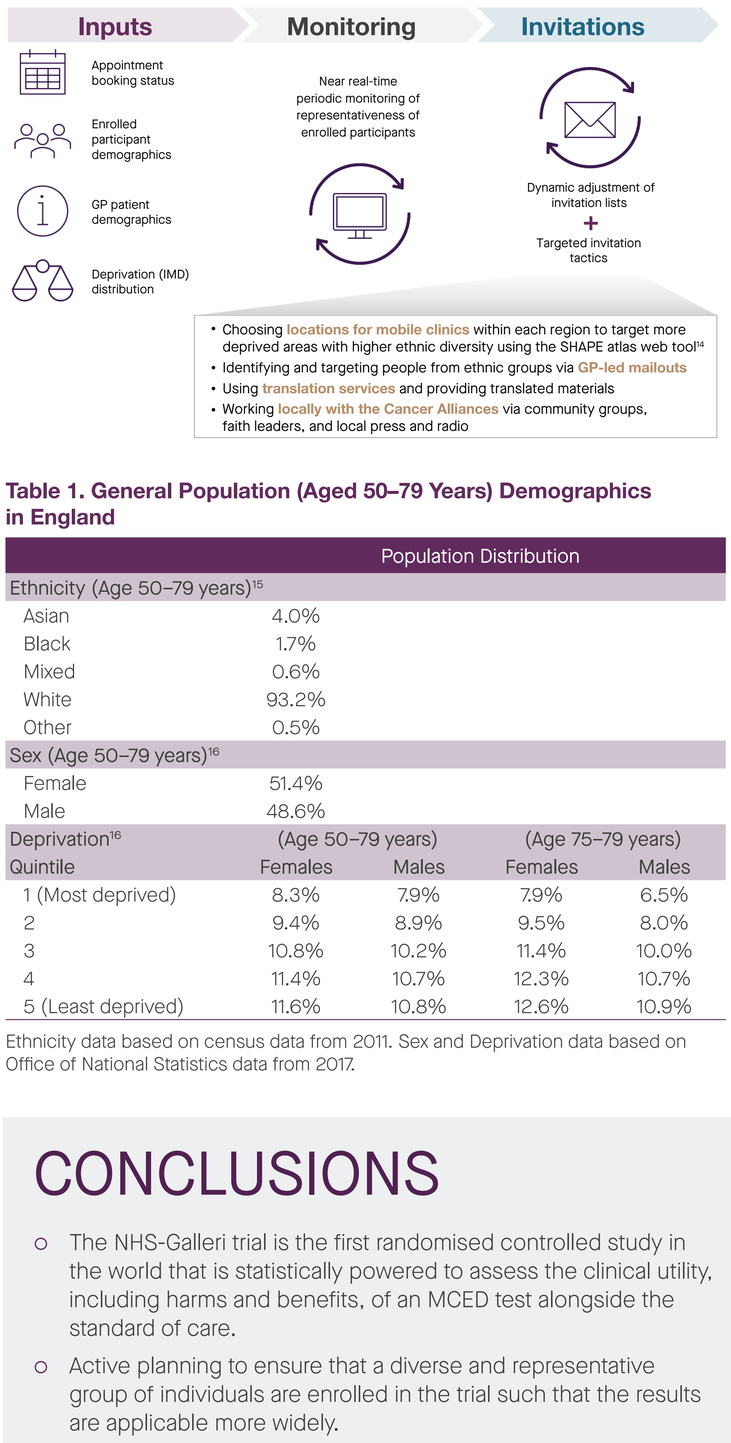


Table 1. General Population (Aged 50–79 Years) Demographics in England

	Population Distribution			
Ethnicity (Age 50–79 years)[15]				
Asian	4.0%			
Black	1.7%			
Mixed	0.6%			
White	93.2%			
Other	0.5%			
Sex (Age 50–79 years)[16]				
Female	51.4%			
Male	48.6%			
Deprivation[16]	(Age 50–79 years)		(Age 75–79 years)	
Quintile	Females	Males	Females	Males
1 (Most deprived)	8.3%	7.9%	7.9%	6.5%
2	9.4%	8.9%	9.5%	8.0%
3	10.8%	10.2%	11.4%	10.0%
4	11.4%	10.7%	12.3%	10.7%
5 (Least deprived)	11.6%	10.8%	12.6%	10.9%

Ethnicity data based on census data from 2011. Sex and Deprivation data based on Office of National Statistics data from 2017.

CONCLUSIONS

- The NHS-Galleri trial is the first randomised controlled study in the world that is statistically powered to assess the clinical utility, including harms and benefits, of an MCED test alongside the standard of care.
- Active planning to ensure that a diverse and representative group of individuals are enrolled in the trial such that the results are applicable more widely.
- Invitation and recruitment tactics aim to optimise representativeness in study enrolment.
- The results of the study will inform whether the MCED test should be used in a population screening setting.
- Future research may implement clinical trial recruitment tactics to aim towards enrolling more representative participant populations.

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Disclosures

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