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Trial in Progress: Cancer Screening Study With or Without Low Dose Lung CT to Validate a Multi-cancer Early Detection Blood Test: SUMMIT

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INTRODUCTION

- Screening for breast, colorectal, and cervical cancers is recommended in the US, Canada, and most European countries, though guideline-recommended modalities, screening age range, and screening frequency vary substantially.[1]
- Evidence for screening for lung cancer using low-dose computed tomography (LDCT) comes from the US National Lung Screening Trial of asymptomatic individuals with a substantial smoking history, which showed a 20% reduction in lung cancer mortality[2] and the Dutch-Belgium NELSON trial, which reported CT screening reduced the risk of lung cancer–related deaths at 10 years by 26%.[3]
- However, uptake of LDCT screening in the US has been very low due to barriers at the patient, physician, and healthcare system levels (eg, smoking stigma, fear of radiation, lack of awareness of screening guidelines among physicians and patients, and variable access).[4,5]
- A simple blood test that accurately detects cancer early and identifies its tissue of origin via measurement of tumor cell-free DNA (cfDNA) could reduce the number of false positive results and other potential harms associated with cancer screening, improve the patient experience, and improve patient outcomes.[6,7]

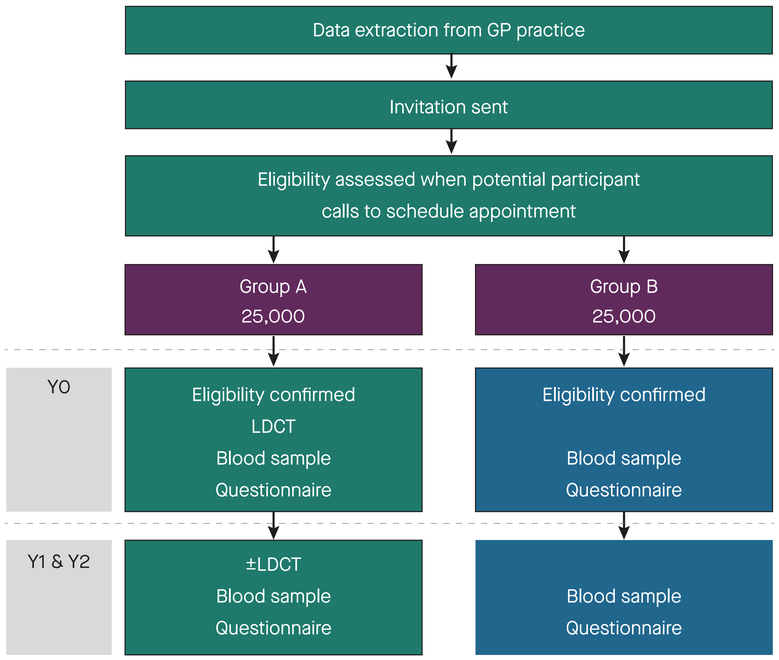
METHODS

- The SUMMIT Study is designed to validate the ability of a blood test to detect multiple cancer types among a high-risk population undergoing LDCT for lung cancer screening, as well as in a lower risk population.
- The SUMMIT Study will also examine the implementation of an LDCT screening service, including the participant experience.

Study Design

- SUMMIT is designed to enroll 50,000 participants (aged 50–77 years) into one of two study arms (**Figure 1**):
  - Group A: Individuals at high-risk for lung and other cancers due to substantial smoking history and meet the United States Preventive Services Task Force (USPSTF) LDCT screening criteria or have a ≥1.3% risk of developing lung cancer over the next six years based on the Prostate, Lung, Colorectal and Ovarian ($PLCO_{m2012}$) risk score.
  - Group B: Individuals not meeting Group A criteria.
    - Exclusion criteria: Participants currently receiving treatment (including watchful waiting) for an active cancer are excluded.

Figure 1. SUMMIT Study Overview



Invited participants are distributed into Group A (individuals meeting USPSTF criteria for lung cancer screening or having a ≥1.3% risk of developing lung cancer in the next six year per $PLCO_{m2012}$) and Group B (Individuals not meeting Group A criteria). At all visits, Group A and B participants answer a questionnaire and provide a blood sample; in addition, Group A participants also undergo LDCT at Y0. Y0: baseline visit; Y1: year 1 visit (approximately 12 months after baseline); Y2: year 2 visit (approximately 24 months after baseline); GP: general practitioner; LDCT: low-dose computed tomography.

Study Participants

- Participants will be identified from the records of approximately 500 general practices across sectors of North Central and East London (**Figure 2**), and are invited by letter to attend a dedicated LDCT scanning unit (Group A) or clinical unit (Group B).
- When participants call to schedule an appointment, likely eligibility is assessed by the phone screener and an appointment is scheduled at a Group A or Group B unit.
  - Consent is obtained after eligibility confirmation at the units.
- Participants will be followed for 10 years after the last participant is enrolled via medical records and the national cancer registry.
  - Data will be collected electronically via case report forms and participant-reported questionnaires.

Figure 2. Current SUMMIT Study Participant Coverage

Locations currently enrolling participants are depicted.

Study Objectives

- The primary objectives of the SUMMIT Study are to:
  - Validate a cell-free nucleic acid blood test for detection of multiple cancers; and
  - Examine the performance of delivering an LDCT screening service for lung cancer to a high-risk population in London.
- Key secondary objectives are to:
  - Compare the cfDNA blood test results to LDCT results; and
  - Evaluate behavioral outcomes and participant acceptability associated with an LDCT screening programme.
- Primary endpoints for the SUMMIT Study include evaluating cancer incidence and stage at diagnosis and screening service performance measures.

Study Procedures

- Group A study procedures are outlined below:
  - Participants will provide a blood sample, complete a questionnaire, and receive a baseline LDCT.
  - Current smokers will receive a smoking cessation intervention.
  - At 12 and 24 months post-baseline, participants will provide a blood sample, complete a questionnaire, and if a current smoker, will receive a smoking cessation intervention.
    - Participant-reported outcomes related to anxiety and quality of life will be quantified using the SF-12 and EQ-5D validated instruments.
  - Participants with a negative baseline LDCT (without lung nodules) will be randomised at their Year 1 visit to either have a LDCT at 12 and 24 months or no further scans.
  - Participants with lung nodules at baseline will require follow-up scans in line with the study nodule follow-up protocol.
  - Participants with abnormal LDCT findings suspicious of cancer or other significant incidental findings will receive an urgent referral for diagnosis and treatment.
- Group B study procedures are outlined below:
  - Participants will provide a blood sample and complete a questionnaire at three study appointments (baseline, 12 months, 24 months).
- Blood test results will not be returned to physicians or participants in either Group A or B.

Statistical Considerations

- The evaluation of the cfNA blood test performance will be performed using a nested case-control design: blood samples will be analyzed from all participants who developed any type of cancer and a randomly selected subcohort of participants who did not.
  - Measures of performance will include sensitivity, false-positive rate (specificity), positive predictive value, and negative predictive value.
- The evaluation of the implementation of a LDCT screening service, including participant experience, will be descriptive with summary results expressed as per 1,000 screen or percentages.

PROGRESS TO DATE

- Enrollment of the Group A cohort began in April 2019; Group B enrollment is targeted to start approximately early 2020.
- Table 1 depicts details of the 3,114 participants enrolled to date (as of August 25, 2019).

Table 1. Currently Enrolled Group A Participant Demographic and Characteristics

	No. Participants (n, %)
Total (as of 8/25/19)	**3,114**
Age, years	
≤65	1,563 (50.2)
>65	1,551 (49.8)
Sex	
Male	1,781 (57.2)
Female	1,333 (42.8)
Race/Ethnicity	
White	2,290 (73.5)
Black	105 (3.4)
Southeast Asian/Chinese	192 (6.2)
Mixed Race	525 (16.9)
Not Reported	2 (0.06)
Smoking Status	
Former	1,662 (53.4)
Current	1,450 (46.6)
Not Reported	2 (0.06)
Personal History of Cancer	
No	2,675 (85.9)
Yes	437 (14.03)
Not Reported	2 (0.06)
Radiology Report[a]	
Follow-up Scan[b]	556 (18.89)
Urgent Referral[c]	164 (5.57)

[a]Radiology reporting not yet available/reported for all participants.
[b]Required upon nodule or other abnormality identified by LDCT.
[c]Required upon abnormality suspicious of cancer identified by LDCT.

SUMMARY

- The SUMMIT Study is designed to determine the performance of this investigational multi-cancer blood test compared to or combined with LDCT for identifying lung cancer, and in detecting cancers for which there are no effective screening tests.
- The SUMMIT Study will evaluate the implementation of an LDCT screening programme in the London population.
- The SUMMIT Study may therefore inform new approaches to finding cancer early.

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