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PROMINENT Smoking Cessation Study

Submission date 19/07/2024	**Recruitment status** Recruiting	[_] Prospectively registered [X] Protocol
Registration date 02/09/2024	**Overall study status** Ongoing	[_] Statistical analysis plan [_] Results
Last Edited 09/02/2026	**Condition category** Cancer	[_] Individual participant data [X] Record updated in last year

Plain English summary of protocol

Background and study aims

Tobacco smoking is known to increase the risk of cancer in both humans and mouse models. The causal link between smoking and tumours of the lung, and up to 14 other cancer types, has been well established. While there is compelling epidemiological evidence to link tobacco smoking with cancer risk, the underlying biological mechanisms are not well understood. Importantly, we do not understand how smoking impacts the phenotypes of normal tissues and how it promotes cancer development.

To determine the specific role of tobacco smoking in tumour promotion, we will conduct an observational study to investigate the effect of changes in smoking on tissue biology. Specifically, the PROMINENT Smoking Cessation Study will collect serial samples of buccal and nasal cells from volunteers undergoing a smoking cessation lifestyle modification. The underlying hypothesis is that through the comparison of samples obtained prior to the intervention and at subsequent time points thereafter, we will be able to observe differences in the molecular and clonal architecture of normal tissues. These changes will help us understand the mechanisms by which smoking promotes cancer development and could help identify molecular targets for prevention.

This key line of investigation will identify the changes that occur in human buccal and nasal cells upon smoking cessation, which may underlie the observed decreased risk of cancer development observed in people who cease smoking. A clear contribution of tobacco smoking to the mutation rate in certain tissues has been firmly established. However, whether it acts exclusively through a contribution to the somatic variation of tissues, or (in addition, or exclusively) as promoters of tumorigenesis is not well understood. In the case of smoking, there is clear evidence of its role in the development of mutations that are drivers of tumours in the lung and other organs. However, recent evidence suggests that quitting smoking promotes replenishment of the bronchial epithelium from mitotically quiescent cells that have avoided tobacco-induced mutagenesis.

In addition, there is growing interest in the effects of e-cigarettes on health. Although now widely used for smoking cessation, nicotine and other compounds contained in e-cigarettes can induce oxidative stress in human bronchial and lung epithelial cells resulting in inflammation, cytotoxicity and increased endothelial cell permeability. Therefore, it is of public health interest to understand the physiological impact of e-cigarettes. Within this study we will be able to assess the impact of smoking cessation on normal cells in those who go on to use e-cigarettes versus those who use other means.

Buccal cells will be obtained through oral rinse which has also been shown to be an effective

method for providing cells amenable to molecular profiling. The nasal mucosa has a strong functional and immunological relationship with the lungs. The nasal mucosa may therefore act as a surrogate for the bronchial epithelium, without the need for invasive tests such as bronchoscopy or induced sputum. We will also include nasal sampling in this study.

Main research question: What is the impact of smoking cessation on the molecular characteristics on nasal and buccal cells, and does exposure to e-cigarettes lead to specific molecular changes in these tissues?

Who can participate?
Any individual (aged 40 years or older) who currently smokes and wishes to stop smoking and accesses the Greater Manchester Lung Health Check programme and/ or the Manchester Conversation-Understand-Replace-Experts/Evidence-base (CURE) programme

What does the study involve?
1. Consent
2. Providing information on health and medical history, education and occupation history, alcohol use, smoking history and oral health via a questionnaire
3. Providing personal information such as name, contact details, NHS number etc
4. Taking your breath carbon monoxide measurement
5. Donating mouth, nose and blood samples
The study lasts 9 -12 months.

What are the possible benefits and risks of participating?
Benefits:
The results of this study are unlikely to be of direct benefit to you as it may take several years to analyse the data, but we hope the information we gain from the study will improve our understanding of lung disease for future patients.
Risks:
Blood samples: The risks involved in donating a blood sample are the same as for routine blood tests. There may be discomfort or pain in the skin and tissue around the vein where the blood is taken. There may be bruising over the vein after the procedure. Blood will be taken by trained professionals who are experienced in the procedure.
We do not anticipate any significant problems or risks. The collection of the nasal brush sample may cause minor irritation.

Where is the study run from?
Manchester University NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
June 2022 to April 2027

Who is funding the study?
Jointly funded by Cancer Research UK and National Cancer Institute (NCI), USA

Who is the main contact?
Chinenye Amadi, chinenye.amadi@manchester.ac.uk

Contact information

Type(s)

Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
330336

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
CGCATF-2021/100007

Central Portfolio Management System (CPMS)
61744

Study information

Scientific Title
Discovering the molecular signatures of cancer PROMotion to INform prevENTion (PROMINENT): Smoking Cessation Study

Acronym
PROMINENT

Study objectives
Primary objectives:
1. Understand how smoking cessation affects normal nasal and buccal cells to modify tumorigenesis risk.

2. Understand how e-cigarettes affects normal nasal and buccal cells compared to individuals who continue to smoke and individuals who have stopped smoking without the use of e-cigarettes.

Secondary objectives:
1. Compare molecular changes with clinical characteristics from lung cancer screening.
2. Assess the effectiveness of smoking cessation interventions in a screening cohort

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 05/06/2024, East of England – Cambridge South Research Ethics Committee (Equinox house, City Link, East Midlands REC Centre, Nottingham, NG2 4LA, United Kingdom; +44 207 104 8208; cambridgesouth.rec@hra.nhs.uk), ref: 24/EE/0071

Study design
Observational cohort study

Primary study design
Observational

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Lung cancer

Interventions
Participants will have two study visits - the first one will be at the same time as their lung health check/ clinic appointment, or on a different day if this is more convenient for them and the second visit will take place several months after their scan (usually between 9 and 12 months after). At each visit, participants will complete a study questionnaire and be asked to donate nose (nose tissue and nose brush) and mouth (mouth swab and mouth wash) samples. Blood samples may also be collected. In-between visits, participants will be contacted by the research team every 3 months, by telephone, to ascertain their smoking status and eligibility to continue in the study.

Intervention Type
Other

Primary outcome(s)
Molecular signals measured by molecular signature as observed in mouth and nose samples, at baseline and follow-up (9 – 12 months)

Key secondary outcome(s))
There are no secondary outcome measures

Completion date
30/04/2027

Eligibility

Key inclusion criteria
1. ALL
1.1. Self-reported current cigarette smoker
1.2. Carbon Monoxide (CO) reading >=5 ppb
1.3. Intends to quit smoking / undertake a smoking quit attempt within 3 months
1.4. No prior history of cancer
1.5. Able to provide informed consent

2. Lung Health Check attendees
2.1. Aged >=55 years
2.2. PLCOM2012 score >=1.51% (or eligible for screening if alternative risk model is used)

3. MFT-CURE attendees
3.1. Aged >=40 years

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
40 years

Upper age limit
100 years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. All
1.1. Never or former smoker (has not smoked within the last 2 weeks)
1.2. Carbon Monoxide (CO) reading <5 ppb
1.3. Prior history of cancer

2. Lung Health Check attendees
2.1. Aged <55 years
2.2. Decline or unable to undertake LDCT screening

3. MFT-CURE attendees
3.1. Aged <40 years

Date of first enrolment
01/08/2024

Date of final enrolment
31/01/2027

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Manchester University NHS Foundation Trust
Cobbett House
Oxford Road
Manchester
England
M13 9WL

Sponsor information

Organisation
University of Manchester

ROR
https://ror.org/027m9bs27

Funder(s)

Funder type
Charity

Funder Name
Cancer Research UK

Alternative Name(s)
CR_UK, Cancer Research UK - London, Cancer Research UK (CRUK), CRUK

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be stored in a publically available repository (further details to be added)

IPD sharing plan summary
Stored in publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version 2.1	05/06/2024	01/08/2024	No	Yes
Participant information sheet	version 4.0	14/05/2025	06/10/2025	No	Yes
Protocol file	version 4.0	14/05/2025	06/10/2025	No	No
Protocol file	version 5.0	19/01/2026	09/02/2026	No	No
Study website		11/11/2025	11/11/2025	No	Yes