

PROMINENT Smoking Cessation Study

Submission date 19/07/2024	Recruitment status Recruiting	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
Registration date 02/09/2024	Overall study status Ongoing	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
Last Edited 02/09/2024	Condition category Cancer	<input type="checkbox"/> Individual participant data <input checked="" type="checkbox"/> 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 May 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

Study website

<https://cancergrandchallenges.org/teams/prominent>

Contact information

Type(s)

Scientific

Contact name

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Contact details

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Additional identifiers

EudraCT/CTIS number

Nil known

IRAS number

330336

ClinicalTrials.gov number

Nil known

Secondary identifying numbers

CPMS 61744, CGCATF-2021/100007, IRAS 330336

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

Old ethics approval format

Ethics approval(s)

24/EE/0071; 05/06/2024

Study design

Observational cohort study

Primary study design

Observational

Secondary study design

Cohort study

Study setting(s)

Other

Study type(s)

Treatment

Participant information sheet

See outputs table

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

Phase

Not Specified

Primary outcome measure

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

Secondary outcome measures

There are no secondary outcome measures

Overall study start date

22/06/2022

Completion date

31/05/2027

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 $\geq 1.51\%$ (or eligible for screening if alternative risk model is used)

3. MFT-CURE attendees

- 3.1. Aged ≥ 40 years

Participant type(s)

Patient

Age group

Adult

Lower age limit

40 Years

Sex

Both

Target number of participants

200

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

31/07/2026

Locations

Countries of recruitment

England

United Kingdom

Study participating centre

Manchester University NHS Foundation Trust

Cobbett House

Oxford Road

Manchester

United Kingdom

M13 9WL

Sponsor information

Organisation

University of Manchester

Sponsor details

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Sponsor type

University/education

Website

<http://www.manchester.ac.uk/>

ROR

<https://ror.org/027m9bs27>

Funder(s)

Funder type

Charity

Funder Name

Cancer Research UK

Alternative Name(s)

CR_UK, Cancer Research UK - London, CRUK

Funding Body Type

Private sector organisation

Funding Body Subtype

Other non-profit organizations

Location

United Kingdom

Results and Publications

Publication and dissemination plan

The conclusions from this project will be disseminated by publications in peer-reviewed scientific journals and presentations in scientific meetings and conferences. With the assistance of our collaborators and patient representatives, we will disseminate the trial findings to a wide NHS and general audience

Intention to publish date

31/05/2028

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