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Exposure to nicotine and tobacco products during pregnancy

Submission date
25/11/2019

Recruitment status
No longer recruiting

Registration date
27/11/2019

Overall study status
Completed

Last Edited
17/01/2025

Condition category
Pregnancy and Childbirth

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Health professionals and pregnant women are cautious about recommending or using e-cigarettes (ECs) in pregnancy, due to lack of detailed safety information. The main aim of the study is to measure toxins and cancer causing substances in the urine of women who used to smoke and now just use ECs compared with women who just smoke.

Who can participate?
Pregnant women who are smokers, users of ECs, nicotine replacement therapy, smoke and use ECs, or have never smoked.

What does the study involve?
Pregnant women will be invited to take part when they attend a routine antenatal appointment. If they agree to participate, they will be asked by a researcher to provide a urine sample (or a routinely collected sample will be used if available) and to complete a questionnaire (about themselves and use of nicotine/tobacco products, alcohol, cannabis). They will also be asked to blow into a device that measures exposure to tobacco smoke. They will then be asked to meet with the researcher again at a further routine antenatal visit, in order to repeat the assessments.

What are the possible benefits and risks of participating?
None

Where is the study run from?
1. St George's University Hospitals NHS Foundation Trust, UK
2. Lancashire teaching Hospitals NHS Foundation Trust, UK
3. Bradford Teaching Hospital NHS Foundation Trust, UK
4. The Newcastle Upon Tyne Hospitals NHS Foundation Trust, UK
5. Gateshead Health NHS Foundation Trust, UK

When is the study starting and how long is it expected to run for?
November 2019 to October 2021

Who is funding the study?
Cancer Research UK

Who is the main contact?
Prof. Michael Ussher
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Contact information

Type(s)
Scientific

Contact name
Prof Michael Ussher

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
269631

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
V4.0; IRAS project ID: 269631

Study information

Scientific Title
Maternal exposure to carcinogens, toxicants and nicotine during pregnancy among e-cigarette users, smokers, nicotine replacement therapy users and among those who have never used nicotine or tobacco products

Study objectives
During pregnancy, we hypothesise that eletronic cigarette (EC) users will have significantly lower levels of urinary acrolein than smokers. As secondary objectives we will explore levels of a range of biomarkers in exclusive EC users compared with exclusive smokers, dual users of cigarettes and ECs, exclusive nicotine replacement therapy (NRT) users; dual users of cigarettes and NRT, and 'never users of tobacco or nicotine products'. Generally, the hypothesis is that less tobacco smoke exposure will equate to less toxin and carcinogen exposure.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 29/10/2019, London - Brighton & Sussex Research Ethics Committee (Health Research Authority, Skipton House, 80 London Road, London, SE1 6LH; +44(0)207 104 8052; NRESCommittee.SECoast-BrightonandSussex@nhs.net), ref: 19/LO/1599

Study design
Observational cross-sectional multicentre study

Primary study design
Observational

Secondary study design
Longitudinal study

Study setting(s)
Hospital

Study type(s)
Other

Participant information sheet
Not available in web format, please use contact details to request a participant information sheet.

Health condition(s) or problem(s) studied
Use of nicotine and tobacco products during pregnancy

Interventions
Pregnant women will be invited to take part when they attend a routine antenatal appointment. If they agree to participate, they will be asked by a researcher to provide a urine sample (or a routinely collected sample can be used if available) and to complete a questionnaire (about themselves and use of nicotine/tobacco products, alcohol, cannabis). They will also be asked to blow into a device that measures exposure to tobacco smoke. They will then be asked to meet with the researcher again at a further routine antenatal visit, in order to repeat the assessments. Urine samples will be stored in a freezer and at the end of the study will be sent to an external laboratory for testing. The results will provide valuable information for women who are pregnant, for healthcare professionals who care for those women and for regulators, about the potential safety of using ECs during pregnancy.

Intervention Type

Other

Primary outcome measure

Current primary outcome measure as of 13/12/2021:
Maternal urinary levels of the volatile organic compound Acrolein (metabolite HPMA) measured using urine test at the time of participation. Acrolein has two metabolites (3HPMA & 2CoEMA); the single primary outcome will be 3HPMA because 3HPMA has a higher ratio in smokers vs non-smokers compared with 2CoEMA. The metabolite 2CoEMA will be analysed as a secondary outcome.

Previous primary outcome measure:
Maternal urinary levels of the volatile organic compound Acrolein (metabolites HPMA and CEMA) measured using urine test at the time of participation

Secondary outcome measures

Current secondary outcome measures as of 13/12/2021:
All tested in maternal urine at time of participation:
1. Tobacco exposure will be assessed with a test for minor tobacco alkaloids (anabasine, anatabine), expired carbon monoxide levels
2. Levels of nicotine, cotinine and their metabolites, to derive total nicotine equivalents
3. Nicotine metabolite ratio (NMR)
4. Two tobacco-specific nitrosamines (TSNAs) (i.e., 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNAL) and N-nitrosonornicotine (NNN)), two heavy metals (i.e., cadmium (Cd) and lead (Pb)) and one polycyclic aromatic hydrocarbon (PAH) (i.e., 2-naphthol)
5. 13 volatile organic compounds (VOCs) parent (metabolite): acrolein (2CoEMA), 1,3-butadiene (MHB3), acrylamide (AAMA), acrylonitrile (CYMA), Benzene (PMA), crotonaldehyde (HPMM), cyanide (ATCA), isoprene (IPM3), ethylbenzene (PHGA), propylene oxide (HPM2), styrene (MADA), toluene/benzyl alcohol (BMA), and m,p-xylene (34MH)
6. Human chorionic gonadotropin (hCG)
7. Pregnancy-associated plasma protein A (PAPPA-A)
8. Use of alcohol and cannabinoids

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6. Human chorionic gonadotropin (hCG)
7. Pregnancy-associated plasma protein A (PAPPA-A)
8. Use of alcohol and cannabinoids

Overall study start date

01/09/2019

Completion date
31/10/2021

Eligibility

Key inclusion criteria
1. Pregnant women
2. Aged at least 16 years of age
3. Able to speak and read English
4. Do not report having had an active infection (chest infection, cold or flu, sore throat, or fever) within 24 hours of either of the two assessments
5. Willing and able to give informed consent for participation in the study
6. Meet criteria for one of six groups related to level and type of use of nicotine and tobacco products:
6.1. Group A. ‘Exclusive smokers’: Smoked more than 5 cigarettes every day for more than the last six months and have not vaped or used NRT in the last month
6.2. Group B. ‘ECs only’: Not smoked cigarettes for at least a month and have vaped every day for at least the last two weeks. Also, have not used NRT in the last month
6.3. Group C. ‘NRT only': Not smoked cigarettes for at least a month and have used NRT every day for at least the last two weeks. Also, have not vaped in the last month
6.4. Group D. Dual users of cigarettes and ECs: Smoked cigarettes on most days of the week for more than 6 months. Also, have been using e-cigarettes on most days of the week for at least the last two weeks
6.5. Group E. Dual users of cigarettes and NRT: Smoked cigarettes on most days of the week for more than 6 months. Also, have been using NRT on most days for at least the last two weeks
6.6. Group F. ‘never smokers’: Have never smoked or used any nicotine or tobacco products

Participant type(s)
Patient

Age group
Mixed

Lower age limit
16 Years

Sex
Female

Target number of participants
204

Total final enrolment
149

Key exclusion criteria
Current participant exclusion criteria as of 20/10/2021:
1. Have used tobacco products other than cigarettes in the last month (e.g., cigars, heat-not-burn)
2. Have used both NRT and ECs in the last month

3. Have used nicotine free e-cigarettes in the last month
4. Report having had an active infection (chest infection, cold or flu, sore throat, or fever) within 24 hours of either of the two assessments
5. Reported as not currently smoking with an expired carbon monoxide reading of >3 parts per million (where an expired carbon monoxide reading has been obtained)

Previous participant exclusion criteria:
1. Have used tobacco products other than cigarettes in the last month (e.g., cigars, heat-not-burn)
2. Have used both NRT and ECs in the last month
3. Have used nicotine free e-cigarettes in the last month
4. Report having had an active infection (chest infection, cold or flu, sore throat, or fever) within 24 hours of either of the two assessments

Date of first enrolment
14/11/2019

Date of final enrolment
30/04/2020

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
St George's University Hospitals NHS Foundation Trust
Blackshaw Road
London
United Kingdom
SW17 0QT

Study participating centre
Lancashire teaching Hospitals NHS Foundation Trust
Preston Royal Hospital
Sharoe Green Lane
Preston
United Kingdom
PR2 9HT

Study participating centre
Bradford Teaching Hospital NHS Foundation Trust
Bradford Royal Infirmary

Smith Lane
Bradford
United Kingdom
BD9 6RJ

Study participating centre
The Newcastle Upon Tyne Hospitals NHS Foundation Trust
The Royal Victoria Infirmary
Queen Victoria Road
Newcastle upon Tyne
United Kingdom
NE1 4LP

Study participating centre
Gateshead Health NHS Foundation Trust
Queen Elizabeth Hospital
Queen Elizabeth Avenue
Sheriff Hill
Gateshead
United Kingdom
NE9 6SX

Sponsor information

Organisation
St George’s University Hospitals NHS Foundation Trust

Sponsor details
Blackshaw Road
London
England
United Kingdom
SW17 0QT
+44(0)208 725 0892
sahollin@sgul.ac.uk

Sponsor type
Hospital/treatment centre

Website
https://www.stgeorges.nhs.uk/

ROR

https://ror.org/039zedc16

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 findings will be presented at international conferences (e.g., Society for Research on Nicotine and Tobacco) and, towards the end of the study period, will be submitted to a high impact journal (e.g., BMJ). We will also disseminate the findings to policy makers, NGOs and health professionals.

Intention to publish date
28/02/2025

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available as consent has not be obtained for this purpose.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Plain English results			17/01/2025	No	Yes