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Smoking, Nicotine and Pregnancy 3 Trial

Submission date
13/10/2021

Recruitment status
Recruiting

Registration date
13/10/2021

Overall study status
Ongoing

Last Edited
14/11/2024

Condition category
Pregnancy and Childbirth

[X] 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
Nicotine replacement therapy (NRT) provides nicotine without the toxins contained in cigarette smoke. When used with specialist support, it helps pregnant women stop smoking. The NRT instruction booklet includes use for preloading, reduction and lapse recovery; studies suggest that allowing people to smoke and use NRT together helps with stopping. Currently, NHS stop smoking support advises pregnant women not to smoke when using NRT. This study will test whether relaxing this message could help pregnant women to quit and improve babies' health. The aim of this study is to test support for the following three uses of NRT:
1. Preloading - using nicotine patches for a short time when still smoking but preparing to stop
2. NRT in 'slip ups' (smoking occasional cigarettes) – advice to keep on with NRT during short 'slip ups'; this may help them stop smoking for good
3. For women who cannot quit, using NRT to smoke less – this could also help them stop smoking; if not, breathing in less harmful cigarette smoke should make babies healthier

Who can participate?
Pregnant women (pregnant for 25 weeks or less) who smoke

What does the study involve?
Participants will be randomly assigned into two groups. One group will receive usual NHS stop smoking support (counseling and NRT). The second group will also receive support with preloading NRT patches for up to 4 weeks before they try to quit and using NRT during 'slip-ups'. Women who cannot stop after 6 weeks will receive support and an offer of NRT to help them to reduce their smoking. The researchers will collect saliva and breath samples before/during the study to measure nicotine and CO levels respectively. They will ask women about their smoking 6 weeks into the study and when they are 36 weeks pregnant. They will collect data on birth outcomes. Data will be compared between the two groups.

What are the possible benefits and risks of participating?
The researchers cannot promise that the study will directly benefit participants, but all participants will receive support to stop smoking based on the best NHS standards of practice. The information they provide during the study will be invaluable in helping the researchers design future ways of helping pregnant women stop smoking. The researchers do not foresee

there being any risks from taking part in this study. However, taking part will take time and may therefore be inconvenient. Some participants may be upset when discussing the risks of smoking in pregnancy.

Where is the study run from?
University of Nottingham (UK)

When is the study starting and how long is it expected to run for?
April 2019 to October 2026

Who is funding the study?
National Institute for Health Research (NIHR) Health Technology Assessment (HTA) Programme (UK)

Who is the main contact?
Dr Katarzyna Campbell
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Study website
https://www.nottingham.ac.uk/research/groups/tobaccoandalcohol

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
291236

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CPMS 49947, IRAS 291236

Study information

Scientific Title
Open-label randomized controlled trial of enhanced support and nicotine replacement therapy (NRT) offered for preloading, lapse recovery and smoking reduction: impact on smoking in pregnancy

Acronym
SNAP 3

Study objectives
To find out if additional support for preloading (using nicotine replacement therapy [NRT] patches in preparation for quit) and recovery of lapses ('slip ups' to smoking during quit attempt) and an offer of NRT for preloading, when added to usual care (UC), i.e. usual NHS smoking cessation support, increase pregnant women's chances of long term smoking cessation, compared to UC alone.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 13/09/2021, West Midlands - Coventry and Warwickshire Research Ethics Committee (The Old Chapel, Royal Standard Place, Nottingham, NG1 6FS, UK; +44 (0)207 104 8084; coventryandwarwick.rec@hra.nhs.uk), REC ref: 21/WM/0172

Study design
Randomized; Interventional; Design type: Treatment, Education or Self-Management, Psychological & Behavioural

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Community, GP practice, Hospital, Internet/virtual, Other

Study type(s)
Prevention

Participant information sheet
See study outputs table

Health condition(s) or problem(s) studied
Smoking in pregnancy

Interventions
Current interventions as of 21/11/2023:
The study design is randomised control trial (RCT) recruiting from antenatal settings and via online recruitment. There will be two trial arms. The control arm will receive standard stop smoking cessation care available for pregnant women, which may include the provision of nicotine replacement therapy (NRT) during the quit attempt (UC group). The intervention arm participants, in addition to standard care, will receive behavioural support and NRT for preloading (using NRT to gradually reduce smoking, until they quit on their agreed quit date) and advice on using NRT in brief smoking lapses during the quit attempt. Women who are unable to quit 6 weeks post-randomisation will receive NRT and advice on using it to reduce smoking.

Outcomes updated 15/12/2022 Protocol v 3.1
The researchers will compare the following between the intervention and the UC group:
1. Long-term abstinence from smoking reported between six weeks after randomisation and 36 weeks gestation or childbirth, whichever is earlier, confirmed by saliva and/or breath sample;
2. Reported and validated 7-day smoking abstinence at 36 weeks gestation
3. Reported ≥ 50% reduction in daily cigarettes at 36 weeks gestation
4. Exhaled CO concentration at delivery
5. Whether or not brief smoking lapse experienced, reported at 6 weeks post randomisation
6. Adverse pregnancy outcome rates(e.g. low birth weight for gestational age, premature birth)

The researchers will recruit 1430 pregnant women who are ≤25 weeks gestation, smoke, are willing to use NRT and wish to receive support to stop smoking. They will ask the woman's GP to confirm there are no contraindications to NRT use. The researchers anticipate the recruitment will take 30 months. Participants will be recruited from approximately 8 weeks gestation. They will collect follow up data from participants at 6 weeks post-randomisation and at around 36 weeks gestation. They will collect birth and maternal outcome data from the hospital after birth, and no later than 10 weeks postpartum. Therefore, the maximum duration of the study for any participant would be approximately 42 weeks.

Updated 15/12/2022 Protocol v3.1
Staff involved in the trial procedures will include:
1. Site trial staff: Clinical Research Network (CRN) staff, research nurses, research midwives or any local site staff delegated by the site PI
2. Central research team: smoking in pregnancy (SIP) researchers, SIP administrators or any staff delegated by the CI

1. Participant identification and screening:
A screening questionnaire (paper or electronic) will be used in all settings to identify potentially eligible women. A paper or electronic copy of the patient information sheet (PIS) will be made available to women at this point. Those potentially eligible and interested will be asked to provide their contact details and will have the opportunity to discuss the study with a researcher. Participants will be identified in the following settings:
1. Antenatal hospital recruitment settings - face to face by the usual clinical care team. The care team may pre-identify potential participants and send them a letter or email with a screening questionnaire, PIS and consent form before their appointment. Alternatively, the care team or local site trial staff may approach women during appointments, introduce the study/offer PIS and ask women to complete the screening questionnaire. Posters will also be put in relevant

clinical areas and women will be able to access the screening questionnaire and PIS via a link or by scanning a code on the poster.
2. Participant Identification Centres (PICs) in antenatal hospital settings and GP surgeries - the usual care team or site trial staff will identify potential participants as above and will pass their details to the central research team.
3. Community midwives may also refer potentially eligible and interested women to the central or local research teams, using the screening questionnaire.
4. Stop smoking practitioners may also refer potentially eligible and interested women to central or local research teams
5. Online adverts targeted towards pregnant women who smoke - women will be directed to a link to the PIS and screening questionnaire. Their details will be passed on to the central research team.
Research team staff will contact women identified in PICs, by community midwives, stop smoking practitioners and online, to discuss the study in more detail.

Recruitment:
1. Participants identified in hospital recruitment settings will discuss the study with site trial staff who will talk them through the PIS and answer any questions. Women who had the chance to fully understand the study and are happy to give their consent will be recruited during the appointment. Women who would like more time to decide will be contacted at least 24 hours later to further discuss their participation. The site trial staff will collect consent, either face to face or by telephone.
2. Participants identified in PICs, by community midwives and online will be contacted via telephone/video call by a central research team member, who will discuss the study with them. For those who do not recall receiving a PIS, a copy will be sent electronically at least 24 hours before consent.

2. Baseline appointment:
Consent:
Informed consent will be collected from all participants before any intervention or data collection. An Investigator or their delegate will go through the consent form with the potential participant, answer questions and obtain consent. Consent will be collected either face to face or using 'distanced' consent via telephone or video call. Women will be asked to tick or initial each consent item and sign the consent form, either using paper (face to face only) or electronic form (e-consent; face to face or distanced). When obtaining distanced consent, if e-consent is not possible (e.g. if there is no internet connection) verbal telephone consent will be obtained, following a strict scripted protocol, which will follow the same consent items as the 'hard copy' consent form.
Eligibility will be formally confirmed once consent is collected.
Very brief advice (VBA) for smoking cessation in pregnancy:
As part of the baseline appointment, all women will receive VBA as defined by the National Centre for Smoking Cessation Training (NCSCT). This is part of standard care for smoking cessation in pregnancy. VBA comprises (1) carbon monoxide (CO) testing, (2) advice that intensive behavioural support enhances success with quitting and (3) referral for this, if available locally.
Data collection at baseline:
Participants will complete baseline measures, including demographics, smoking beliefs and behaviours and provide necessary details about the pregnancy/antenatal care. The baseline questionnaire will be completed verbally, either face to face or during a telephone/video call.
Samples: Saliva/Breath samples may be collected, at the clinic appointment or by the participant. If sample collection in the clinic is not possible, we may post saliva sample kits and individual-use carbon monoxide (iCO) monitors, with instructions, may be sent to participants by post. Women

will be asked to send the saliva sample via post in a pre-paid envelope. iCO monitor will be used with a mobile app, which will send the results to the central research team electronically. Saliva sample will only be collected from women recruited in clinic, and randomised to intervention group.

Randomisation:
Participants will be allocated into one of the two groups by chance, by the Investigator or delegate, using a randomisation website.

Referral for stop smoking support:
Once randomised, women in the UC group will be referred for standard stop smoking support available in their area at the end of their baseline appointment, as per standard care.
Women in the intervention group will receive enhanced preloading telephone support (see below) and will be referred for UC smoking cessation support at the end of the preloading component of the intervention (at quit date, up to 4 weeks post-randomisation).
3. Post-randomisation study pack via post:
All women will receive a study starter pack via post. For all women, this will contain:
- a "What happens next" information sheet
- a standard care information leaflet
- if applicable, saliva sample kit(s) with instructions
- if applicable, iCO monitor with instructions
The intervention group will also receive
- 1 week worth of NRT patches (15 mg/16 h), with instructions
- a preloading information leaflet
- an access to the study website, which will reiterate the information contained in the preloading booklet
These resources will complement the advice provided during enhanced preloading telephone support.

4. Intervention (intervention group only)
Preloading phase and NRT provision and advice on using NRT in brief lapses:
- shortly after dispatch of the starter pack, central research team members will contact participants in the intervention group. They will receive up to 4 weekly telephone/video support calls delivered by a university researcher. The number of calls will depend on when the quit date is set up (e.g. if the quit date is set up in 1 week, participants will only receive the first call, at the end of which they will be referred for standard smoking cessation support).
Call 1 - The researcher will explain how to use the NRT received in the starter pack for preloading. The use of NRT in brief smoking lapsed will also be discussed. The researcher will help women set a quit date, at least 1 week but no more than 4 weeks ahead.
Calls 2-3 - The researcher will ask women how they got on with the NRT; reinforce preloading /brief lapse advice; more NRT will be issued if needed.
Final call - During the final call before the quit date, the researcher will refer women for standard smoking cessation support in their area, as described above.

Data collection - Preloading phase (Pilot only):
During the first 9 months of the trial (in-trial pilot) saliva and/or CO sample will be collected from a sub-sample of women who use NRT for preloading.
5. Standard smoking cessation support which combines behavioural support and provision of NRT, will be offered to all participants (UC group - at baseline; intervention group - after preloading phase). Smoking cessation support varies in different areas. If no specialist services are available in an area, the researchers will refer women for cessation support to their GP /midwife.

6. Data collection - follow up (FU) 1 (6 weeks post-randomisation):
An online questionnaire (approx. 10 minutes) including smoking behaviours since randomisation, NRT use and access to stop smoking services.
If unable to collect data via an online questionnaire, the research team will attempt to obtain data via telephone, text message or post.
7. Intervention (intervention group only)

Reduction phase - advice and NRT provision:
Women who report smoking at FU1 will be contacted by the central team researcher via telephone and offered a re-referral for smoking cessation support. Those who refuse will be offered the reduction phase of the intervention. If they accept this, they will receive 2 weeks supply of NRT via post. The researcher will advise them to use NRT (patches and/or inhalators) daily and smoke less than usual.
NRT will be repeated on demand unless the participant reports smoking more than at baseline or more than 10 cigarettes each day, for 2 consecutive weeks. They will also receive bi-weekly telephone/video call support and supportive text messages, until up to 36 weeks gestation.
NicUse App - throughout the reduction phase, women will be instructed to report smoking and NRT/e-cigarette use via a smartphone application, daily. They will receive instructions, a link to the app and login details. This is for self-monitoring purposes.
8. Data collection - FU2, at 36 weeks gestation or at childbirth, whichever is soonest. An online questionnaire (approx. 10 minutes), including smoking behaviours, stop smoking support. If unable to collect data via an online questionnaire, the central research team will attempt to obtain data via telephone, text message or post. Data may be obtained by site trial staff during antenatal appointments. Validation of smoking status - women who report long term quit (between FU1 and FU2) or at least 50% smoking reduction, will be asked to provide saliva and/or breath sample (using methods as described at baseline) to confirm smoking status.
9. Maternal and birth outcomes - after birth (up to 10 weeks postpartum) we will request these data from the hospital or GP.
10. Interviews to improve recruitment (Pilot only):
Potentially eligible women who provide contact details via screening questionnaire, both those who agree to participate in the trial and those who decline, will be invited to take part in a telephone interview, lasting approx. 40 minutes. They will be asked to discuss the factors that influenced their decision to join or not. Interviews will be audio recorded.

Incentives:
Women will be offered £5 shopping vouchers for completing each FU questionnaire. They will be offered a £20 voucher for saliva/CO samples (except baseline) and a £20 voucher for taking part in the interview.

Previous interventions from 08/03/2022 to 21/11/2023:

The study design is randomised control trial (RCT) recruiting from antenatal settings and via online recruitment. There will be two trial arms. The control arm will receive standard stop smoking cessation care available for pregnant women, which may include the provision of nicotine replacement therapy (NRT) during the quit attempt (UC group). The intervention arm participants, in addition to standard care, will receive behavioural support and NRT for preloading (using NRT to gradually reduce smoking, until they quit on their agreed quit date) and advice on using NRT in brief smoking lapses during the quit attempt. Women who are unable to quit 6 weeks post-randomisation will receive NRT and advice on using it to reduce smoking.

The researchers will compare the following between the intervention and the UC group:
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2. Reported 7-day smoking abstinence at 6 weeks after randomisation
3. Reported and validated 7-day smoking abstinence at 36 weeks gestation (or childbirth, if sooner)
4. Reported and validated ≥50% reduction in daily cigarettes at 36 weeks gestation
5. Exhaled CO concentration at delivery
6. Adverse pregnancy outcome rates(e.g. low birth weight for gestational age, premature birth)

The researchers will recruit 1430 pregnant women who are ≤25 weeks gestation, smoke, are willing to use NRT and wish to receive support to stop smoking. They will ask the woman's GP to confirm there are no contraindications to NRT use. The researchers anticipate the recruitment will take 30 months. Participants will be recruited from approximately 8 weeks gestation. They will collect follow up data from participants at 6 weeks post-randomisation and at around 36 weeks gestation. They will collect birth and maternal outcome data from the hospital after birth, and no later than 10 weeks postpartum. Therefore, the maximum duration of the study for any participant would be approximately 42 weeks.

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1. Site trial staff: Clinical Research Network (CRN) staff, research nurses, research midwives or any local site staff delegated by the site PI
2. Central research team: smoking in pregnancy (SIP) researchers, SIP administrators or any staff delegated by the CI

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2. Participant Identification Centres (PICs) in antenatal hospital settings - the usual care team or site trial staff will identify potential participants as above and will pass their details to the central research team.
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Research team staff will contact women identified in PICs, by community midwives, stop smoking practitioners and online, to discuss the study in more detail.
(Note - currently the researchers have not identified any PIC sites, but we may include sites that wish to act as PICs in the future).

Recruitment:
1. Participants identified in hospital recruitment settings will discuss the study with site trial staff who will talk them through the PIS and answer any questions. Women who had the chance to fully understand the study and are happy to give their consent will be recruited during the appointment. Women who would like more time to decide will be contacted at least 24 hours later to further discuss their participation. The site trial staff will collect consent, either face to face or by telephone.
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2. Baseline appointment:
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Data collection at baseline:
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Samples: Saliva and breath samples will be collected, either at the clinic appointment or by the participant. If sample collection in the clinic is not possible, we will post saliva sample kits and individual-use carbon monoxide (iCO) monitors, with instructions, may be sent to participants by post. Women will be asked to send the saliva sample via post in a pre-paid envelope. iCO monitor will be used with a mobile app, which will send the results to the central research team electronically. Saliva sample will only be collected from women recruited in clinic, and randomised to intervention group.

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component of the intervention (at quit date, up to 4 weeks post-randomisation).
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Data collection - Preloading phase (Pilot only):
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NRT will be repeated on demand unless the participant reports smoking more than at baseline

or more than 10 cigarettes each day, for 2 consecutive weeks. They will also receive bi-weekly telephone/video call support and supportive text messages, until up to 36 weeks gestation.
NicUse App - throughout the reduction phase, women will be instructed to report smoking and NRT/e-cigarette use via a smartphone application, daily. They will receive instructions, a link to the app and login details. This is for self-monitoring purposes.
8. Data collection - FU2, at 36 weeks gestation or at childbirth, whichever is soonest. An online questionnaire (approx. 10 minutes), including smoking behaviours, stop smoking support. If unable to collect data via an online questionnaire, the central research team will attempt to obtain data via telephone, text message or post. Data may be obtained by site trial staff during antenatal appointments. Validation of smoking status - women who report long term quit (between FU1 and FU2) or at least 50% smoking reduction, will be asked to provide saliva and/or breath sample (using methods as described at baseline) to confirm smoking status.
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Potentially eligible women who provide contact details via screening questionnaire, both those who agree to participate in the trial and those who decline, will be invited to take part in a telephone interview, lasting approx. 40 minutes. They will be asked to discuss the factors that influenced their decision to join or not. Interviews will be audio recorded.

Incentives:
Women will be offered £5 shopping vouchers for completing each FU questionnaire. They will be offered a £20 voucher for saliva/CO samples (except baseline) and a £20 voucher for taking part in the interview.

Original interventions:

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The researchers will recruit 1430 pregnant women who are ≤25 weeks gestation, smoke, are willing to use NRT and wish to receive support to stop smoking. They will ask the woman's GP to confirm there are no contraindications to NRT use. The researchers anticipate the recruitment will take 30 months. Participants will be recruited from approximately 12 weeks gestation. They

will collect follow up data from participants at 6 weeks post-randomisation and at around 36 weeks gestation. They will collect birth and maternal outcome data from the hospital after birth, and no later than 10 weeks postpartum. Therefore, the maximum duration of the study for any participant would be approximately 38 weeks.

Staff involved in the trial procedures will include:
1. Site trial staff: Clinical Research Network (CRN) staff, research nurses, research midwives or any local site staff delegated by the site PI
2. Central research team: smoking in pregnancy (SIP) researchers, SIP administrators or any staff delegated by the CI

1. Participant identification and screening:
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(Note - currently the researchers have not identified any PIC sites, but we may include sites that wish to act as PICs in the future).

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1. Participants identified in hospital recruitment settings will discuss the study with site trial staff who will talk them through the PIS and answer any questions. Women who had the chance to fully understand the study and are happy to give their consent will be recruited during the appointment. Women who would like more time to decide will be contacted at least 24 hours later to further discuss their participation. The site trial staff will collect consent, either face to face or by telephone.
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2. Baseline appointment:
Consent:
Informed consent will be collected from all participants before any intervention or data

collection. An Investigator or their delegate will go through the consent form with the potential participant, answer questions and obtain consent. Consent will be collected either face to face or using 'distanced' consent via telephone or video call. Women will be asked to tick or initial each consent item and sign the consent form, either using paper (face to face only) or electronic form (e-consent; face to face or distanced). When obtaining distanced consent, if e-consent is not possible (e.g. if there is no internet connection) verbal telephone consent will be obtained, following a strict scripted protocol, which will follow the same consent items as the 'hard copy' consent form.
Eligibility will be formally confirmed once consent is collected.
Very brief advice (VBA) for smoking cessation in pregnancy:
As part of the baseline appointment, all women will receive VBA as defined by the National Centre for Smoking Cessation Training (NCSCT). This is part of standard care for smoking cessation in pregnancy. VBA comprises (1) carbon monoxide (CO) testing, (2) advice that intensive behavioural support enhances success with quitting and (3) referral for this, if available locally.
Data collection at baseline:
Participants will complete baseline measures, including demographics, smoking beliefs and behaviours and provide necessary details about the pregnancy/antenatal care. The baseline questionnaire will be completed verbally, either face to face or during a telephone/video call.
Samples: Saliva and breath samples will be collected, either at the clinic appointment or by the participant. If sample collection in the clinic is not possible, we will post saliva sample kits and individual-use carbon monoxide (iCO) monitors, with instructions, by post. Women will be asked to send the saliva sample via post in a pre-paid envelope. iCO monitor will be used with a mobile app, which will send the results to the central research team electronically.

Randomisation:
Participants will be allocated into one of the two groups by chance, by the Investigator or delegate, using a randomisation website.

Referral for stop smoking support:
Once randomised, women in the UC group will be referred for standard stop smoking support available in their area at the end of their baseline appointment, as per standard care.
Women in the intervention group will receive enhanced preloading telephone support (see below) and will be referred for UC smoking cessation support at the end of the preloading component of the intervention (at quit date, up to 4 weeks post-randomisation).
3. Post-randomisation study pack via post:
All women will receive a study starter pack via post. For all women, this will contain:
- a "What happens next" information sheet
- a standard care information leaflet
- if applicable, saliva sample kit(s) with instructions
- if applicable, iCO monitor with instructions
The intervention group will also receive
- 1 week worth of NRT patches (15 mg/16 h), with instructions
- a preloading information leaflet
- an access to the study website, which will reiterate the information contained in the preloading booklet
These resources will complement the advice provided during enhanced preloading telephone support.

4. Intervention (intervention group only)
Preloading phase and NRT provision and advice on using NRT in brief lapses:
- shortly after dispatch of the starter pack, central research team members will contact

participants in the intervention group. They will receive up to 4 weekly telephone/video support calls delivered by a university researcher. The number of calls will depend on when the quit date is set up (e.g. if the quit date is set up in 1 week, participants will only receive the first call, at the end of which they will be referred for standard smoking cessation support).
Call 1 - The researcher will explain how to use the NRT received in the starter pack for preloading. The use of NRT in brief smoking lapsed will also be discussed. The researcher will help women set a quit date, at least 1 week but no more than 4 weeks ahead.
Calls 2-3 - The researcher will ask women how they got on with the NRT; reinforce preloading /brief lapse advice; more NRT will be issued if needed.
Final call - During the final call before the quit date, the researcher will refer women for standard smoking cessation support in their area, as described above.

Data collection - Preloading phase (Pilot only):
During the first 9 months of the trial (in-trial pilot) saliva and/or CO sample will be collected from a sub-sample of women who use NRT for preloading.
5. Standard smoking cessation support which combines behavioural support and provision of NRT, will be offered to all participants (UC group - at baseline; intervention group - after preloading phase). Smoking cessation support varies in different areas. If no specialist services are available in an area, the researchers will refer women for cessation support to their GP /midwife.
6. Data collection - follow up (FU) 1 (6 weeks post-randomisation):
An online questionnaire (approx. 10 minutes) including smoking behaviours since randomisation, NRT use and access to stop smoking services.
If unable to collect data via an online questionnaire, the research team will attempt to obtain data via telephone, text message or post.
7. Intervention (intervention group only)

Reduction phase - advice and NRT provision:
Women who report smoking at FU1 will be contacted by the central team researcher via telephone and offered a re-referral for smoking cessation support. Those who refuse will be offered the reduction phase of the intervention. If they accept this, they will receive 2 weeks supply of NRT via post. The researcher will advise them to use NRT (patches and/or inhalators) daily and smoke less than usual.
NRT will be repeated on demand unless the participant reports smoking more than at baseline or more than 10 cigarettes each day, for 2 consecutive weeks. They will also receive bi-weekly telephone/video call support and supportive text messages, until up to 36 weeks gestation.
NicUse App - throughout the reduction phase, women will be instructed to report smoking and NRT/e-cigarette use via a smartphone application, daily. They will receive instructions, a link to the app and login details. This is for self-monitoring purposes.
8. Data collection - FU2, at 36 weeks gestation or at childbirth, whichever is soonest. An online questionnaire (approx. 10 minutes), including smoking behaviours, stop smoking support. If unable to collect data via an online questionnaire, the central research team will attempt to obtain data via telephone, text message or post. Data may be obtained by site trial staff during antenatal appointments. Validation of smoking status - women who report long term quit (between FU1 and FU2) or at least 50% smoking reduction, will be asked to provide saliva and/or breath sample (using methods as described at baseline) to confirm smoking status.
9. Maternal and birth outcomes - after birth (up to 10 weeks postpartum) we will request these data from the hospital or GP.
10. Interviews to improve recruitment (Pilot only):
Potentially eligible women who provide contact details via screening questionnaire, both those

who agree to participate in the trial and those who decline, will be invited to take part in a telephone interview, lasting approx. 40 minutes. They will be asked to discuss the factors that influenced their decision to join or not. Interviews will be audio recorded.

Incentives:
Women will be offered £5 shopping vouchers for completing each FU questionnaire. They will be offered a £20 voucher for saliva/CO samples (except baseline) and a £20 voucher for taking part in the interview.

Intervention Type
Mixed

Primary outcome measure
Biochemically validated, prolonged abstinence from smoking self-reported between 6 weeks after randomisation and 36 weeks gestation or childbirth, whichever is earlier. Biochemical validation: cotinine/anabasine levels in saliva sample and/or CO levels tested using CO monitor. Timepoint: 36 weeks gestation or at childbirth, whichever is the soonest.

Secondary outcome measures
Current secondary outcome measures as of 21/11/2023:
Smoking-related:
1. Reported and validated 7-day smoking abstinence at 36 weeks gestation (measured by self-reported follow-up questionnaire, saliva sample analysed for cotinine and/or anabasine, exhaled breath sample for carbon monoxide levels)
2. Self-reported ≥50% reduction in daily cigarettes at 36 weeks gestation
3. Exhaled CO concentration at delivery (measured by exhaled breath sample for carbon monoxide levels)
4. Whether or not brief smoking lapse experienced, reported at 6 weeks post randomisation (self report)

Pregnancy and safety-related (collected from medical records at birth or up to 10 weeks postpartum):
1. Miscarriage (patient notes)
2. Stillbirth (patient notes)
3. Low birth weight for gestational age (patient notes)
4. Unadjusted birthweight and birthweight z score (patient notes)
5. Premature birth (patient notes)
6. Gestation at birth (patient notes)
7. Congenital abnormality (patient notes)
8. Mode of delivery (patient notes)
9. Admission to special care (patient notes)
10. Neonatal death (patient notes)

Exploratory outcomes:
1. Cigarettes per day when using NRT for ‘preloading’ or to cut down smoking (self report)
2. Exhaled CO when using NRT for ‘preloading’ or to cut down smoking (measured by exhaled breath sample for carbon monoxide levels) at around day 7
3. Saliva cotinine concentration when using NRT for ‘preloading’ or to cut down smoking (saliva sample analysed for cotinine and/or anabasine) at around day 7
4. Use of stop smoking support (self report) measured using self-report – follow up 1 questionnaire at 6 weeks after randomisation

Previous secondary outcome measures:
Smoking-related:
1. Reported 7-day smoking abstinence at 6 weeks after randomisation
2. Reported and validated 7-day smoking abstinence at 36 weeks gestation (cotinine/anabasine levels in saliva sample and/or CO levels tested using CO monitor)
3. Reported and validated ≥50% reduction in daily cigarettes at 36 weeks gestation
4. Exhaled CO concentration measured using CO monitor at delivery
5. Whether or not brief smoking lapse experienced, reported at 6 weeks after randomisation
NB: If delivery occurs before 36 weeks gestation, outcomes intended for collection at 36 weeks will be collected then

Pregnancy and safety-related (collected from medical records at birth or up to 10 weeks postpartum):
1. Miscarriage
2. Stillbirth
3. Low birth weight for gestational age
4. Unadjusted birthweight and birthweight z score
5. Premature birth
6. Gestation at birth
7. Congenital abnormality
8. Mode of delivery
9. Admission to special care
10. Neonatal death

Exploratory outcomes:
1. Exhaled CO when using NRT for 'preloading' or to cut down smoking measured using CO monitor at around day 7
2. Saliva cotinine concentration when using NRT for 'preloading' or to cut down smoking measured using saliva sample at around day 7
3. Use of stop smoking support measured using self-report – follow up 1 questionnaire at 6 weeks after randomisation
4. Reported use of NRT before the quit date and in brief smoking lapses measured using self-report – FU1 questionnaire

Overall study start date
05/04/2019

Completion date
31/10/2026

Eligibility

Key inclusion criteria
Current inclusion criteria as of 08/03/2022:

Women of any age who:
1. Are <25 weeks' gestation and have been referred for or have received or attended an intment as part of standard antenatal care
2. Smoke ≥ 5 daily cigarettes
3. Willing to set a quit date and accept referral to SSS
4. Willing to use NRT patch to try to stop smoking

5. Able to understand written and spoken English
6. Able to give consent

_____

Previous inclusion criteria:

Women of any age who:
1. Are ≤25 weeks' gestation with dating ultrasound-confirmed pregnancies
2. Smoke ≥5 daily cigarettes
3. Willing to set a quit date and accept referral to SSS
4. Are willing to use an NRT patch to try to stop smoking
5. Able to give consent

Participant type(s)
Patient

Age group
Mixed

Sex
Female

Target number of participants
Planned Sample Size: 1430; UK Sample Size: 1430

Key exclusion criteria
Current exclusion criteria as of 21/11/2023:
1. Already in a cessation study
2. Contraindications to NRT including: known severe reaction/hypersensitivity to NRT, recent cardiovascular/cerebrovascular event or changes and taking theophylline/clozapine
3. Currently uses e-cigarette every day or more frequently

Previous exclusion criteria:
1. Already in a cessation study
2. Currently uses e-cigarettes daily or more frequently
3. Contraindications to NRT including: severe cardiovascular disease, unstable angina, cardiac arrhythmias, recent cerebrovascular accident or transient ischaemic attack (TIA), chronic, generalized skin disorders or sensitivity to nicotine patches, chemical dependence/alcohol addiction or major fetal anomalies
4. Not able to read or understand text written in English

Date of first enrolment
01/04/2022

Date of final enrolment
31/12/2025

Locations

Countries of recruitment

England

United Kingdom

Wales

Study participating centre
Royal Berkshire Hospital
London Road
Reading
United Kingdom
RG1 5AN

Study participating centre
New Cross Hospital
Wolverhampton Road
Heath Town
Wolverhampton
United Kingdom
WV10 0QP

Study participating centre
Warrington Hospital
Lovely Lane
Warrington
United Kingdom
WA5 1QG

Study participating centre
Milton Keynes University Hospital
Standing Way
Eaglestone
Milton Keynes
United Kingdom
MK6 5LD

Study participating centre
Worcestershire Royal Hospital
Charles Hastings Way

Worcester
United Kingdom
WR5 1DD

Study participating centre
Birmingham Children's Hospital
Steelhouse Lane
Birmingham
United Kingdom
B4 6NH

Study participating centre
Leighton Hospital
Leighton
Crewe
United Kingdom
CW1 4QJ

Study participating centre
University Hospital of Hartlepool
Holdforth Road
Hartlepool
United Kingdom
TS24 9AH

Study participating centre
University of Nottingham
School of Medicine and Health Sciences
University Park
Nottingham
United Kingdom
NG7 2RD

Study participating centre
The Royal London Hospital
80 Newark Street
London
United Kingdom
E1 2ES

Study participating centre
The Hillingdon Hospitals NHS Foundation Trust
Pield Heath Road
Uxbridge
United Kingdom
UB8 3NN

Study participating centre
North Cumbria Integrated Care NHS Foundation Trust
Pillars Building
Cumberland Infirmary
Infirmary Street
Carlisle
United Kingdom
CA2 7HY

Study participating centre
Wirral University Teaching Hospital NHS Foundation Trust
Arrowe Park Hospital
Arrowe Park Road
Upton
Wirral
United Kingdom
CH49 5PE

Study participating centre
Walsall Healthcare NHS Trust
Manor Hospital
Moat Road
Walsall
United Kingdom
WS2 9PS

Study participating centre
The Princess Alexandra Hospital
Hamstel Road
Harlow
United Kingdom
CM20 1QX

Study participating centre
Manchester University NHS Foundation Trust
St Marys Hospital
Oxford Road
Manchester
United Kingdom
M13 9WL

Study participating centre
Sandwell and West Birmingham Hospitals NHS Trust
City Hospital
Dudley Road
Birmingham
United Kingdom
B18 7QH

Study participating centre
University Hospitals Dorset NHS Foundation Trust
Management Offices
Poole Hospital
Longfleet Road
Poole
United Kingdom
BH15 2JB

Study participating centre
Royal Free London NHS Foundation Trust
Royal Free Hospital
Pond Street
London
United Kingdom
NW3 2QG

Study participating centre
Sherwood Forest Hospitals NHS Foundation Trust
Kings Mill Hospital
Mansfield Road
Sutton-in-ashfield
United Kingdom
NG17 4JL

Study participating centre
Buckinghamshire Healthcare NHS Trust
Amersham Hospital
Whielden Street
Amersham
United Kingdom
HP7 0JD

Study participating centre
Stoke Mandeville Hospital
Mandeville Road
Aylesbury
United Kingdom
HP21 8AL

Study participating centre
Royal Cornwall Hospitals NHS Trust
Royal Cornwall Hospital
Treliske
Truro
United Kingdom
TR1 3LJ

Study participating centre
Great Western Hospitals NHS Foundation Trust
Great Western Hospital
Marlborough Road
Swindon
United Kingdom
SN3 6BB

Study participating centre
Cwm Taf NHS Trust
Dewi Sant Hospital
Albert Road
Pontypridd
United Kingdom
CF37 1LB

Study participating centre

Bolton NHS Foundation Trust
The Royal Bolton Hospital
Minerva Road
Farnworth
Bolton
United Kingdom
BL4 0JR

Study participating centre
Powys Teaching Lhb
Bronllys Hospital
Bronllys
Brecon
United Kingdom
LD3 0LS

Study participating centre
London North West University Healthcare NHS Trust
Northwick Park Hospital
Watford Road
Harrow
United Kingdom
HA1 3UJ

Study participating centre
Swansea Lhb
Kidwelly House, Charter Court
Phoenix Way
Swansea Enterprise Park
Swansea
United Kingdom
SA7 9FS

Study participating centre
Epsom and St Helier University Hospitals NHS Trust
St Helier Hospital
Wrythe Lane
Carshalton
United Kingdom
SM5 1AA

Study participating centre
East Lancashire Hospitals NHS Trust
Royal Blackburn Hospital
Haslingden Road
Blackburn
United Kingdom
BB2 3HH

Study participating centre
Cardiff & Vale University Lhb
Woodland House
Maes-y-coed Road
Cardiff
United Kingdom
CF14 4HH

Study participating centre
Aneurin Bevan Lhb - Caerphilly Locality Office
Llanarth House
Newbridge Gateway
Bridge Street
Newport
United Kingdom
NP11 5GH

Study participating centre
County Durham and Darlington NHS Foundation Trust
Darlington Memorial Hospital
Hollyhurst Road
Darlington
United Kingdom
DL3 6HX

Study participating centre
Hull University Teaching Hospitals NHS Trust
Bay 2 - Specialist Midwives Office
Antenatal Day Unit
Women’s & Children’s Hospital
Anlaby Road
Hull
United Kingdom
HU3 2JZ

Study participating centre
York and Scarborough Teaching Hospitals
Surgery and Family Health
LARC
York Hospital
Wigginton Road
York
United Kingdom
YO31 8HE

Sponsor information

Organisation
University of Nottingham

Sponsor details
Research and Innovation
East Atrium
Jubilee Conference centre
Triumph Road
Nottingham
England
United Kingdom
NG8 1DH
+44 (0)11584667906
sponsor@nottingham.ac.uk

Sponsor type
University/education

Website
http://www.nottingham.ac.uk/

ROR
https://ror.org/01ee9ar58

Funder(s)

Funder type
Government

Funder Name

NIHR Evaluation, Trials and Studies Co-ordinating Centre (NETSCC); Grant Codes: NIHR129210

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal. The protocol and statistical analysis plan will be available at a later date.

Intention to publish date
31/01/2027

Individual participant data (IPD) sharing plan
The current data-sharing plans for this study are unknown and will be available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Interview version 1.0	25/08/2021	13/10/2021	No	Yes
Participant information sheet	Pilot version 1.0	25/08/2021	13/10/2021	No	Yes
Participant information sheet	Trial version 1.0	25/08/2021	13/10/2021	No	Yes
HRA research summary			26/07/2023	No	No