



2023 exceptional surveillance of tobacco: preventing uptake, promoting quitting and treating dependence (NICE guideline NG209)

Surveillance report

Published: 21 February 2023

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Surveillance decision

We will not update the recommendation in the [NICE guideline on tobacco: preventing uptake, promoting quitting and treating dependence](#). Following publication of a single study there remains uncertainty about the effectiveness and safety of using nicotine-containing e-cigarettes to help women stop smoking in pregnancy. We will refresh the information on this subject by making some [editorial amendments](#).

New published evidence

The purpose of this exceptional review was to examine any impact on NICE's guideline on tobacco, following completion of the [NIHR funded study on helping pregnant smokers quit: a multi-centre randomised controlled trial \(RCT\) of e-cigarette and nicotine patches](#), which published its findings in the [Nature Medicine journal in 2022](#). The full Health Technology Assessment (HTA) report is awaiting publication (see the [NIHR webpage](#) for updates). This is the first RCT that compared the effectiveness and safety of licensed nicotine patches against e-cigarettes to help women stop smoking in pregnancy.

Context

Prevalence of smoking tobacco in pregnancy is at 10.7%, but there is considerable variation in this when factors such as age, income, and geographical area are taken into consideration. Information on the harmful and teratogenic effects of tobacco smoke, including from tar or carbon monoxide, is well documented. Information on the safety and effectiveness of nicotine-containing [e-cigarettes](#), including the effects of switching from smoking to vaping in the perinatal phase, is less clear. The need for new evidence in this area is significant as, among other reasons, e-cigarettes are popular among young people and people who are attempting to quit, the effects of e-cigarettes (chemicals and nicotine) on the fetus remain uncertain and we don't know about the effects of e-cigarettes on cessation and reduction in pregnancy, see [Nicotine vaping in England 2022](#) and [Vaping in England: an evidence update including mental health and pregnancy 2020](#).

Guideline background

During development of the NICE guideline in 2021, the committee noted there was no

evidence of safety or effectiveness for e-cigarettes in pregnancy and were unable to make recommendations. There was available evidence of effectiveness for nicotine replacement therapy (NRT), which showed that when added to a behavioural intervention it may help women stop smoking in pregnancy. The guideline recommends that service providers:

- Provide the pregnant woman with intensive and ongoing support (brief interventions alone are unlikely to be sufficient) throughout pregnancy and beyond.
- Consider NRT alongside behavioural support to help women stop smoking in pregnancy (see [BNF information on NRT](#)).

The lack of evidence on safety or effectiveness for e-cigarettes in pregnancy made this a priority area for research; 2 recommendations for research were made to answer the following questions:

- [Health effects of e-cigarettes](#): What are the short- and long-term health effects of e-cigarette use? Are there any specific health effects relating to use in pregnancy, or use by children and young people?
- [Nicotine replacement therapy and e-cigarettes and pregnancy](#): Are nicotine replacement therapy or nicotine-containing e-cigarettes effective to help women stop smoking in pregnancy (and at what dose)?

The committee also made a recommendation for research to help understand the [views and concerns of pregnant women and their healthcare professionals about using nicotine-containing e-cigarettes in pregnancy](#).

Exceptional surveillance review methods

The exceptional surveillance process consisted of:

- Considering the new evidence that triggered the exceptional review.
- Feedback from topic experts on the impact of the new evidence.
- Considering the evidence used to develop the guideline in 2021.
- Examining the NICE event tracker for relevant ongoing and published events.

We decided that full updated literature searches were not needed because the information

we had from the NIHR study was enough to establish whether an update to the guideline was needed. We did ask topic experts if they were aware of additional new or ongoing trials involving e-cigarettes in pregnancy, but none were identified.

For further details about the process and the possible update decisions that are available, see [ensuring that published guidelines are current and accurate in developing NICE guidelines: the manual](#).

Reasons for the decision

Helping pregnant smokers quit - NIHR study methods

This NIHR funded trial included pregnant women who smoke in England and Scotland. They were randomised to e-cigarettes or nicotine patches (combined with other NRT products if required) during pregnancy; behavioural support was offered in both arms. The primary outcome was prolonged abstinence reported throughout pregnancy and validated biochemically at the end of pregnancy by salivary cotinine levels. Participants lost to follow-up or anyone with missing smoking status data for any reason at follow-up, were classified as still smoking. Secondary outcomes (self-reported abstinence at 4 weeks post-quit and at end of pregnancy, and 7-day point-prevalence abstinence) and safety outcomes (including pre-term birth, birthweight, low birthweight [less than 2.5 kg] and gestational age) were also analysed on an intention to treat basis. For further information on the study methods, see the [Nature Medicine journal](#) or the [NIHR study protocol](#).

Helping pregnant smokers quit - NIHR study results

The study recruited 1,140 pregnant women who smoked (median age 27 years) across 23 hospitals in the England and 1 NHS stop smoking service in Scotland. The main smoking cessation outcomes reported in the Nature Medicine journal included:

- For the primary outcome (validated prolonged abstinence at the end of pregnancy), the proportion of women who quit smoking in the e-cigarettes arm was 6.8% versus 4.4% in the patches arm and did not differ significantly (relative risk [RR]=1.55, 95% confidence interval [CI] 0.95 to 2.53, p=0.08).

- There were low return rates of useable saliva samples in those who self-reported abstinence (108 of 196; 66 in the e-cigarettes arm and 42 in the NRT arm) and for validated prolonged abstinence (39 in the e-cigarettes arm and 25 in the NRT arm).
- In anticipation that some participants in the nicotine patch group would also use e-cigarettes during the study, a pre-specified sensitivity analysis was conducted (excluding abstinent participants who used non-allocated e-cigarettes products in the nicotine patch group), it found that e-cigarettes were more effective than patches (6.8% versus 3.6%; RR=1.93, 95% CI 1.14 to 3.26, p=0.02).

The main birth outcomes reported were:

- Safety data were available from 1,110 of the 1,140 women in the study (556 of 571 in the e-cigarettes arm versus 554 of 569 in the NRT arm, 97.4% in each arm).
- Mean birthweight was the same in both study arms, despite the higher use of nicotine products in the e-cigarettes arm: 3.1 versus 3.1 kg (mean difference 0.03 [-0.04 to 0.10, p=0.45]).
- There were more babies with low birth weight (less than 2.5 kg) in the NRT use group: e-cigarettes 52 (9.6%) versus NRT 80 (14.8%; RR=0.65, 95% CI 0.47 to 0.9, p=0.01).
- Adverse outcomes in the 2 study arms were similar, including for miscarriage, stillbirth, neonatal death and pre-term birth.

Topic expert feedback

In this exceptional review we engaged with topic experts who were recruited to the NICE Centre for Guidelines Expert Advisers Panel to represent their specialty. We received feedback from 4 topic experts with 3 (a public health consultant, reader in tobacco studies and a tobacco dependence specialist) indicating that the guideline should be updated to take account of the helping pregnant smokers quit trial. One expert (public health specialist) did not believe the new trial would support a change to the guideline.

The 3 experts in support of an update noted that the trial goes some way to fill the evidence gap that prevented the guideline committee from making recommendations in this area. In particular, they believe that the new evidence indicates e-cigarettes are likely to be as effective as NRT in supporting pregnant women to quit. They also expressed that e-cigarettes, like NRT, are not likely to be a first line treatment, but are preferable than smoking if a pregnant woman is unable to quit tobacco without support of a nicotine-

containing product.

For the 1 expert who did not believe the trial could support an update of the recommendations, the main issue of contention was the low return of saliva samples for validated abstinence in the primary outcome. The expert also commented that biochemical validation of abstinence is the 'gold standard' in tobacco studies. As noted by the study authors, validation results were available from just over half of the self-reported abstinent participants and reduced the power to detect a difference between the 2 study arms.

Other considerations

When considering available evidence in the general population, the 2021 guideline committee agreed that there was insufficient evidence to tell whether e-cigarettes cause long-term effects. E-cigarettes are relatively new devices, and they agreed it is important to understand whether they cause any health harms or benefits aside from their potential to reduce smoking related harm.

While the trial provides new evidence on cessation and birth outcomes there were no outcomes recorded beyond birth for the mother and child. This is in a context where medium- and long-term outcome evidence for e-cigarettes is lacking during and beyond pregnancy. In this respect, this trial alone does not address the evidence gap or provide the assurances about safety that the committee hoped to address through the recommendation for research concerning health effects of e-cigarettes.

Furthermore, as with many studies concerning the use of NRT and e-cigarettes during pregnancy they are designed to investigate effectiveness and not adverse events, meaning they may not have been large enough to show an effect. In addition, we have no new evidence about birth outcomes in a trial comparing e-cigarettes with placebo and non-placebo (behavioural support only) controls.

Given the potential risks of using e-cigarettes during pregnancy, there remains important evidence gaps in this area.

Equalities

Smoking prevalence among pregnant women is higher among those aged under 20 than among older women. Pregnant women from manual occupation groups are 5 times more

likely to smoke than women from managerial and professional occupations.

The preference for e-cigarettes to help stop smoking among these groups and others ([Nicotine vaping in England 2022](#)) makes this an area of unmet need in the research literature; additional evidence for e-cigarettes could potentially help address smoking related health inequalities.

An equalities and health inequalities assessment was completed during this surveillance review. See [appendix A for details](#).

Overall decision

The NICE guideline on tobacco does not make recommendations on the use of e-cigarettes to help women stop smoking in pregnancy as there was no evidence about their effectiveness, and only limited evidence about safety at the time of guideline development. The guideline does make recommendations about the use of NRT in this population.

The helping pregnant smokers quit trial is a large study which is relevant to the [recommendation for research on nicotine replacement therapy and e-cigarettes and pregnancy](#) and provides new evidence on effectiveness, when comparing NRT and e-cigarettes. However, the authors acknowledge that collecting saliva samples for validation of results proved challenging, and they were available from only a little over half of the self-reported abstinent participants. This limitation of the research undermines confidence in the findings and highlights a need for further confirmatory effectiveness evidence in this area.

This trial alone provides only limited evidence to address the relevant [recommendation for research on health effects of e-cigarettes](#). The findings do not suggest that e-cigarettes use in pregnancy poses larger risks than the use of NRT. Overall, this study provides some new evidence that e-cigarettes may have similar birth outcomes as NRT among women who use these products to support a quit attempt. However, the key evidence gaps that the guideline committee wanted to address through NICE recommendations for research remain, notably there were no outcomes recorded over the longer-term including after birth. Further, the events rates were very low in most cases and we have no evidence of e-cigarettes in comparison to placebo and non-placebo (behavioural support only) controls.

Following consideration of the results from the trial and topic expert feedback, the new evidence alone does not have an impact on the NICE guideline. As this trial is the only evidence to date on the use of e-cigarettes during pregnancy for cessation, it seems prudent to await for further evidence on the effectiveness and safety of e-cigarettes during pregnancy. There remains a need for evidence to clarify what advice should be given to women who are unable to quit without the support of nicotine and prefer to use e-cigarettes over NRT.

Editorial amendments

The guideline information about nicotine-containing e-cigarettes to help women stop smoking in pregnancy will be refreshed following publication of the [NIHR funded single study on helping pregnant smokers quit: a multi-centre RCT of e-cigarette and nicotine patches](#).

Publication of the study now means evidence is available, but it is insufficient to support development of recommendations about nicotine-containing e-cigarettes to help women stop smoking in pregnancy.

The following subheading and statement will be included in the section of the guideline for [recommendations on treating tobacco dependence in pregnant women](#):

Evidence on nicotine-containing e-cigarettes to help women stop smoking in pregnancy

It is not possible to make recommendations because there is insufficient evidence:

- about the effectiveness of nicotine-containing e-cigarettes to help stop smoking in pregnancy;
- to tell whether using nicotine-containing e-cigarettes in pregnancy causes harm to the fetus or long-term to the child after birth. **[2023]**

E-cigarettes are relatively new devices, and it is important to understand whether they cause any health harms or benefits and their potential to support a quit attempt during pregnancy. To support future development of the guideline, [recommendations for research were made to help understand the health effects of e-cigarettes in pregnancy, whether they are effective to help women stop smoking in pregnancy and the views and concerns of pregnant women and their healthcare professionals about using nicotine-containing e-](#)

cigarettes in pregnancy.

ISBN: 978-1-4731-5043-0