

## JSNA Supporting Evidence: Rapid Evidence and Economic Review (Pregnancy and pre-operative smoking cessation)

This is a rapid literature review and summary of evidence to support the JSNA. It focusses on smoking cessation in relation to engagement and delivery of services to some of the targeted groups (pregnancy and pre-op) established for the core specialist team from 1<sup>st</sup> April 2018.

Evidence has been found using the NICE evidence search <https://www.evidence.nhs.uk/>.

### Pregnancy

#### NICE guidelines

**[Smoking: stopping in pregnancy and after childbirth Public health guideline \[PH26\]](#). Published date: June 2010**

This guideline covers support for women to stop smoking during pregnancy and in the first year following childbirth.

The recommendations include:

- Identifying pregnant women who smoke and referring them to NHS Stop Smoking Services. This is aimed at midwifery and includes measuring levels of carbon monoxide in all pregnant women and referring those who smoke to services.
- All other health and social care professionals, such as GPs, health visitors, sonographers, youth workers, etc., should be identifying pregnant women who smoke and refer to NHS Stop Smoking Services.
- Provide initial on-going support including the provision of interventions throughout pregnancy and after delivery. It recommends the use of Carbon monoxide testing and the provision of support to women who recently quit, including the use of Nicotine Replacement Therapy when needed.
- Ensure services meet the needs of disadvantaged pregnant women who smoke, including collaboration with agencies who support women with complex needs, such as substance misuse services, teenage pregnancy support and mental health services.
- Ensure partners and others, related to pregnant women, who smoke, are offered stop smoking support and advice on passive smoking.
- Stop Smoking Services to contact all women by phone and attempting to see those whose contact was not possible at key maternity appointments. It also recommends offering appointments at other venues, including home visits. There are also recommendations on how to relay information to pregnant women on the phone.
- Training should be provided to relevant professionals on delivering stop smoking interventions to pregnant women, namely midwives. All other relevant professionals should be trained on how to deliver brief interventions to initiate a referral to stop smoking services
- Discuss the risks and benefits of NRT with pregnant women who smoke, particularly those who do not wish to accept the offer of help from the local specialist stop smoking service. If a woman expresses a clear wish to receive NRT, use professional judgement when deciding whether to offer a prescription.
- Advise pregnant women using nicotine patches to remove them before going to bed.
- Neither varenicline or bupropion should be offered to pregnant or breastfeeding women.

The [evidence review](#) behind the 2010 guideline also highlighted:

- At the first contact with a pregnant woman, ask her whether she smokes and advise her to stop in a way that is sensitive to her preferences, needs and circumstances. Provide information about the risks of smoking to the unborn child and the hazards of exposure to secondhand smoke. Address any concerns she and her partner or family may have about stopping smoking.
- Interventions which employ cognitive behavioural approaches to cessation are effective. Those using a 'stages of change' approach showed borderline effectiveness and there was no evidence that using the results of feedback tests (such as reports of urinary cotinine levels) increased cessation.
- Financial incentives for smoking cessation during pregnancy were found to be the single most effective intervention based on the results of four trials conducted in the USA but that further research is required to explore their applicability in the UK.
- Insufficient evidence for the effectiveness of NRT for smoking cessation in pregnancy.
- Self-help interventions for cessation during pregnancy are effective however there was a lack of evidence that more intensive (i.e. longer or more frequently used) self-help materials had a greater impact than less intensive ones.

[New smoking cessation guidelines](#) were published on March 28<sup>th</sup> 2018 but do not update the recommendations for smoking in pregnancy. A search of the literature in relation to smoking cessation in pregnancy was conducted for this rapid review to provide any updates since 2010 where possible and suggestions for further more detailed evidence reviews. Summaries of the evidence obtained can be found in the appendix.

### Nicotine Replacement Therapy (NRT)

The NICE guidelines highlight mixed evidence on the use of NRT in smoking cessation in pregnancy. A more recent [2015 Cochrane systematic review](#) looking at 9 trials shows borderline evidence to suggest NRT combined with behavioural support might help women to stop smoking in later pregnancy. However, when only the higher quality placebo controlled trials were analysed, NRT was found to be no more effective than a placebo. There is also a large degree of uncertainty around the cost effectiveness of delivering the intervention. One study highlighted improved developmental outcomes in children of mothers who received the NRT intervention, although this was not taken into account in assessing its cost effectiveness.

Adherence to NRT during pregnancy has been raised as an issue within the literature, with one possible reason being a more rapid nicotine metabolism during pregnancy affecting the dose required to be effective. Further studies are required to determine whether higher dose NRT in pregnancy would improve outcomes.

**As the initial search and review of evidence remains inconclusive it is recommended that NICE guidelines continue to be followed and a more detailed evidence search and review be conducted looking at NRT in pregnant women as further evidence becomes available.**

### Self-help interventions

Self-help interventions delivered via automated, interactive text messages were not found to statistically significantly improve rates of smoking cessation. [The results](#) are subject to a wide margin of error and further studies would be required to verify these findings.

The most effective intervention for improving smoking cessation in pregnancy is a financial incentive based scheme. A 2015 [UK trial](#) that paid participants up to £400 in shopping vouchers for setting a quit date and verifying abstinence at three appointments during pregnancy achieved a quit rate of 22.5%, compared to 8.6% for the control group. As identified in the NICE guidance [Research from the USA](#) has also found financial incentives to be an effective intervention.

The authors of the UK trial on financial incentives speculate that shopping vouchers may contribute needed income in advance of the baby's arrival for women in lower socioeconomic groups, who are more likely to smoke in pregnancy. Further analysis of Northamptonshire's cohort of pregnant smokers may be able to identify target populations that may benefit from this type of intervention.

Financial incentive programmes have been introduced in other areas in the UK, including Greater Manchester, Stoke-on-Trent and Tayside. Case studies from these areas would provide further insight into the replicability of the study's results prior to implementing such a scheme locally.

**It is recommended that case studies be obtained from these areas if commissioners wish to explore this option further.**

### E-Cigarettes

At the time of writing, there are no e-cigarettes on the UK market that have a medicinal licence, therefore they cannot be prescribed and no particular product can be recommended as an aid to smoking cessation. [Guidance](#) aimed at midwives and healthcare professionals around the use of e-cigarettes in pregnancy promote quitting through the use of licensed NRT products and conventional smoking cessation services, but does not discourage the use of e-cigarettes if they help the expectant mother stay smoke free. The view in the guidance is that e-cigarettes are likely to be significantly less harmful to the mother and unborn baby than cigarettes.

There is limited evidence on the risks of e-cigarette use in pregnancy. An [animal study](#) has shown that exposure to chemicals found in e-cigarettes can cause facial birth defects. Risks may also vary between products depending on the flavourings and concentration of nicotine used in the e-cigarette liquid. **Further research is required to determine the relative safety of using e-cigarettes compared to normal cigarettes.**

## Acute settings

### NICE Guidelines

[NICE guidelines Smoking: acute, maternity and mental health services](#). **Public health guideline [PH48]. Published date: November 2013**

Stopping smoking at any time has considerable health benefits for people who smoke, and for those around them. For people using secondary care services, there are additional advantages, including shorter hospital stays, lower drug doses, fewer complications, higher survival rates, better wound healing, decreased infections, and fewer re-admissions after surgery.

Secondary care providers have a duty of care to protect the health of, and promote healthy behaviour among, people who use, or work in, their services. This duty of care includes providing them with effective support to stop smoking or to abstain from smoking while using or working in secondary care services.

This guidance aims to support smoking cessation, temporary abstinence from smoking and smoke free policies in all secondary care settings. It recommends:

- Strong leadership and management to ensure secondary care premises (including grounds, vehicles and other settings involved in delivery of secondary care services) remain smoke free – to help to promote non-smoking as the norm for people using these services.
- All hospitals have an on-site stop smoking service.
- Identifying people who smoke at the first opportunity, advising them to stop, providing pharmacotherapy to support abstinence, offering and arranging intensive behavioural support, and following up with them at the next opportunity.
- Providing intensive behavioural support and pharmacotherapy as an integral component of secondary care, to help people abstain from smoking, at least while using secondary care services.
- Ensuring continuity of care by integrating stop smoking support in secondary care with support provided by community-based and primary care services.
- Ensuring staff are trained to support people to stop smoking while using secondary care services.
- Supporting all staff to stop smoking or to abstain while at work.
- Ensuring there are no designated smoking areas, no exceptions for particular groups, and no staff-supervised or staff-facilitated smoking breaks for people using secondary care services.

The [evidence](#) from the guidance covers the efficacy of interventions delivered to surgical patients. It highlights that brief interventions prior to surgery lack efficacy even if accompanied by NRT. Also stop smoking messages delivered under sedation are not effective. However, extended support accompanied by medication is effective. NRT accompanied by behavioural support is effective, whereas combinations of patches and inhaler was not more effective than each medication on its own and Bupropion and varenicline provided without on-going face to face support lacks efficacy.

[NICE economic analysis](#) of smoking cessation in secondary care (2013) concluded smoking cessation interventions were cost effective across populations with different conditions, including patients presenting at secondary care with COPD and cardiac conditions and pre-operative patients. For the majority of interventions and population groups, the conclusion from the economic model – i.e. that the interventions are cost-effective and thus value for money – holds not only when the lifetime benefits of smoking cessation are considered, but also when a more short term perspective is adopted.

Results from smoking cessation interventions suggest that even relatively short periods of abstinence such as in preparation for surgery have the potential to generate benefits that outweigh the cost of interventions.

The review found for preoperative patients, smoking cessation generates cost savings up to £4,800 per patient over lifetime (£800 being health care cost savings and the remaining £4,000 representing productivity savings).

As with any modelling exercise, the results are subject to uncertainty and numerous assumptions. However, given that the ICERs generally fall well below the £30,000 threshold (and the interventions are even cheaper and more effective than their comparators), it is unlikely that the conclusions are sensitive to those assumptions. In fact, the sensitivity analysis showed that most interventions remain cost-effective even when the costs and effects of the interventions are randomly varied.

Moreover, the benefits associated with smoking cessation captured in our analysis are limited to a number of health outcomes and only health care cost and productivity cost savings have been considered. Improvements in these and other health outcomes associated with smoking cessation are also likely to lead to reduced use of social care resources and savings in individuals costs – such as direct health care payments and transport costs.

[A Cochrane review](#) from 2014 also highlighted that evidence from preoperative smoking interventions providing behavioural support and offering NRT increase short term smoking cessation and may reduce post-operative morbidity. Based on limited evidence they suggest that weekly counselling and NRT 4-8 weeks prior to surgery is more likely to have an impact on complications and long term smoking cessation.

**It is recommended that any local service is evaluated to ensure this potential is realised locally.**

## Appendix

### **Cochrane review of drug treatments for stopping smoking in pregnancy**

<http://cochranelibrary-wiley.com/doi/10.1002/14651858.CD010078.pub2/full>

#### Main results:

This review includes a total of nine trials which enrolled 2210 pregnant smokers: eight trials of NRT and one trial of bupropion as adjuncts to behavioural support/CBT. The risk of bias was generally low across trials with virtually all domains of the 'Risk of bias' assessment tool being satisfied for the majority of studies. We found no trials investigating varenicline or ENDS. Compared to placebo and non-placebo controls, there was a difference in smoking rates observed in later pregnancy favouring use of NRT (risk ratio (RR) 1.41, 95% confidence interval (CI) 1.03 to 1.93, eight studies, 2199 women). However, subgroup analysis of placebo-RCTs provided a lower RR in favour of NRT (RR 1.28, 95% CI 0.99 to 1.66, five studies, 1926 women), whereas within the two non-placebo RCTs there was a strong positive effect of NRT, (RR 8.51, 95% CI 2.05 to 35.28, three studies, 273 women; P value for random-effects subgroup interaction test = 0.01). There were no differences between NRT and control groups in rates of miscarriage, stillbirth, premature birth, birthweight, low birthweight, admissions to neonatal intensive care, caesarean section, congenital abnormalities or neonatal death. Compared to placebo group infants, at two years of age, infants born to women who had been randomised to NRT had higher rates of 'survival without developmental impairment' (one trial). Generally, adherence with trial NRT regimens was low. Non-serious side effects observed with NRT included headache, nausea and local reactions (e.g. skin irritation from patches or foul taste from gum), but these data could not be pooled.

#### Authors' conclusions:

NRT used in pregnancy for smoking cessation increases smoking cessation rates measured in late pregnancy by approximately 40%. There is evidence, suggesting that when potentially-biased, non-placebo RCTs are excluded from analyses, NRT is no more effective than placebo. There is no evidence that NRT used for smoking cessation in pregnancy has either positive or negative impacts on birth outcomes. However, evidence from the only trial to have followed up infants after birth, suggests use of NRT promotes healthy developmental outcomes in infants. Further research evidence on NRT efficacy and safety is needed, ideally from placebo-controlled RCTs which achieve higher adherence rates and which monitor infants' outcomes into childhood. Accruing data suggests that it would be ethical for future RCTs to investigate higher doses of NRT than those tested in the included studies.

### **The SNAP trial: a randomised placebo-controlled trial of nicotine replacement therapy in pregnancy – clinical effectiveness and safety until 2 years after delivery, with economic evaluation**

<https://www.ncbi.nlm.nih.gov/pubmed/25158081>

#### Results:

One thousand and fifty women enrolled (521 NRT, 529 placebo). There were 1010 live singleton births and 12 participants had live twins, while there were 14 fetal deaths and no birth data for 14 participants. Numbers of adverse pregnancy and birth outcomes were similar in trial groups, except for a greater number of caesarean deliveries in the NRT group. Smoking: all participants were included in the intention-to-treat (ITT) analyses; those lost to follow-up (7% for primary outcome) were assumed to be smoking. At 1 month after randomisation, the validated cessation rate was higher in the NRT group {21.3% vs. 11.7%, odds ratio [OR], [95% confidence interval (CI)] for cessation with NRT, 2.05 [1.46 to 2.88]}. At delivery, there was no difference between groups'

smoking cessation rates: 9.4% in the NRT and 7.6% in the placebo group [OR (95% CI), 1.26 (0.82 to 1.96)]. Infants: at 2 years, analyses were based on data from 888 out of 1010 (87.9%) singleton infants (including four postnatal infant deaths) [445/503 (88.5%) NRT, 443/507 (87.4%) placebo] and used multiple imputation. In the NRT group, 72.6% (323/445) had no impairment compared with 65.5% (290/443) in placebo (OR 1.40, 95% CI 1.05 to 1.86). The incremental cost-effectiveness ratio for NRT use was £4156 per quitter (£4926 including twins), but there was substantial uncertainty around these estimates.

### **Financial incentives for smoking cessation in pregnancy: randomised controlled trial**

<http://www.bmj.com/content/350/bmj.h134>

Abstract:

*Objective:* To assess the efficacy of a financial incentive added to routine specialist pregnancy stop smoking services versus routine care to help pregnant smokers quit.

*Design:* Phase II therapeutic exploratory single centre, individually randomised controlled parallel group superiority trial.

*Setting:* One large health board area with a materially deprived, inner city population in the west of Scotland, United Kingdom.

*Participants:* 612 self reported pregnant smokers in NHS Greater Glasgow and Clyde who were English speaking, at least 16 years of age, less than 24 weeks pregnant, and had an exhaled carbon monoxide breath test result of 7 ppm or more. 306 women were randomised to incentives and 306 to control.

*Interventions:* The control group received routine care, which was the offer of a face to face appointment to discuss smoking and cessation and, for those who attended and set a quit date, the offer of free nicotine replacement therapy for 10 weeks provided by pharmacy services, and four, weekly support phone calls. The intervention group received routine care plus the offer of up to £400 of shopping vouchers: £50 for attending a face to face appointment and setting a quit date; then another £50 if at four weeks' post-quit date exhaled carbon monoxide confirmed quitting; a further £100 was provided for continued validated abstinence of exhaled carbon monoxide after 12 weeks; a final £200 voucher was provided for validated abstinence of exhaled carbon monoxide at 34-38 weeks' gestation.

*Main outcome measure:* The primary outcome was cotinine verified cessation at 34-38 weeks' gestation through saliva (<14.2 ng/mL) or urine (<44.7 ng/mL). Secondary outcomes included birth weight, engagement, and self reported quit at four weeks.

*Results:* Recruitment was extended from 12 to 15 months to achieve the target sample size. Follow-up continued until September 2013. Of the 306 women randomised, three controls opted out soon after enrolment; these women did not want their data to be used, leaving 306 intervention and 303 control group participants in the intention to treat analysis. No harms of financial incentives were documented. Significantly more smokers in the incentives group than control group stopped smoking: 69 (22.5%) versus 26 (8.6%). The relative risk of not smoking at the end of pregnancy was 2.63 (95% confidence interval 1.73 to 4.01)  $P < 0.001$ . The absolute risk difference was 14.0% (95% confidence interval 8.2% to 19.7%). The number needed to treat (where financial incentives need to be offered to achieve one extra quitter in late pregnancy) was 7.2 (95% confidence interval 5.1 to 12.2). The mean birth weight was 3140 g (SD 600 g) in the incentives group and 3120 (SD 590) g in the control group ( $P = 0.67$ ).

*Conclusion:* This phase II randomised controlled trial provides substantial evidence for the efficacy of incentives for smoking cessation in pregnancy; as this was only a single centre trial, incentives should

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now be tested in different types of pregnancy cessation services and in different parts of the United Kingdom.

### **Are financial incentives cost-effective to support smoking cessation during pregnancy?**

<https://www.ncbi.nlm.nih.gov/pubmed/26370095>

*Findings:* The incremental cost per quitter at 34-38 weeks pregnant was £1127 (\$1716). This is similar to the standard look-up value derived from Stapleton & Wests published ICER tables (72), £1390 per quitter, by looking-up the CPIT trial incremental cost (£157) and incremental 6 month quit outcome (0.14). The lifetime model resulted in an incremental cost of £17 (95% CI: -£93, £107) and a gain of 0.04 QALYs (95% CI: -0.058, 0.145), giving an ICER of £482/QALY (\$734/QALY). Probabilistic sensitivity analysis indicates uncertainty in these results, particularly regarding relapse after birth. The expected value of perfect information was £30 million (at a willingness to pay of £30,000/QALY), so given current uncertainty, additional research is potentially worthwhile.

*Conclusion:* Financial incentives for smoking cessation in pregnancy are highly cost-effective, with an incremental cost per QALY of £482, which is well below recommended decision thresholds.

### **Large multicentre pilot randomised controlled trial testing a low-cost, tailored, self-help smoking cessation text message intervention for pregnant smokers (MiQuit)**

<http://eprints.nottingham.ac.uk/41557/>

*Abstract:*

*Aims:* To estimate the effectiveness of pregnancy smoking cessation support delivered by SMS text message and key parameters needed to plan a definitive trial.

*Design:* Multicentre, parallel-group, single-blinded, individual randomised controlled trial.

*Setting:* 16 antenatal clinics in England.

*Participants:* 407 participants were randomised to the intervention (n=203) or usual care (n=204). Eligible women were <25 weeks gestation, smoked at least 1 daily cigarette (> 5 pre-pregnancy), were able to receive and understand English SMS texts and were not already using text-based cessation support.

*Intervention:* All participants received a smoking cessation leaflet; intervention participants also received a 12-week programme of individually-tailored, automated, interactive, self-help smoking cessation text messages (MiQuit).

*Outcome Measurements:* Seven smoking outcomes including validated continuous abstinence from 4 weeks post-randomisation until 36 weeks gestation, design parameters for a future trial and cost-per-quitter.

*Findings:* Using the validated, continuous abstinence outcome, 5.4% (11/203) of MiQuit participants were abstinent versus 2.0% (4/204) of usual care participants (odds ratio [OR] 2.7, 95% confidence interval [CI] 0.93 to 9.35). The Bayes Factor for this outcome was 2.23. Completeness of follow up at 36 weeks gestation was similar in both groups; provision of self-report smoking data was 64% (MiQuit) and 65% (usual care) and abstinence validation rates were 56% (MiQuit) and 61% (usual care). The incremental cost-per-quitter was £133.53 (95% CI -£395.78 to £843.62).

*Conclusions:* There was some evidence, though not conclusive, that a text messaging programme may increase cessation rates in pregnant smokers when provided alongside routine NHS cessation care.

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