Outpatient Tobacco Addiction Treatment Pathway
Additional Notes

First Line: Varenicline

(provide in conjunction with counselling/support, but if such support is refused or is not available, this should not preclude treatment with varenicline)

Mode of Action:

Varenicline is a nicotinic receptor agonist and antagonist. It causes dopamine release via its agonist action and alleviates cravings for nicotine and also prevents dopamine release from nicotine in cigarette smoke through its antagonist action. It is a highly effective treatment for tobacco addiction through both relief of carvings and preventing positive impact from smoking that reinforces the addiction.

Evidence Base:

The EAGLES study is the only randomised controlled trial to evaluate the effectiveness of the three main pharmacotherapy strategies (nicotine replacement therapy, varenicline and bupropion) in tobacco addiction head to head and versus placebo. Over 8000 patients were randomised between the four arms. ***Varenicline was the most effective treatment (33.5% quit rate at 9-12 weeks):***

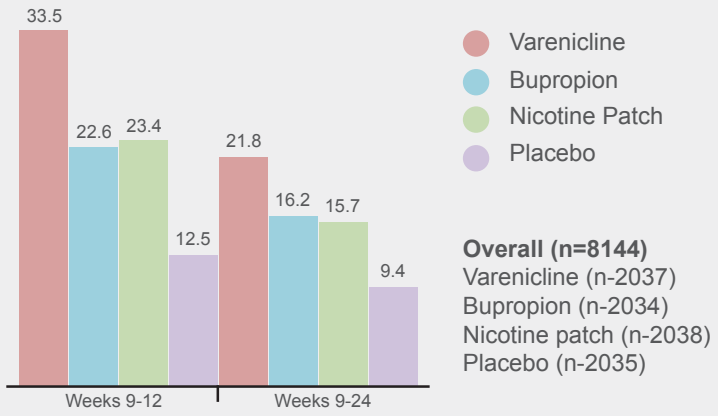


Figure 1: *Abstinence rates in the EAGLES study*

Varenicline versus placebo OR 3.61, p<0.0001 (95% CI 3.07-4.24)

Varenicline versus NRT OR 1.75, p<0.001 (95% CI 1.46-1.93)

Varenicline versus bupropion OR 1.75, p<0.0001 (95% CI 1.52-2.01)

Side effects:

Warn about nausea (advise to take medication with food and water), sleep disturbance and vivid dreams

Contraindications:

End-stage renal failure eGFR<10mls/min, pregnant or breast feeding mothers

Varenicline is safe to use in patients with a history of mental health disease however we ask that the mental health disease has been stable for the last 3 months with no changes in medication dose or new medication started

Dose:

0.5mg once daily Day 1-3
0.5mg twice daily Day 4-7
1mg twice daily Day 8+

Prescribing notes:

Varenicline is started prior to the quit date. This quit date is ideally within 1-2 weeks of starting varenicline but can be at any time within the 12 weeks of treatment.
The dose can be reduced to 0.5mg if intolerable side effects
The course length is 12 weeks but can be extended to 24 weeks
Further courses of varenicline in the event of relapse are appropriate

Note:

There is no increased risk of moderate to severe neuropsychiatric adverse events with varenicline (EAGLES study 2016, The Lancet). The act of stopping smoking carries a small risk of moderate to severe neuropsychiatric events and this is regardless of the treatment used. The risk is higher in those with a history of psychiatric illness (5%) versus those without (2%). Advise patients to seek help in the event of a neuropsychiatric event. In the long term, stopping smoking improves mental health disease, e.g. stopping smoking is more effective than antidepressants in treating depression.

Second Line: Nicotine Replacement Therapy

(provide in conjunction with counselling/support, but if such support is refused or is not available, this should not preclude treatment with NRT)

Mode of Action:

Nicotine replacement therapy provides nicotine without the toxic components of combustible tobacco. NRT alleviates cravings for tobacco and is an effective and safe smoking cessation tool. ***Nicotine is a relatively harmless substance with similar effects to caffeine. It is safe in long term use with no increase in mortality, serious adverse events, cardiovascular disease or cancer (NICE PH45).***

Evidence Base:

Nicotine replacement therapy increases the chance of abstinence by approximately 60% compared to placebo (RR 1.60 95%CI 1.53-1.68, Cochrane Review 2012, 117 trials, Stead et al). NRT is cost-effective even when modelling at the lowest quit rate (9%) and most expensive NRT (£763 per person); cost per QALY £634 (2018 NICE PHG94).

In the EAGLES study NRT was more effective than placebo in smoking cessation (23.4% quite rate at 9-12 weeks versus 12.5%, OR 2.15 95% CI 1.82-2.54, p<0.0001).

A recent RCT of 'preloading' with NRT prior to a quit date was suggestive of a benefit but not conclusive. Adding this trial to the previous inconclusive meta-analysis of nicotine patch preloading versus standard use gives a risk ratio of 1.24 (1.07 to 1.43) for long term abstinence from nicotine patch preloading (BMJ 2018).

Side Effects:

Warn about sleep disturbance. Nicotine patches can cause mild skin irritation. Short acting nicotine absorbed through the buccal membrane can cause dyspepsia, nausea, hiccups if nicotine is swallowed rather than absorbed at the gums.

Contradictions:

Nil

Note:

There is no increased risk of moderate to severe neuropsychiatric adverse events with NRT. The act of stopping smoking carries a small risk of moderate to severe neuropsychiatric events and this is regardless of the treatment used. The risk is higher in those with a history of psychiatric illness (5%) versus those without (2%). **Advise patients to seek help in the event of a neuropsychiatric event.** In the long term, stopping smoking improves mental health disease, e.g. stopping smoking is more effective than antidepressants in treating depression.

Prescribing notes:

- NRT should be prescribed for 12 weeks and can be extended to 24 weeks
- NRT can be started prior to a quit date. This quit date is ideally within 1-2 weeks of starting NRT but can be at any time within the 12 weeks of treatment.
- Ongoing prescription may be required to facilitate ongoing abstinence (decided on a case by case basis).
- Encourage patients to use the short acting nicotine regularly e.g. on the hour every hour.

Cravings for nicotine are extremely powerful and NRT is weaker than cigarettes. Patients cannot overdose on nicotine except for causing mild symptoms such as light-headiness or nausea. However, under-dosing will affect how well NRT can alleviate cravings!

Nicotine replacement therapy comes in two forms: short acting and long acting. Think of NRT as a trying to put out a fire (cravings). Long acting nicotine is like a sprinkler system – providing a constant flow of water to control the fire. Short acting nicotine is like a fire extinguisher – a rapid burst of water to put the fire out there and then.

Short acting nicotine

Short acting nicotine comes in many forms, each as effective as the other. Each device has its own technique and 'top tips' for ensuring smokers get the best relief of their cravings.

Nicotine inhalator

The inhalator is not a very accurate name for this device because the user does not inhale the nicotine. The user 'puffs' on the device so the medication enters the mouth and is absorbed through the gums. It is not inhaled into the lungs. Patients often like this device because it mimics the hand to mouth action of smoking. It is not as powerful as a cigarette and you should ***advise your patients to use the inhalator for 20 minutes at a time to have an effect similar to a cigarette.***

Nicotine dose - **10 puffs from a nicotine inhalator = 1 puff on a cigarette**

Nicotine chewing gum

Nicotine chewing gum is not to be chewed like normal chewing gum. ***Advise your patients to chew the gum until they notice a hot fiery taste, then park the gum between their lip and gum to let the nicotine be absorbed through the gum.*** If they chew it like normal gum they are likely to swallow the nicotine which can cause heartburn, nausea and hiccups.

Nicotine lozenges

Nicotine lozenges are sucked like a sweet to release the nicotine. The nicotine is then absorbed through the gums. However, if there are any symptoms of the nicotine being swallowed (heartburn, nausea, hiccups) then ***advise your patients to park the lozenge between the lip and gum to allow the nicotine to be absorbed through the gum.***

Nicotine microtabs

These are very small tablets that are placed under tongue. They are not chewed, sucked or swallowed. The nicotine is absorbed through the gums.

Nicotine nasal spray

Nicotine is sprayed into the nostrils and absorbed into bloodstream through the lining of the nose. Give the following advice to your patients: ***'Tip your head back slightly and insert the spray tip into one of your nostrils. Press nozzle firmly and quickly. Spray into your other nostril. If you experience sneezing, a runny nose, or watery eyes, these effects should decrease after the first few days.'***

Nicotine inhalator	15mg/cartridge (maximum 6 cartridges in 24 hours) ***On the hour every hour initially*** Whenever cravings occur
Nicotine chewing gum	2mg as required (maximum 15 in 24 hours) ***On the hour every hour initially*** Whenever cravings occur
Nicotine lozenges	2mg as required (maximum 15 in 24 hours) ***On the hour every hour initially*** Whenever cravings occur
Nicotine microtabs	2mg as required (maximum 15 in 24 hours) ***On the hour every hour initially*** Whenever cravings occur
Nicotine nasal spray	2 sprays each nostril ***On the hour every hour initially*** Whenever cravings occur

Long acting nicotine

Long acting nicotine comes in the form of patches. Patches ideally need to be applied to a hairless area of skin such as the upper arm. Patches can cause skin irritation though this is usually mild. Patches come in 16 hour and 24 hour forms. One of the most powerful indicators of a smoker's addiction is how quickly they smoke after waking up. We use this information to help decide whether a 16 hour patch or a 24 hour patch is best for them.

If they smoke within 30 minutes of waking up then they need a 24 hour patch to help alleviate these early morning cravings. However the 24 hour patch is likely to cause more sleep disturbance.

If it takes longer than 30 minutes to smoke after waking then they can have a 16 hour patch with is likely to cause less sleep disturbance and shouldn't affect early morning cravings.

When prescribing nicotine replacement therapy ask two simple questions:

How many cigarettes do you smoke?

How long have you been awake before you smoke your first cigarette?

These questions can stratify smokers into three levels of addiction which informs the choice of NRT:

Low level addiction <10 cigarettes per day	Prescribe a short acting nicotine according to patient preference
Moderate level addiction 10-19 cigarettes per day	Prescribe either a short acting or a long acting nicotine replacement therapy (consider combination therapy) 14mg/24hr patch (smokes within 30 minutes of waking) 15mg/16hr patch (does NOT smokes within 30 minutes of waking)
High level addiction >20 cigarettes per day	Prescribe both short acting and long acting nicotine replacement 21mg/24hr patch (smokes within 30 minutes of waking) 25mg/16hr patch (does NOT smokes within 30 minutes of waking)

Always use clinical judgement and opt for a higher level of NRT treatment if you suspect a higher level of addiction. Remember nicotine does not cause serious adverse events and must be given in adequate doses to alleviate cravings.

Third Line: Buproprion

(Should only be initiated by Specialist Tobacco Addiction Services)

Mode of Action:

Bupropion is a nicotinic receptor antagonist. It prevents dopamine release from nicotine in cigarette smoke through its antagonist action. It is an effective treatment for tobacco addiction through the preventing positive impact from smoking that reinforces the addiction. However it has a number of drug interactions and side effects such that it should only be prescribed following multiple unsuccessful quit attempts with varenicline or NRT and under the guidance of a specialist tobacco addiction treatment service.

Evidence Base:

In the EAGLES study bupropion was more effective than placebo in smoking cessation (22.6% quite rate at 9-12 weeks versus 12.5%, OR 1.89 95% CI 1.56-2.29, p<0.0001). One therapy was not shown to be superior to another between bupropion and NRT (OR 0.96 95% CI 0.83-1.11, p0.58)

Side Effects:

Warn about seizures, mania, insomnia and hypertension ***(weekly BP monitoring if given with NRT).***

Contradictions:

Avoid in acute alcohol withdrawal, acute benzodiazepine withdrawal, bipolar disorder, CNS tumour, eating disorders, history of seizures and severe hepatic cirrhosis.

Cautions:

Due to seizure risk avoid in patients with the potential for lowered seizure threshold e.g. alcohol abuse, diabetes with hypoglycaemic episodes, head trauma. Due to mania risk avoid in bipolar disease. Avoid prescription with tamoxifen – reduced serum levels of tamoxifen.

Dose:

150mg OD day 1-6
150mg BD day 7+

Prescribing notes:

Treatment course = 7-9 weeks. **Discontinue if abstinence not achieved at 7 weeks**
Reduce dose to 150mg OD in the elderly, renal impairment, hepatic impairment or any of the following medications: anti-psychotics, anti-depressants, anti-malarials, tramadol, theophylline, corticosteroids, quinolones, anti-histamines.

Note:

There is no increased risk of moderate to severe neuropsychiatric adverse events with bupropion (EAGLES study 2016, The Lancet). The act of stopping smoking carries a small risk of moderate to severe neuropsychiatric events and this is regardless of the treatment used. The risk is higher in those with a history of psychiatric illness (5%) versus those without (2%). **Advise patients to seek help in the event of a neuropsychiatric event**. In the long term, stopping smoking improves mental health disease, e.g. stopping smoking is more effective than antidepressants in treating depression.

E-cigarettes

E-cigarettes are a highly debated and at times controversial topic in the tobacco addiction community. Whatever your thoughts on e-cigarettes they are a very popular device amongst smokers. 60% of smokers in the UK have tried an e-cigarette and approximately 20% are regular users. It is important that Greater Manchester Healthcare Professionals have provide a consistent message about e-cigarettes to our patients.

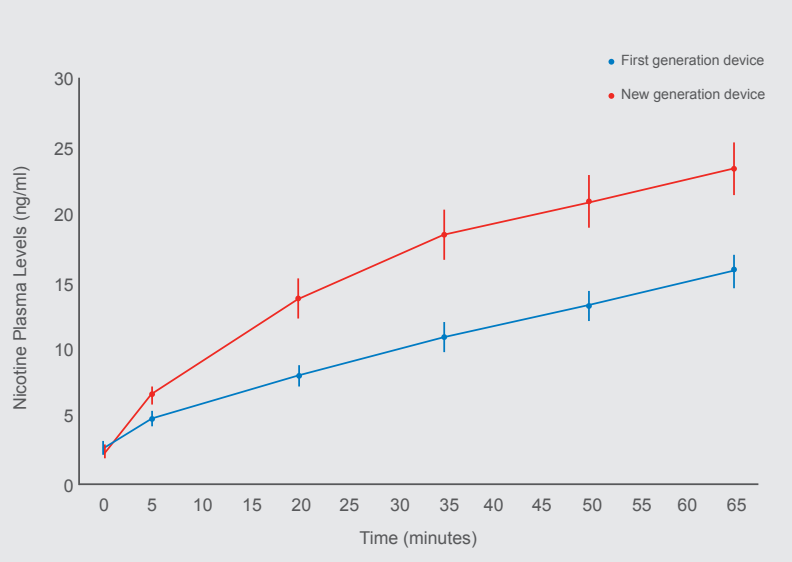
'E-cigarettes' is not a good name for these devices are they are **not cigarettes** and they contain ***no tobacco***. They contain a liquid that is heated to create a vapour that is inhaled into the lungs. E-cigarettes contain:

- Nicotine liquid
- Glycerine (the substance used to make dry smoke in theatres)
- Propylene glycol
- +/- flavouring

E-cigarettes are significantly less harmful than cigarettes and will expose users to less toxic chemicals, though not none entirely, and they **are less harmful, not safe**.

The best way to think about e-cigarettes is another device for providing short acting nicotine.

- Like the nicotine inhalator, they are likely to be popular as they mimic the action of smoking cigarettes.
- One advantage of an e-cigarette, particularly the third/fourth generation devices, is they are able to deliver a high dose of nicotine at a speed far closer to cigarettes than NRT



- Just like with short acting nicotine it is important to encourage patients to use regularly and remind them they cannot overdose on nicotine and need to use it in sufficient quantity to alleviate carvings and reduce the chance of relapse to cigarettes. Advise smokers to use the higher doses of nicotine liquid for maximal reduction of cravings
- Advice smokers to switch entirely to an e-cigarette with zero cigarette use. Approximately 50% of the risk of a heart attack comes in the first cigarette and 30% of the stroke risk. Exposure to toxic chemicals is relatively similar between dual cigarette and e-cigarette users and cigarette users.
- E-cigarettes can be combined with other tobacco addiction treatments such as NRT and varenicline in a multi-faceted approach to a quit attempt.
- It is imperative smokers are offered the treatments with a robust evidence for effectiveness, particularly NRT and varenicline. Those smokers that chose to include e-cigarettes within their quit attempt strategy should be supported in doing so.

E-cigarettes

E-cigarettes are not medicinal and cannot be prescribed. They are a consumer device. To ensure the least risk of harm e-cigarettes must be carefully and thoroughly regulated and the chemicals contained within the liquid also regulated. Advise patients to buy e-cigarette and its components from a licenced vender.

A licenced vender will also be able to advise on different generations of e-cigarettes and the technique used to maximise nicotine intake, something that is slightly different to the technique of smoking a cigarette.

Some patients find adding a non-tobacco flavour to an e-cigarette makes them more usable and helps to break the addiction and association to tobacco, this is of course a personal choice.

There are wider concerns about e-cigarettes including a potential gateway to smoking in young adults and children, the renormalisation of smoking in today's society and strengthening the tobacco industry's presence in this market once again. Clearly these are important cultural issues for us to debate but for an individual smoker seeking specialist support in Greater Manchester, in whom stopping smoking is the single greatest intervention for their health they can do, we will offer that smoker evidence based treatments and support them with appropriate information and counselling if they chose to use this form of short acting nicotine device.