MENTAL HEALTH
Living well for longer

2017 update

Pharmacy Guidance on Smoking and Mental Disorder

KEY LEARNING POINTS

- Smoking is the single largest cause of preventable death in the UK and a major determinant of health inequality for those with a mental disorder.
- With appropriate support, those with a mental disorder are able to stop smoking.
- Doses of some psychiatric medication require significant reduction following smoking cessation.
- A range of pharmacological interventions (such as combination nicotine replacement therapy or varenicline) and non-pharmacological interventions are effective in supporting smoking cessation for people with a mental disorder.
- Pharmacists have a key role in improving access to smoking cessation and reduction interventions for smokers with a mental disorder as well as facilitating appropriate changes of medication doses.

Smoking – the biggest killer

Smoking is associated with an increased risk of several chronic diseases[1] and is the single largest cause of preventable death with smokers dying on average 10 years earlier than non-smokers[2]. In 2014, there were 78,000 deaths attributable to smoking in England[3].

Smoking and mental disorder

People with different mental disorders have a 10-20 year lower life expectancy[1] with smoking recognised as the single largest preventable cause. Since 42% of adult tobacco consumption in England is by those with a mental disorder[4], this group experiences a significant proportion of overall tobacco related harm. Furthermore, the annual health service cost of smoking by those with a mental disorder in the UK was £719m in 2009/10[5].

Smoking cessation and reduction in those with a mental disorder

Smoking cessation results in improved physical and mental health[1]. Furthermore, evidence suggests that the impact of smoking cessation on anxiety and depressive symptoms is at least as large as antidepressants[6]. Smoking cessation is the single largest way to reduce the 10-20 year premature mortality experienced by those with a mental disorder.

Pharmacotherapy and non-pharmacological support are effective in supporting smoking cessation in those with a mental disorder[1]. Furthermore, interventions can also support people who are not ready to stop smoking completely by helping them to reduce the amount they smoke. Over time this can help to double smoking cessation rates[7].

Despite being as motivated to stop as the general population, those with a mental disorder are less likely to receive smoking cessation interventions. Taking action to support those with a mental disorder to quit smoking should be even more imperative, given the rates of comorbid physical health problems and reduced life expectancy within this population.

Medication dose reduction following smoking cessation

Smoking increases the metabolism of different medications, including some antidepressants (tricyclics and mirtazapine), antipsychotics (clozapine, olanzapine and haloperidol)[8, 9], some benzodiazepines and opiates[10]. This can result in significantly lower plasma levels[11] and therefore, larger doses are required for a similar therapeutic effect. Stopping smoking can reduce metabolism of some medication resulting in higher, sometimes toxic plasma levels over a few days[11, 12]. Therefore, close monitoring is required and doses of the medications above need to be reduced within days of cessation and by up to 50% within a month of cessation. It is recommended that[12]:

- Plasma levels of clozapine (and olanzapine if assays are available) should be measured before smoking cessation to enable more accurate and timely monitoring

and adjustment of medications. Doses of clozapine and olanzapine should be reduced by 25% during the first week of cessation and then further plasma levels taken on a weekly basis until levels have stabilised
- Doses of fluphenazine and some benzodiazepines should be reduced by up to 25% in the first week of cessation
- Tricyclic antidepressants may need to be reduced by 10-25% in the first week
- Further dose reductions may be required with continued cessation

Dose reduction of psychotropic medication following smoking cessation in those with a mental disorder in the UK would result in associated annual NHS savings of £40m[5].

Medication dose reduction following smoking reduction

Smoking reduction decreases the associated harm and increases the chances of stopping smoking among smokers in the general population[13]. Smoking reduction can also decrease the metabolism of some medication. However, there is an important research gap regarding required dose changes for people who reduce their smoking but do not stop completely. In such cases, monitoring which includes regular blood tests for drug levels should inform such changes.

Role of pharmacists

Pharmacists are highly accessible to different groups of the local population and are in an ideal position to:

- Explain how smoking cessation can improve mental health as well as physical health
- Encourage people to stop smoking through promoting healthy lifestyles which is part of the pharmacy contractual framework
- Check drug interactions between medicines prescribed and/or taken as supplements
- Highlight to patients and prescribers the need for planned reduction of doses of some medications upon smoking cessation (as outlined above)
- Encourage the use of combined NRT to all including those who continue to smoke which supports smoking reduction as a first step to cessation
- Supply smoking cessation pharmacotherapy through Patient Group Directions (PGDs) or as part of a local Enhanced Service
- Coordinate pharmacy support with community and inpatient mental health services, primary care providers and local Stop Smoking Services to offer ongoing smoking cessation support as part of a more integrated service

Pharmacy staff who are trained to provide advice on stopping smoking are likely to improve the support pharmacies can offer to people who wish to stop.

Smoking cessation and reduction pharmacotherapy

Several different types of smoking cessation pharmacotherapy exist. When comparing different types of pharmacotherapy for the general population, be aware that[15, 16]:

- Different types of NRT are similarly effective for smoking cessation with nasal spray being slightly more effective followed by tablets/lozenges, inhalers, patches and gum which is slightly less effective
- NRT and bupropion are equally effective
- Varenicline is more effective than bupropion or single forms of NRT
- Varenicline is as effective as combined NRT
- Addition of bupropion or nortriptyline does not increase effectiveness of NRT

A combination of different forms of NRT and NRT/bupropion reduces smoking consumption in people with a mental disorder[5, 13, 14].

Nicotine replacement therapy (NRT)

NRT is effective (OR 1.84, 1.71-1.99)[15]. Several different forms of NRT can be prescribed[16, 17]. The choice of which form to use should reflect patient needs, tolerability and cost considerations. Patches are likely to be easier to use than gum, nasal spray or inhaler although patches cannot be used for relief of acute cravings[16]. The use of local Enhanced Services can also be considered in order to improve access:

- Patches: 16-hour and 24-hour patches are available with no difference in efficacy. Both types come in several strengths to allow gradual weaning. A high dose patch should be used for those who normally smoke more than 20 cigarettes per day
- Gum: 2mg, 4mg or 6mg, up to 15 pieces daily can be chewed at regular intervals
- Sublingual tablets: one (2mg) tablet per hour for those smoking 20 cigarettes daily and two tablets per hour for those smoking 40 cigarettes daily
- Oral film: 2.5mg dissolved in the mouth up to 15 times a day
- Nasal spray: (500mcg) maximum dose 2 sprays per nostril per hour for up to 16 hours per day
- Oral spray: 1 or 2 sprays of 1mg, up to 4 sprays per hour to a maximum of 64 sprays a day
- Inhalator: mouthpiece. The initial dose should be up to twelve 10mg cartridges, or six 15mg cartridges per day
- Lozenges: 1mg, 1.5mg, 2mg and 4 mg up to maximum 15 per day

Combining a nicotine patch with a rapid-delivery form of NRT is more effective than a single type of nicotine replacement[15, 16] particularly for more dependent smokers including those with a mental disorder who may need longer than the recommended 8-12 weeks treatment[5, 14]. Only cigarette smoking induces hepatic enzymes to alter drug plasma levels in the ways described above; NRT has no effect on enzyme activity and therefore drug doses are not affected although require accompanying dose reductions of medications outlined above upon smoking cessation.

Side effects[15, 17]

- Patches: Skin sensitivity and irritation
- Gum: Hiccoughs, gastrointestinal problems, jaw pain and orodental problems
- Sublingual tablets: Hiccoughs, burning, sore throat, coughing and dry lips
- Nasal/oral spray and inhalers: Local irritation
- Serious adverse effects are absent from trial reports although there have been reports of possible increased risk of chest pain and heart problems

E-cigarettes

Although there is a lack of evidence about long term safety and more research is needed, e-cigarettes are widely considered to be much less harmful than cigarette smoking[18] and used by 4% of adults in England[3]. The main reasons for e-cigarette use are to aid stop smoking (53%) and being less harmful than cigarettes[3]. As for other forms of NRT, e-cigarettes do not induce enzymes and so require accompanying dose reductions of medications outlined above if completely replacing tobacco smoking.

Bupropion

Bupropion is an atypical antidepressant which acts as an adrenaline and dopamine reuptake inhibitor as well as nicotinic antagonist thereby reducing nicotine cravings and withdrawal symptoms. Bupropion is effective in the general population for smoking cessation (OR 1.82, 1.60-2.06) with a combination of NRT and bupropion more effective than bupropion alone[15]. For people with schizophrenia, bupropion almost triples cessation rates at six months[19].

Dosing: start 1-2 weeks before planned quit date at 150mg daily for 6 days, then 150mg twice daily for maximum 7-9 weeks.

Side effects

- Dry mouth (10%), constipation, nausea, insomnia (30-40%) and allergic reactions[15]
- Serious adverse effects (SAEs)
  - » Seizures: Seizure rate (0.1%) was low although a report found it was much higher in accidental and intentional overdoses (6%). Rates were lower for sustained-release formulations
  - » Spontaneous abortion
  - » MHRA described reports of bupropion being associated with the development of depression, suicidal thoughts and behaviours, hallucinations, delusions, disordered thoughts and extreme mood swings. These effects were more likely in people who have had mental health problems before[20]
  - » In 2009, the FDA required bupropion to carry the agency's strongest safety warning due to side effects including changes in behaviour, hostility, agitation, depressed mood, suicidal thoughts and behaviour, and attempted suicide including in those with no previous history of psychiatric illness[21]
  - » However, a meta-analysis of six trials found no difference in neuropsychiatric SAEs between bupropion and placebo[15]. A further large prospective study found no increased risk of depression or suicidal behaviour[22]
  - » A meta-analysis of bupropion for people with schizophrenia found no reported serious adverse events[19]. A more recent trial involving more than 4,000 people with a history of psychiatric disorder

found that bupropion did not significantly increase the risk of neuropsychiatric adverse events[23]

Contraindications
Bupropion is contraindicated for people with bipolar disorder and epilepsy. It should not be prescribed to people who have recently stopped taking sedatives or medicines to treat anxiety, eating disorder or who are heavy drinkers[20].

Interactions
Bupropion should not be prescribed with other drugs which increase risk of seizure such as tricyclic antidepressants, monoamine oxidase inhibitors (MAOIs) and some antipsychotic medication including clozapine, chlorpromazine and depot injections[12]. Bupropion can increase blood levels of citalopram so should not be taken concurrently and should be avoided for two weeks after stopping[17]. However, the two drugs have been used safely as co-therapy[24].

Varenicline

Varenicline (OR 2.88, 2.40-3.47) is a nicotine receptor partial agonist and as effective as combination NRT although more effective than either single form NRT or bupropion[15].

Dosing: Usually started 1-2 weeks before target stop date at 500mcg daily for 3 days, then 500mcg twice daily for 4 days and then increased to 1mg twice daily for a further 11 weeks.

Side effects

- Main side effect is nausea while other common side effects include insomnia, abnormal dreams and headaches[15]
- Serious adverse effects (SAEs)
  - » A meta-analysis found no increased rate of any SAE or neuropsychiatric SAE in people taking varenicline compared to placebo[15]. A further large prospective study found no increased risk of depression or suicidal behaviour[22]. A more recent trial involving more than 4,000 people with a history of psychiatric disorder found that varenicline did not significantly increase the risk of neuropsychiatric adverse events[23]
  - » In 2009, the FDA required varenicline to carry the agency's strongest safety warning due to side effects including changes in behaviour, hostility, agitation, depressed mood, suicidal thoughts and behaviour, and attempted suicide including in those with no previous history of psychiatric illness[21]. However, the EMA has recently removed the black box warning[25] following further evaluation outlined above
  - » Changes in behaviour or thinking, anxiety, psychosis, mood swings, aggressive behaviour, depression, suicidal ideation and behaviour and suicide attempts have been reported in patients taking varenicline in post-marketing surveillance[25]

Need for close monitoring while taking bupropion and varenicline

- If patients taking varenicline or bupropion develop suicidal thoughts, agitation, depressed mood, or display any changes in behaviour which are of concern for the doctor, pharmacist, patient, family, or carer, they should stop bupropion or varenicline and contact their doctor immediately[20, 25]
- Care should be taken with patients with a history of psychiatric illness and patients should be advised accordingly[25]
- Close, regular monitoring by health professionals including psychiatrists, GPs and community health staff should occur through a clearly negotiated plan of support and contact especially in the first 2-3 weeks with clear strategies for responding in the event of changes
- If varenicline or bupropion is stopped due to neuropsychiatric symptoms, patients should be monitored closely until the symptoms resolve
- Family members and carers should also be alerted to the potential for such changes and be an active part of any negotiated support plan, with the person's consent

Nortriptyline and cytisine

Evidence also highlights the effectiveness of nortriptyline (OR 2.03, 1.48-2.78) and cytisine (OR 3.98, 2.01-7.87) without significant adverse effects[15]. However, these treatments are unlicensed in the UK.

Level of smoking cessation pharmacotherapy provision and associated expenditure

Over the last ten years in England, the number of smoking cessation prescription items dispensed has reduced from 2 million to 1.3 million[3]. This has been primarily due to a reduction of NRT items dispensed from 2.1 million to 0.8 million. There has been a similar 42% reduction in net ingredient cost from £65.9 million in 2010/11 to £38.1 million in 2014/15 (3). In contrast, there are 2.2 million current users of e-cigarettes. ■

Useful Resources

Royal College of Psychiatrists (2016) Improving the physical health of adults with severe mental illness: essential actions (OP100). Working Group for Improving the Physical Health of People with SMI
http://www.rcpsych.ac.uk/files/pdfversion/OP100.pdf

HSCIC (2015) Statistics on NHS Stop Smoking Services: England 2015
http://www.hscic.gov.uk/catalogue/PUB17526/stat-smok-eng-2015-rep.pdf

Campion J, Shiers D, Britton J, Gilbody S, Bradshaw T (2014) Primary care guidance on smoking and mental disorders – 2014 update. Royal College of General Practitioners & Royal College of Psychiatrists
http://www.rcpsych.ac.uk/pdf/PrimaryCareGuidanceonSmokingandMentalDisorders2014update.pdf

Royal Pharmaceutical Society (2014) Policy statement on e-cigarettes
http://www.rpharms.com/policy-pdfs/e-cigarettes---ps---201402.pdf

National Centre for Smoking Cessation and Training (2014) Local Stop Smoking Services: Service and delivery guidance 2014.
http://www.ncsct.co.uk/publication_service_and_delivery_guidance_2014.php

Royal College of Physicians/Royal College of Psychiatrists (2013) Smoking and mental health. A joint report.
https://www.rcplondon.ac.uk/sites/default/files/smoking_and_mental_health_-_full_report_web.pdf

NICE (2013) Smoking: acute, maternity and mental health services.
https://www.nice.org.uk/guidance/PH48

NICE (2013) Tobacco harm reduction.
http://www.nice.org.uk/ph45

NHS Smokefree Support Services.
http://www.nhs.uk/smokefree/help-and-advice/support#IzL011SJDPOypz8q.97 and Helpline on 0300 123 1044

Free local NHS Stop Smoking Service.
http://www.nhs.uk/smokefree/help-and-advice/local-support-services-helplines

Help at Hand leaflet produced by the Royal College of Psychiatrists provides information to smokers and staff and can be downloaded at
http://www.rcpsych.ac.uk/mentalhealthinfo/problems/smokingandmentalhealth.aspx

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Iris

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