

# Smoking and mental illness

## A clinical guide to quitting

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People with mental illness are much more likely to smoke than the general population but much less likely to be offered smoking cessation services, possibly partly because of misconceptions about smoking and mental illness among medical practitioners. The 5 As framework and most pharmacological quit strategies can be used in patients with a mental illness, with some cautions about side effects and drug interactions.

Australia is rightly proud of its achievements in reducing overall rates of cigarette smoking. However, a significant number of Australians still smoke (about 15% of the population), and people with mental illness continue to smoke at a higher rate than the general population. Indeed, in people with schizophrenia and related disorders there has been almost no reduction in smoking rates despite public health messaging and targeted projects. For example, the 2010 Study of High Impact Psychoses (SHIP) found that 71% of men and 58% of women with psychosis were current smokers. They smoked a high volume of cigarettes daily and had high indices of dependence.<sup>1</sup>



### Key points

- Rates of smoking in people with mental illness remain high and have not decreased in line with rates in the rest of the population.
- Smoking contributes significantly to higher morbidity and mortality in people with mental illness.
- Smoking cessation has beneficial effects on mental health.
- Having a mental illness should not preclude a patient from smoking cessation services.

**Table 1. Overview of pharmacological therapies to assist smoking cessation**

	NNT (12-month quitter)	Dose	Precautions
Bupropion	20	150 mg daily for 3 days, then 150 mg twice daily for 9 weeks	Bipolar affective disorder, seizures (avoid use)
Nicotine replacement therapy	10	See Table 2	Hepatic and renal impairment (reduce dose) Cardiovascular disease: recent myocardial infarction; unstable or progressive angina pectoris; severe cardiac arrhythmias; acute phase stroke (avoid use)
Varenicline	10	0.5 mg daily for 3 days, then 0.5 mg twice daily for 3 days, then 1 mg twice daily for 12 weeks	Significant renal disease: mild-to-moderate renal disease (CrCl ≥30mL/min) – no dosage adjustment required; severe renal disease (CrCl <30 mL/min) – 0.5mg once daily initially, may increase to 0.5mg every 12 hours; end-stage renal disease requiring haemodialysis – dose not to exceed 0.5mg once daily Use with caution in people with mental illness

Abbreviations: CrCl = creatinine clearance; NNT = number needed to treat for one person to successfully quit.

The reasons behind such high ongoing rates of smoking among people with mental illness are complex. They include social affiliation, oral gratification, perceived benefit in terms of reduced anxiety symptoms and also pro-cognitive effects, reduced akathisia associated with antipsychotic medications and potential effects on the negative symptoms of schizophrenia (e.g. lethargy and apathy).

Despite the high rates of smoking in people with mental illness, they are less likely to be offered help with smoking cessation than smokers without a mental illness. Reasons include misconceptions about smoking and mental illness held by many medical practitioners, a lack of clinician confidence about helping people with a mental illness quit smoking and a paucity of specific treatment services. Arguably, people with a mental illness should be specifically targeted for smoking cessation, notably because smoking adds to their already heavy cardiovascular risk burden.<sup>2</sup>

This article describes some of the misconceptions about smoking cessation in people with a mental illness and ways in which GPs can help support them to quit smoking.

**Common misconceptions about smoking and mental illness**

Several unhelpful and inaccurate beliefs about smoking and smoking cessation in people with mental illness are common among medical practitioners. However, the evidence shows that these beliefs are incorrect, as follows.

**‘People with mental health problems do not want to give up smoking’**

Although it is true that motivations to quit may differ between people with a mental illness and those without, the former do not actually lack the motivation to quit. Indeed, the SHIP study found that 72% of smokers with a psychosis had attempted quitting, and

many had multiple attempts.<sup>1</sup> However, people with a mental illness tend to be less successful in their quit attempts than people without a mental illness, and they have a high relapse rate. Thus, people with a mental illness might need more concerted and longer-term quit support.

**‘Quit strategies that have proven efficacy in the general population do not work for people with a mental illness’**

It is not true that quit strategies that are effective in the general population are not effective for people with a mental illness. For example, the large-scale EAGLES trial, which compared nicotine replacement therapy (NRT), bupropion and varenicline with placebo in smokers with and without psychiatric disorders, found that people with a broad array of mental illnesses could successfully quit.<sup>3</sup> A study specifically targeting people with a severe mental illness achieved quit rates of 18.6% at 12 weeks.<sup>4</sup> Again, the issue is how to maintain abstinence.

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**‘Mental health worsens on quitting’**

Although quitting a drug of dependence carries the risk of acute exacerbation of certain mental health symptoms, the withdrawal effects reported among people with a mental illness largely mirror those seen in people without a mental illness. For example, insomnia, agitation, depression and even suicidality have been described in both groups. However, the EAGLES study found rates of neuropsychiatric side effects were low across all four trial arms, albeit rates of moderate-to-severe effects were slightly higher in those with a baseline mental illness (6.5% vs 1.3%).<sup>3</sup>

In the longer term, there have been concerns about depression and suicidality in smokers with a mental illness who quit. In fact, ceasing smoking is associated with decreased depressive symptoms and reduced alcohol use in patients with depression, as well as improved quality of life.<sup>5,6</sup> A recent review found that nicotine dependence cessation was associated with a decreased likelihood of suicide attempts compared with people currently dependent on nicotine.<sup>7</sup>

### Framework for smoking cessation in people with a mental illness

A suggested framework to help clinicians achieve smoking cessation among their patients is based on the '5 As':

- ask all patients about smoking
- assess readiness to quit
- advise all smokers to quit
- assist
- arrange follow up.

Additional supports that are appropriate for people with mental illness as well as the general population are available online from organisations such as Quit ([www.quit.org.au](http://www.quit.org.au)).

### Role of medications in smoking cessation

Pharmacological strategies to assist smoking cessation that have proven successful in the general population can be used in patients with a mental illness. However, cautions are needed regarding particular side effects as well as the potential for drug-drug interactions (Table 1).

### Nicotine replacement therapy

NRT reduces both the need to smoke and withdrawal symptoms from ceasing. It is probably about twice as effective as placebo in smoking cessation. NRT is available as patches, gum, lozenges, mouth spray and an inhaler. Evidence suggests that the mouth spray and inhaler may be more effective than other forms of NRT.<sup>8</sup>

Compliance with NRT is generally poor, and underuse is associated with worse outcomes. Each additional lozenge used per day is associated with a 10% increased rate of quitting.<sup>9</sup> Higher relapse rates are associated with underdosing of NRT and not using it for long enough. Therefore, NRT is most likely to be successful when given in conjunction with behavioural support, which is available from telephone helplines and trained smoking cessation counsellors listed on state health department websites. Using a combination of patches and the oral form of NRT is associated with higher cessation rates. The recommended dosage of NRT is influenced by the patient's level of nicotine dependence (Table 2).<sup>10</sup>

### Varenicline

Varenicline is a partial agonist at alpha-4 beta-2 nicotinic receptors in the brain, a target for nicotine. Varenicline is associated with

**Table 2. Dosage of nicotine replacement therapy (NRT) according to patient's levels of dependence**

Dependence level	NRT dosage (not combination therapy)*
High • more than 20 cigarettes daily and/or • first cigarette less than 30 mins from waking	<ul style="list-style-type: none"> <li>• Patch 21 mg/24 h or</li> <li>• Lozenge 4 mg 1-hourly when necessary to a maximum of 12 daily</li> <li>• Consider combination therapy*</li> </ul>
Medium • 10 to 20 cigarettes daily and/or • first cigarette 30 to 60 mins from waking	<ul style="list-style-type: none"> <li>• Patch 14 mg/24 h or</li> <li>• Lozenge 2 to 4 mg 1-hourly when necessary to a maximum of 6 to 12 daily or</li> <li>• Inhaler 1-hourly when necessary to a maximum of 6 to 12 cartridges daily</li> </ul>
Low • fewer than 10 cigarettes daily and/or • first cigarette more than 60 mins from waking	<ul style="list-style-type: none"> <li>• May not need NRT</li> <li>• Monitor withdrawal symptoms</li> <li>• Patch 14 mg/24 h if required</li> </ul>

\* Combination therapy comprises:<sup>10</sup>

- patch (21 mg/24 h) plus an inhaler or lozenge (1-hourly when necessary to a maximum of six inhalers or lozenges daily) OR
- adding second patch simultaneously (note that if patient experiences disturbing nightmares then the second or both patches may be removed after 16 hours).

both a decrease in the pleasurable effects of smoking caused by dopamine release and a decrease in cravings for nicotine. Studies suggest it is more effective in smoking cessation than either NRT or bupropion, and three times more effective than placebo.<sup>8,11</sup>

### Pharmacological strategies to assist smoking cessation that have proven successful in the general population can be used in patients with a mental illness

Initially, there were significant concerns about the use of varenicline in patients with mental health diagnoses, and there are case reports of it having significant detrimental effects on mental health.<sup>11,12</sup> However, as outlined above, more recent studies suggest that this effect might have been overstated. A 2016 review found no clear evidence that varenicline is associated with an increased risk of neuropsychiatric adverse events.<sup>12</sup> The EAGLES study found no significant increase in neuropsychiatric symptoms with varenicline compared with bupropion or NRT.<sup>3</sup>

These findings led the US Food and Drug Administration to remove its 'black box warning' from varenicline, although caution is still needed in people with pre-existing depression and anxiety or psychosis. However, these concerns should not stop clinicians using this highly effective agent.

### Bupropion

Bupropion is a selective noradrenaline-dopamine reuptake inhibitor and a nicotinic receptor antagonist. It is approved for use as an antidepressant in some overseas jurisdictions but not in Australia, where it is listed on the PBS for smoking cessation. It appears to work by reducing cravings, and evidence suggests that patients are twice as likely to cease smoking with bupropion treatment compared with placebo.<sup>13</sup> The effect seems distinct from its antidepressant activity.

Bupropion is associated with a one in 1000 risk of seizures and is therefore relatively contraindicated in patients with epilepsy. It should be used with caution in people with eating disorders, those with bipolar disorder (in whom it might precipitate mania if they are not taking a mood stabiliser) and those with acute benzodiazepine or alcohol withdrawal.

### Effect of smoking cessation on psychotropic medications

Stopping smoking can significantly affect the plasma levels of a number of psychotropic medications. For example, ceasing smoking increases levels of clozapine and olanzapine because of its effects on hepatic metabolism. This means that a dosage adjustment might be necessary following cessation. The interactions involved are caused by aromatic hydrocarbons in the smoke, not nicotine. NRT does not affect plasma levels of these drugs.

Psychotropic medications that have reduced plasma levels in smokers include:

- antidepressants such as agomelatine, duloxetine, fluvoxamine, mirtazapine and tricyclic antidepressants
- antipsychotics such as clozapine, haloperidol and olanzapine.

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### Patient follow up

It is important to continue to monitor and support patients while they quit. This support is likely to improve quitting rates and also allows monitoring of mental state and any changes in medication that might be necessary (e.g. increasing NRT dosage or potentially decreasing antipsychotic dose).

### The future

Of particular note is the potential use of e-cigarettes for smoking cessation and harm minimisation. There is little research into their use for this purpose at present, and nicotine is not currently available in Australia for use in e-cigarettes. However, the fact that nicotine delivery by e-cigarettes more closely resembles that of smoking may make them more popular with smokers.

### Conclusion

The persistently high levels of smoking among people with mental illness contribute significantly to increased morbidity and mortality in this group. The medical profession needs to persist in its efforts to help people with mental illness to quit smoking and to emphasise the potential benefits for physical and mental health and wellbeing.

**RMT**

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