

# In the KNOW

*New research has identified a link between antidepressants and dementia, but ditching your prescription for fear of forgetfulness in older age might do more harm than good* BY ANGELA TUFVESSON



It's estimated that one in nine New Zealand adults are prescribed antidepressants each year, and research shows our use of this type of drug is higher than the OECD average. Across the ditch, antidepressants are the third most commonly prescribed class of medication in Australia after antibiotics and cholesterol-lowering drugs.

There's no doubt antidepressants are a popular treatment for depression, but there are concerns the drugs may increase the risk of long-term health problems. In particular, an emerging body of research is investigating a possible link between antidepressants and dementia, which is set to affect more than 170,000 Kiwis by 2050. So what are the long-term risks of taking antidepressants, and should you be talking to your doctor about alternative treatment options for depression?

## DEMENTIA LINK

In the largest study of its kind, published in the *British Medical Journal*, researchers in the UK, Ireland and the US reviewed the healthcare records of more than 300,000 people to look for links between dementia and drugs that belong to a group of medicines known as anticholinergic drugs, which are known to cause problems with thinking. These drugs block a chemical called acetylcholine, which can affect a wide range of the body's organs.

Because of this, anticholinergic drugs are used to treat a range of conditions, including incontinence, Parkinson's disease and, crucially, depression. A type of antidepressant called tricyclic antidepressants – which may be prescribed as nortriptyline, clomipramine, dothiepin, imipramine and amitriptyline – tend to have strong anticholinergic activity.

The study found that anticholinergic drugs were linked with about a 10% increase in dementia risk. "We examined the medication history of people diagnosed with dementia and compared them to the medication history of older people not diagnosed with dementia," says lead author, Dr Kathryn Richardson from the University of East Anglia. "We were looking at medications with anticholinergic activity and a large number of these are certain types of antidepressants. We found that these medications had been more commonly used, and for longer, in those with dementia." Dr Richardson says it's unclear what may be happening in the body to increase dementia risk.

"One small study has suggested that anticholinergics are linked to a build up of amyloid plaques that cause Alzheimer's disease [which is a type of dementia] while another has shown brain changes in MRI scans associated with anticholinergics, but these are far from

conclusive," she says. This study is significant but it's important to note that it doesn't establish a causative link between antidepressants and dementia.

According to Professor Malcolm Hopwood from the Department of Psychiatry at the University of Melbourne, "there is no clear evidence directly linking antidepressants to dementia. When you look at this study, it's showing an association between the use of antidepressants and the development of dementia, but this doesn't prove it's a causation."

Indeed, research findings in this area are mixed. According to Dementia Australia, some studies have identified a similar link to Dr Richardson's work while others have found no association between anticholinergic medication use and dementia risk.

## CHICKEN OR THE EGG?

What makes it tricky to understand the link between antidepressants and dementia is that depression itself, which affects one in five Kiwi women, is a known risk factor for dementia.

"We believe there's a link between depression and dementia," says Dr Mark Fisher from Dementia New Zealand. "It's less about the medication and more about the illness that's being treated with the medication – that is what most >>

people would believe. More broadly, there is an awareness that the underlying physiological problems that go with depression are linked with a number of different illnesses.”

In fact, a major 2017 review by *The Lancet* identified depression as one of nine potentially modifiable risk factors linked to dementia. It found depression is responsible for four percent of the risk of developing dementia, explaining that depressive symptoms may increase dementia risk due to their effect on stress hormones and the part of the brain that regulates emotions.

Dr Richard Porter, a spokesperson for the Royal Australian & New Zealand College of Psychiatrists, says many experts believe inflammation is to blame for the link between depression and dementia. “Probably the most common hypothesis is that depression seems to be associated with inflammation that causes problems with the blood vessels in the brain, which then predisposes to dementia. But it’s extremely complex and very difficult to be absolutely clear what the link is.”

Just to make things even more complex, Dr Fisher says a diagnosis of depression later in life may actually be a symptom of dementia rather than a contributing factor. “There is quite a well-established link between people who get depression later in life and subsequent dementia, but it is suspected that that may be a marker for the neurodegenerative process that’s happening in the brain,” he says.

“It’s what’s called ‘reverse causality’ because it looks like you have late onset depression, which then causes dementia, but in actual fact it is the dementia pathology that’s silent and causes the depression to occur in later life.”

### NEW TREATMENTS

The other important caveat to research linking antidepressants with dementia is



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that most people are not prescribed tricyclic antidepressants, the anticholinergic type of antidepressants that have been linked with dementia, in the first instance.

Instead, doctors usually prescribe newer classes of antidepressants. Selective serotonin reuptake inhibitors (SSRIs) are the most widely prescribed type of antidepressants. They’re usually preferred over other types, including serotonin-noradrenaline reuptake inhibitors (SNRIs) and monoamine-oxidase inhibitors – as they cause fewer side effects.

“Not all antidepressants have strong

anticholinergic properties,” says Professor Hopwood. “The newer antidepressants like the SSRIs are the most widely used types, and most of them have relatively weak anticholinergic properties.”

Most people experience only a few mild side effects when taking SSRIs that generally improve with time, including feeling agitated or shaky, dizziness, blurred vision, low sex drive and feeling sick. According to the NHS in the UK, there are some more serious long-term health risks, such as serotonin syndrome, which occurs when levels of serotonin

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in the brain become too high and can include symptoms like confusion, sweating, diarrhoea, constipation, loss of appetite or dizziness, but these are relatively uncommon.

### ALTERNATIVE THERAPIES

Of course, a range of psychological treatments for depression can help to change thinking patterns and improve coping skills, so antidepressants aren’t prescribed to everyone. Cognitive behavioural therapy, which involves working through thought and behaviour patterns with a therapist, is one of the most effective treatments for depression.

And there is a heap of research suggesting that good old-fashioned exercise may increase levels of serotonin in the brain, which is involved in the regulation of mood. Regular exercise can even be an effective treatment by itself for some types of depression.

Dr Porter says there’s no real evidence to suggest that antidepressants are a better treatment than a placebo for mild cases of depression. But for more serious cases, antidepressants are usually most effective and outweigh the risk of side effects. About 50% of people who take an antidepressant find their depression symptoms are halved.

“For mild depression, there is no really good evidence that antidepressants are better than a placebo,” says Dr Porter. “The general consensus and recommendations of, for example, the RANZCP are that for mild depression other treatments like lifestyle changes, exercise and brief psychological intervention are more appropriate than prescribing an antidepressant.

“For moderate depression, however, treatment in most cases should include an antidepressant. In cases of severe depression, certainly we should use an antidepressant.”

Most people need to take antidepressants for six to 12 months to reduce the risk of depression returning. Scientific consensus is a tricky business and if you’re taking antidepressants or are thinking about

taking a course of treatment it’s easy to feel overwhelmed by conflicting research and fearful of a serious condition such as dementia. So what should you do?

“If you’re already taking tricyclic antidepressants, I would not stop taking them, but discuss any concerns you have with your doctor the next time you have an appointment,” Dr Richardson suggests.

Professor Hopwood says antidepressants are an effective treatment for depression and stopping treatment for fear of amplified dementia risk can actually increase the chances of developing the condition because depression itself is a risk factor for dementia.

“I’d be very concerned that because of an overstated fear people stopped treatment of depression too quickly,” he says. “Funnily enough, if they do, that may add to an increased risk of dementia through untreated depression.

“The use of medication to treat mental health problems is unfortunately quite stigmatised, and there’s a lot of scepticism about the role of medications like antidepressants. In the end, we need to be logical and examine the evidence for and against.

“Depression is the leading cause of disability globally and there is clear potential benefit of antidepressants. Any risks need to be weighed against that. My advice is not to stop antidepressants too readily until we understand any possible relationship [between antidepressants and dementia] much more clearly.”

### WHERE TO FROM HERE?

Dr Porter agrees that treating depression will help to reduce your risk of dementia. “The best way to reduce the risk of dementia is to treat the depression adequately,” he explains. “That may or may not be with an antidepressant, but either way it should be treated. “It might be appropriate to come off an antidepressant, but you should go and discuss the pros and cons, and the possible risks with your GP because one risk of coming off antidepressants is that you become depressed again.” ✱

## \* Antidepressants

### THE FACTS

‘Antidepressants aren’t happy drugs and won’t make you feel euphoric. They help you have more realistic emotional responses.’

‘Antidepressants don’t alter personality. Often people find it easier to get along with others because they feel less anxious.’

‘It can take up to six weeks for antidepressants to begin to work.’

‘Along with depression, antidepressants are used to treat anxiety disorders, obsessive compulsive disorders (OCD) and post-traumatic stress disorder (PTSD).’

‘They can reduce symptoms of depression, including feelings of sadness, tiredness, poor appetite and sleep problems.’

## What is dementia?

Dementia is more than a little forgetfulness in older age and it isn’t a natural part of ageing. Confusingly, it isn’t one specific disease; rather, dementia is a syndrome, or group of related symptoms, associated with ongoing decline of brain functioning that typically affects people over 65. This may include problems with memory loss, mental sharpness, language and mood. There are more than 100 diseases that may cause dementia. The most common form of dementia is Alzheimer’s disease, which accounts for two-thirds of

dementia diagnoses, followed by vascular dementia, which caused by reduced blood flow to the brain. In most cases, dementia occurs sporadically and has no clear pattern of family inheritance. Currently, there is no cure for dementia but scientists continue to probe preventative strategies and treatment options. A major 2017 review by *The Lancet* says one in three cases of dementia are preventable by lifestyle changes including increasing physical activity, quitting smoking and increasing social contact.

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