Understanding Antidepressants

Dr Adam Lake GP

A short information leaflet to help make sense of antidepressants and their effects. This leaflet is for general information only and is not a substitute for individual medical advice. If you are concerned about your medication or mood, please speak with your GP.

Introduction

There has been a lot of research into antidepressants, particularly in recent years. Some of the findings may be surprising, and they are not always widely known. As a prescriber, I feel a strong ethical responsibility to make sure people have clear, balanced information before making decisions about these medications.

This leaflet summarises some key points in an accessible way. A longer, fully referenced version is available if you'd like to explore the evidence in more depth.

It's important to keep in mind that all the research is based on averages across thousands of people. Individual responses can vary enormously. In my own practice, I've seen some people benefit greatly from antidepressants with no or minimal side effects, others find them less helpful or experience unwanted effects, and many fall somewhere in between.

How Antidepressants Work

For many years, the most common explanation of depression has been that it is caused by a chemical imbalance in the brain, usually a lack of serotonin. Decades of research have not found evidence to support this theory.

Antidepressants affect serotonin and/or noradrenaline reuptake, altering chemical signalling in the brain. Rather than correcting a known imbalance, antidepressants create an altered brain state. This can be helpful for some people, but it is not a correction from a 'diseased' to a 'normal' state. These changes would occur in anyone taking the drugs, whether or not they are experiencing depression. This way of understanding effects is called a drug-centred model; clinicians differ in how much emphasis they place on this compared with the traditional disease-centred explanation.

How antidepressants lead to changes in mood isn't fully understood. There is some

evidence that many antidepressants reduce REM sleep and therefore increase more restorative stages of sleep. This may help to shift one of the physiological patterns often seen in depression, where there is increased REM and reduced restorative slow-wave sleep.

How Effective Are They?

In short-term trials, many people report improvement after starting antidepressants. On average, medicines do better than placebo, but the difference is modest and varies a lot from person to person. For example, in clinical trials, around 1 in 6 to 1 in 8 people experience an improvement that is greater than placebo on rating scales, though these averages don't predict any individual's response. Research shows that a large part of this improvement is shared with placebo, but that doesn't mean "it's all in the mind" or that the effects aren't real. Placebo responses involve genuine, measurable changes in brain networks related to mood, expectation, and neuroplasticity. This shows how powerful hope, meaning, and context can be in recovery.

Real-World Outcomes

Most drug trials involving antidepressants are 2–3 months, which is much shorter than the usual time people take them for, so there is less data about longer term effects. In the largest longer-term study (STAR-D), around a quarter of participants achieved remission after the first treatment step, and about one in ten maintained remission long-term. When including multiple treatment steps, roughly two-thirds achieved remission at some stage, but many later relapsed. In everyday practice, people are often encouraged to try different antidepressants if the first one only partly helps. However, STAR-D found that each additional switch or combination tended to bring smaller and shorter-lasting benefits, while the overall burden of side effects increased.

In routine practice, outcomes are often modest. While some people achieve meaningful and lasting improvement when taking antidepressants, many experience only partial benefit, relapse, or ongoing symptoms despite treatment. A minority achieve full and sustained remission. Severity plays a role: people with the most severe depression may see a clearer drug effect, though this is still modest on average. For some, antidepressants provide valuable extra support, especially when symptoms have been severe or long-lasting; for others, different or additional approaches may be more helpful.

These outcomes compare with the natural course of depression, which on average lasts around six months, though this varies widely. For some, starting antidepressants can make the treatment journey more complex - for example through cycles of switching,

withdrawal symptoms, or partial responses - which can sometimes prolong symptoms rather than shorten them.

Potential Side Effects

Physical and Emotional Effects

Antidepressants can cause physical side effects such as headaches, stomach upset, or changes in sleep. Emotional effects are less well known but common. Many people describe emotional numbing or flattening, reduced positive and negative feelings, or feeling detached from themselves and others. Some find this helpful for a period; others find it reduces quality of life. These effects usually lessen after tapering off or reducing the dose under medical supervision.

Suicidality

In all age groups, antidepressants can sometimes lead to an increase in suicidal thoughts and behaviours shortly after starting or changing dose, so careful monitoring is important. This is more common in younger people, whereas in adults the overall risk appears neutral or slightly reduced over time. Anyone who develops new or worsening suicidal thoughts after starting antidepressants should seek medical help promptly.

Dependence and Withdrawal

The brain adapts to the presence of antidepressants, so when the dose is reduced or stopped it can take time to readjust. Withdrawal effects are common and may include anxiety, mood changes, sleep disturbance, flu-like symptoms, or sensory changes. For some people these effects are mild; for others they can be more severe or prolonged, lasting weeks, months, or occasionally longer. Because withdrawal symptoms can overlap with depression itself, they are sometimes mistaken for relapse by both patients and clinicians, leading to a cycle of stopping and restarting medication or trying new drugs. Slow, supported tapering under medical supervision - often over several months - is the safest approach, especially after long-term use.

Akathisia

A less common but important side effect is akathisia, a state of intense inner restlessness and agitation, sometimes accompanied by increased suicidal thoughts. This usually appears shortly after starting or changing dose and needs prompt medical attention.

Summary

Antidepressants can be an important and sometimes life-changing tool, particularly in moderate to severe depression, or when people have been trying to manage for weeks

or months and reach a point where they need extra support. I have seen many people experience great benefit from them. Their effects do vary widely from person to person: some experience great benefit with no or minimal side effects, some find them less helpful, and some experience unwanted effects.

NICE guidelines emphasise shared decision-making - choosing from a menu of options based on your preferences and what matters most to you.

Placebo responses highlight the real power of the brain, expectations, and the therapeutic context. Antidepressants are one option among many, and understanding both their potential benefits and limitations helps you make informed choices in partnership with your clinician.

Antidepressants are often most helpful when combined with other approaches such as psychological therapies, lifestyle changes, or practical support. These address different aspects of depression and can complement each other.

If you're considering starting, changing, or stopping antidepressants, discuss it with your GP or pharmacist so you can make a plan that fits your needs

If you'd like to explore this topic in more depth, there's a longer version of this leaflet available with detailed references.