

Four research papers I wish my GP had read before prescribing antidepressants

In 1996, when I was prescribed an antidepressant, there was already published research that showed selective serotonin reuptake inhibitors (SSRIs), commonly known as antidepressants, caused withdrawal effects.¹ However, at that time, the Defeat Depression campaign had successfully created a narrative adopted by most prescribers, in which anxiety or depression were described to the patient as caused by a 'chemical imbalance in the brain' and that SSRIs were safe, effective, and non-addictive. Why would a doctor feel the need to do a full literature review?

WE NOW KNOW A DRUG CAN CAUSE DEPENDENCE WITHOUT CAUSING ADDICTION

Today the word is out that my experience of attempting repeatedly to stop taking the drug and experiencing increasingly severe withdrawal effects is by no means uncommon. We now know a drug can cause dependence without causing addiction. Dependence is simply the physiological consequence of taking a drug that causes the body (especially the brain and central nervous system) to change its structure and functioning in response to the ongoing presence of the drug — for example, an antidepressant. The Public Health England (PHE) report *Dependence and withdrawal associated with some prescribed medicines. An evidence review*, published in 2019,² established that 25% of adults in England were taking a dependence-forming drug. This led to the Royal College of Psychiatrists publishing a new position statement on antidepressant withdrawal, identifying it as potentially 'severe and long-lasting', and something that patients should be made aware of during informed consent for these medications.³

As a busy GP, should you wish to learn more through reading current research, which papers give you the best insight into this subject? I would suggest the following four, chosen because each of them

addresses some element of my 17 years spent on these drugs, helping to make sense of what happened to me, and to explain why it was such a painfully long and unpleasant journey.

KEY PAPERS

Begin with Davies and Read (2019), *A systematic review into the incidence, severity and duration of antidepressant withdrawal effects: are guidelines evidence-based?*⁴ This paper sets the scene, indicating the percentage of patients that doctors treat who may go on to experience antidepressant withdrawal. It describes a systematic literature review to ascertain the incidence, severity, and duration of antidepressant withdrawal reactions. In all, 24 relevant studies were identified, with diverse methodologies and sample sizes.

This systematic review establishes that more than half (56%) of people who attempt to come off antidepressants experience withdrawal effects, with nearly half (46%) of people experiencing withdrawal effects describing them as severe. For patients, it is not uncommon for the withdrawal effects to last for several weeks or months. The National Institute for Health and Care Excellence guidelines have for many years underestimated the severity and duration of antidepressant withdrawal, with significant clinical implications. Recently they were updated to acknowledge that these reactions can be severe and long-lasting for some.⁵

To gain a wider understanding of the impact on patients when prescribers misread/misdiagnose adverse effects or withdrawal effects from antidepressants for relapse, read Guy, Brown, Lewis, Horowitz (2020), *The 'patient voice': patients who experience antidepressant withdrawal symptoms are often dismissed, or misdiagnosed with relapse, or a new medical condition*.⁶

This paper outlines the themes emerging from 158 responders to an open invitation to describe the experience of prescribed psychotropic medication withdrawal for

petitions sent to the Welsh and Scottish parliaments. I was the petitioner for Wales and I am a co-author of this report. We identified eight points along the patient's journey where prescribers failed to recognise prescribed drug dependence and withdrawal, with particular reference to antidepressants lacking. We established a pattern of lack of information (informed consent) given to patients about the risk of antidepressant withdrawal. Doctors then failed to recognise the symptoms of withdrawal and were poorly informed about the best method of tapering prescribed medications. Patients were diagnosed with relapse of the underlying condition or new onset of medical illnesses other than withdrawal, leading to them seeking advice outside of mainstream health care, including from online peer support forums. Although these might not represent the majority of cases, there are enough people affected that we need to pay attention.

Should you only have time to read one paper, choose this next one. It provides the information that would have prevented my misunderstanding of tapering and shortened my withdrawal journey. Horowitz and Taylor (2019), *Tapering of SSRI treatment to mitigate withdrawal symptoms*.⁷

The authors examined the PET imaging data of serotonin transporter occupancy by SSRIs and found that hyperbolically reducing doses (by smaller and smaller amounts each time) reduces their effect on serotonin transporter inhibition in a linear manner. They therefore suggest that SSRIs should be tapered hyperbolically and slowly to doses much lower than those of therapeutic minimums (for example, <1 mg for many antidepressants). Withdrawal symptoms will then be minimised.

Because of the dosage form of many antidepressants, the authors recommend liquid preparations of antidepressants for the small doses — for some medications these cost the same as tablets. Others are more expensive but might be considered a good investment in the long run if it

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allows patients to come off unnecessary medication.

The report describes how to distinguish between withdrawal and relapse, or recurrence of the original condition. Withdrawal comes on quickly (days, rather than weeks), responds equally quickly to the reintroduction of the SSRI, and can present with somatic or psychological symptoms quite distinct from the original illness. It is important to point out here that sometimes withdrawal symptoms appear similar to the original illness, which is what makes the whole issue difficult for doctors and patients alike. The authors also provide an explanation of the neurobiology of SSRI withdrawal, including how the alteration of serotonergic receptors affect key bodily systems including the gut, heart, muscles, and movement.

PATIENTS HAVE DEVELOPED A ROBUST INTERNET-BASED SUBCULTURE OF PEER SUPPORT FOR TAPERING OFF PSYCHIATRIC DRUGS

A key reason why patients turn to others with lived experience online is because there are no support services within the NHS, with the exception of a small Prescribed Medication Support Service in North Wales.² A recent paper by White *et al*, *The role of Facebook groups in the management and raising of awareness of antidepressant withdrawal*,⁸ looked into the experiences of 67 125 people on Facebook withdrawal sites, and questioned why social media seems to be filling a void left by health services.

On a similar theme, my last recommendation is Framer (2021), *What I have learnt from helping thousands of people taper off antidepressants and other psychotropic medications*.⁹ This paper describes how, in the absence of medical literature to assist with withdrawal, patients have developed a robust internet-based subculture of peer support for tapering off psychiatric drugs and recovering from withdrawal. The paper is from the founder of such an online community (<https://www.survivingantidepressants.org>).

Framer describes her experience of SSRI withdrawal and her creation of an online peer support forum, which has about 14 000 registrations and 30 000 visitors each month. She pulls together themes from the stories and queries people have posted, identifying adverse drug reactions, risk factors for withdrawal, tapering techniques, withdrawal symptoms, protracted withdrawal syndrome, and strategies to cope with symptoms, in the context of the existing scientific literature.

Most people who withdraw from antidepressants find to their dismay that more symptoms of withdrawal can appear and the severity escalates after the last dose has been taken. Framer introduces us to PAWS — Post Acute Withdrawal Syndrome — which describes the various physical and emotional symptoms that develop as the body readjusts following the adaptations it has had to make while taking the drug. She also touches on ‘neuro-emotions’ — emotions generated by the neurological effects of withdrawal. These are one of the physiological effects of withdrawal, often unrecognised and easily misdiagnosed as a return of the underlying condition.

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