





ANTIDEPRESSANT WITHDRAWAL

Clinical guidelines on antidepressant withdrawal urgently need updating

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In February 2018 the international debate on antidepressant withdrawal was reignited. ¹⁻⁴ In response to a letter published in the *Times* by Davies et al on the benefits and harms of antidepressants, ¹ the Royal College of Psychiatrists publicly stated that, "[for] the vast majority of patients, any unpleasant symptoms experienced on discontinuing antidepressants have resolved within two weeks of stopping treatment."

To support this claim the college referred to guidelines from the National Institute for Health and Care Excellence (NICE), which state that "[withdrawal] symptoms are usually mild and self-limiting over about 1 week."⁵

When Davies et al issued a freedom of information request to NICE asking for the evidence for its one week claim NICE was able to provide only two short review articles, neither of which supports the one week claim, although both cite numerous sources that contradict it.⁶

We think that NICE's current position on antidepressant withdrawal (first established in 2004) not only was advanced on insufficient evidence but is now widely countered by subsequent research. Several studies, using a range of methods, show that many people experience withdrawal for longer than one week—for example, for over two weeks in 55% of patients, at least six weeks in 40%, at least 12 weeks in 25%, and one

to 13 weeks in 58%¹⁰—with other studies finding mean durations of 11 days¹¹ and 43 days.¹²

Examples of longer durations, of more than a year, are reported in two recent community samples of people experiencing difficulties with withdrawal—by 38.6% (n=185)¹³ and for a mean duration of 90.5 weeks (n=97).¹⁴

Systematic reviews of withdrawal also concur, and one of the largest concludes that withdrawal symptoms "typically ensued within a few days from discontinuation and lasted a few weeks, also with gradual tapering. Late onset and/or a longer persistence of disturbances occurred as well." Another stated that "[withdrawal reactions] typically occur within a few days from drug discontinuation and last a few weeks . . . many variations are possible, including late onset and/or longer persistence of disturbances."

The most recent systematic review, by Davies and Read, also concluded, on the basis of 14 studies of varied methods, that around half of users experience withdrawal when trying to stop or reduce antidepressant treatment, that nearly half of those experiencing withdrawal (46%) report it as severe, and that reports of symptoms lasting several months are common in many recent studies (see examples of duration above).¹⁷

That the evidence base contradicts NICE's official position on antidepressant withdrawal raises concerns for the substantial

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number of antidepressant users who will experience withdrawal for a longer duration than current guidelines recognise. Assuming that doctors abide by such guidelines, we believe that many people may have their antidepressant withdrawal misdiagnosed—for example, as relapse or as a failure to respond to treatment—with antidepressants being reinstated, switched, or increased in dose as a result.

These practices, if routinely enacted, would help partly explain why the average time a person spends taking antidepressants has doubled in the UK since the guidelines were introduced in 2004, ^{18 19} why antidepressant prescriptions are rising overall, and why patients regularly report that their withdrawal is not properly acknowledged, understood, and managed by doctors. ²⁰²¹ In addition, the pooled results of two recent surveys showed that under 2% of around 3000 patients were able to recall being told anything about withdrawal effects, dependence, or potential difficulties in discontinuing treatment. ^{22 23}

It is worrying that antidepressants are causing withdrawal effects that can be long lasting and severe and that this is not being sufficiently recognised by current clinical guidelines—and, by extension, many prescribers. NICE is now in the process of updating its depression guidelines, and we call on it and the royal colleges to revise their practice guidelines and recommendations to bring them in line with the scientific evidence base.

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- Davies J, Moncrieff J, Kinderman P, et al; Council for Evidence-Based Psychiatry. Stigma and efficacy of taking antidepressants. Letter to the editor. *Times* 2018 Feb 23. https:// www.thetimes.co.uk/article/stigma-and-efficacy-of-taking-antidepressants-0zvsg560x.
- Baldwin D, Burns W. Pills for depression. Letter to the editor. Times 2018 Feb 24. https://www.thetimes.co.uk/article/86afb2fc-18c7-11e8-a427-78e8af199a96.
- 3 Hengartner MP. Rapid response to: Adlington K, Pop a million happy pills? Antidepressants, nuance, and the media. BMJ 2018. https://www.bmj.com/content/360/bmj.k1069/rr-1.
- Davies J, Read J, Hengartner M, et al. Rapid response to: lacobucci G, NHS prescribed record number of antidepressants last year. BMJ 2019. https://www.bmj.com/content/364/ bmj.l1508/rr-4.
- National Institute for Health and Care Excellence. Depression in adults: recognition and management. 2009. https://www.nice.org.uk/guidance/cg90/resources/depression-inadults-recognition-and-management-pdf-975742638037.
- Davies J, Read J. A systematic review into the incidence, severity and duration of antidepressant withdrawal effects: Are guidelines evidence-based? Addict Behav 2018;2018:4; [epub ahead of print]. 10.1016/j.addbeh.2018.08.027. 30292574

- Perahia DG, Kajdasz DK, Desaiah D, Haddad PM. Symptoms following abrupt discontinuation of duloxetine treatment in patients with major depressive disorder. J Affect Disord 2005;89:207-12. 10.1016/j.jad.2005.09.003 16266753
- Zajecka J, Fawcett J, Amsterdam J, etal . Safety of abrupt discontinuation of fluoxetine: a randomized, placebo-controlled study. J Clin Psychopharmacol 1998;18:193-7. 10.1097/00004714-199806000-00003 9617977
- Royal College of Psychiatrists. Coming off antidepressants. 2012. http://www.rcpsych.ac. uk/healthadvice/treatmentswellbeing/antidepressants/comingoffantidepressants.aspx. (Accessed Feb 2018.)
- 10 Black K, Shea C, Dursun S, Kutcher S. Selective serotonin reuptake inhibitor discontinuation syndrome: proposed diagnostic criteria. J Psychiatry Neurosci 2000:25:255-61.10863885
- 11 Price JS, Waller PC, Wood SM, MacKay AV. A comparison of the post-marketing safety of four selective serotonin re-uptake inhibitors including the investigation of symptoms occurring on withdrawal. *Br J Clin Pharmacol* 1996;42:757-63. 10.1046/i.1365-2125.1996.00498.x 8971432
- Narayan V, Haddad PM. Antidepressant discontinuation manic states: a critical review of the literature and suggested diagnostic criteria. J Psychopharmacol 2011;25:306-13. 10.1177/0269881109359094 20156925
- Davies J, Pauli R, Montagu L. Antidepressant withdrawal: a survey of patients' experience by the All-Party Parliamentary Group for Prescribed Drug Dependence. 2018. http:// prescribeddrug.org/wp-content/uploads/2018/10/APPG-PDD-Survey-of-antidepressantwithdrawal-experiences.pdf.
- 14 Stockmann T, Odegbaro D, Timimi S, Moncrieff J. SSRI and SNRI withdrawal symptoms reported on an internet forum. Int J Risk Saf Med 2018;29:175-80. 10.3233/JRS-180018 29758951
- Fava GA, Benasi G, Lucente M, Offidani E, Cosci F, Guidi J. Withdrawal symptoms after serotonin-noradrenaline reuptake Inhibitor discontinuation: systematic review. Psychother Psychosom 2018;87:195-203. 10.1159/000491524 30016772
- Fava GA, Gatti A, Belaise C, Guidi J, Offidani E. Withdrawal symptoms after selective serotonin reuptake inhibitor discontinuation: a systematic review. *Psychother Psychosom* 2015;84:72-81. 10.1159/000370338 25721705
- 17 Davies J, Read J. A systematic review into the incidence, severity and duration of antidepressant withdrawal effects: Are guidelines evidence-based? Addict Behav 2018. 10.1016/j.addbeh.2018.08.027. 30292574
- NHS Digital. Prescriptions dispensed in the community—Statistics for England, 2006-2016. https://digital.nhs.uk/data-and-information/publications/statistical/prescriptions-dispensed-in-the-community/prescriptions-dispensed-in-the-community-statistics-for-england-2006-2016-pas.
- 19 Kendrick T. Long-term antidepressant treatment: Time for a review? Prescriber 2015;26:7-810.1002/psb.1389.
- 20 Davies J, Pauli G, Montagu L. A survey of antidepressant withdrawal reactions and their management in primary care. Report from the All Party Parliamentary Group for Prescribed Drug Dependence. 2018. http://prescribeddrug.org/wp-content/uploads/2018/10/APPG-PDD-Survey-of-antidepressant-withdrawal-experiences.pdf.
- 21 Cartwright C, Gibson K, Read J, Cowan O, Dehar T. Long-term antidepressant use: patient perspectives of benefits and adverse effects. *Patient Prefer Adherence* 2016;10:1401-7. 10.2147/PPA.S110632 27528803
- 22 Read J, Cartwright C, Gibson K. How many of 1829 antidepressant users report withdrawal symptoms or addiction? *Int J Ment Health Nurs* 2018. 10.1111/inm.12488.
- 23 Read J, Williams J. Adverse effects of antidepressants reported by a large international cohort: emotional blunting, suicidality, and withdrawal effects. *Curr Drug Saf* 2018;13:176-86. 10.2174/1574886313666180605095130 29866014

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