

## **How common and severe are six withdrawal effects from, and addiction to, antidepressants? The experiences of a large international sample of patients.**

### **HIGHLIGHTS**

- Over half (55%) of people who had tried to come off or reduce antidepressants report some degree of difficulty coming off, with 27% ticking ‘very difficult’
- 61% report ‘withdrawal effects’, with 44% of these describing the effects as ‘severe’
- 40% report ‘addiction’, with 39% of these describing their addiction as ‘severe’
- ‘Anxiety/panic’ (66%) and ‘Irritability (62%) are particularly common
- Less than 1% had been told anything about withdrawal effects or dependence

### **ABSTRACT**

**Introduction:** The incidence and severity of withdrawal effects when coming off antidepressants (ADs) have recently received considerable attention. National guidelines on the topic have proven to be inaccurate. This paper reports the largest direct-to-patient international survey on these issues.

**Methods:** Data generated by an online survey from 867 people from 31 countries, who had taken ADs continuously for at least one month, and had tried to come off (successfully or not) was analysed.

**Results:** The majority (59%) had taken ADs for more than three years. Of those who were still taking them, 29% had been doing so for at least 20 years. 61% reported some degree of withdrawal effects, and 44% of these described the effects as ‘severe’. The most common of six listed withdrawal effects were anxiety/panic (66%) and irritability (62%). The most common spontaneously reported ‘other’ withdrawal effect was suicidality (2%). 40% reported that they felt addicted, with 39% of these describing their addiction as ‘severe’. Over

half (55%) reported some degree of difficulty coming off, with 27% ticking 'very difficult', and 11% 'very easy'. Duration of treatment was related to withdrawal, addiction and difficulty coming off. Younger people experienced more frequent withdrawal effects. Only six people (0.7%) recalled being told anything about withdrawal, dependence or addiction by the initial prescriber.

Conclusions: These findings confirm previous studies, using a range of methodologies, finding high incidences of withdrawal effects, frequently at severe levels. National guidelines, and those of professional organisations, urgently need to be updated to reflect this evidence.

## **1. Introduction**

In the U.K. antidepressant [AD] prescribing has doubled over ten years. By 2016-17 more than seven million adults (16% of the adult population) were prescribed ADs in England (DHSC, 2018). Similar rates occur in Australia, Belgium, Canada, Denmark, Iceland, Portugal, and Sweden (OECD, 2017, 2018), with the highest being in the U.S. (Pratt, Brody, & Qu, 2017).

These high prescription rates do not seem to be explicable in terms of increases in depression or help-seeking (Munoz-Arroyo, Sutton, & Morrison, 2006). UK data on 189,851 GP patients showed that a doubling of prescribing over eight years was probably explained by a doubling of prescriptions per patient, rather than by increases in new prescriptions (Moore et al., 2009). By 2011, half of AD users in England, about 3.5 million people, were taking ADs for longer than two years (Johnson et al., 2012). About half of AD users in the U.S. (about 18 million) take them for at least 5 years (Mojtabai & Olfson, 2014). Average duration has doubled since the mid-2000s in the U.K. (NHS Digital, 2017) and the U.S. (Mojtabai & Olfson, 2014). In the U.K., a third of people taking ADs for more than two years

have no clinical need for them (Cruickshank, MacGillivray, & Bruce, 2008). Similar rates of apparently unnecessary long-term prescribing occur in Australia (Ambresin et al., 2015) and the Netherlands (Eveleigh, 2015).

Difficulty stopping the drugs because of withdrawal effects might explain why long-term prescribing is increasing, including to people who are deemed not to have a clinical need for them. The notion of AD withdrawal effects was officially recognised by a ‘consensus panel’ funded by drug company Eli Lilly in 1996, and was immediately minimised by creating the term ‘discontinuation syndrome’ (Schatzberg et al., 1997), still sometimes unquestioningly deployed today. Since then withdrawal from ADs has been portrayed, by guidelines and professional bodies, as rare, minimal and brief.

The President of the UK’s Royal College of Psychiatry (RCP) and the Chair of the RCP’s Psychopharmacology Committee recently wrote ‘We know that in the vast majority of patients, any unpleasant symptoms experienced on discontinuing antidepressants have resolved within two weeks of stopping treatment’ (Burn & Baldwin, 2018). U.S.A guidelines similarly claim symptoms ‘typically resolve without specific treatment over 1–2 weeks’ (A.P.A., 2010, p. 39). U.K. guidelines state ‘symptoms are usually mild and self-limiting over about 1 week, but can be severe, particularly if the drug is stopped abruptly’ (NICE, 2009, 1.9.2.1 in CG90). Freedom of Information requests revealed that the current NICE guidelines on AD withdrawal are not based on any research studies (Davies & Read, 2019a, p. 119).

Three systematic reviews have now established that such statements and guidelines have been minimising the problem (Davies & Read, 2019a; Fava et al., 2015; 2018). The most recent systematic review (involving the current author) was undertaken at the request of the UK’s All Party Parliamentary Group for Prescribed Drug Dependence, to inform an enquiry by Public Health England (an agency of the Department of Health and Social Care). Fourteen

studies, including small RCTs and large scale surveys, found that withdrawal incidence rates ranged from 27% to 86% with a weighted average of 56%. Four studies produced a weighted average of 46% of those experiencing withdrawal effects endorsing the most extreme ‘severity’ rating. Seven of ten studies with data on duration contradict the U.K. and U.S.A. guidelines, by finding that a significant proportion of people who experience withdrawal do so for far more than two weeks, and that it is not uncommon for people to experience withdrawal for several months. The reviewers (Davies & Read, 2019a, p. 111) concluded:

We recommend that U.K. and U.S.A. guidelines on antidepressant withdrawal be urgently updated as they are clearly at variance with the evidence on the incidence, severity and duration of antidepressant withdrawal, and are probably leading to the widespread misdiagnosing of withdrawal, the consequent lengthening of antidepressant use, much unnecessary antidepressant prescribing and higher rates of antidepressant prescriptions overall. We also recommend that prescribers fully inform patients about the possibility of withdrawal effects.

The Davies and Read review was sharply critiqued by two psychiatrists who characterised it as a ‘War on antidepressants’, claimed that the review had exaggerated the extent, severity and duration of withdrawal effects, and disagreed with our call for guidelines to be urgently reviewed (Jauhar & Hayes, 2019). Our response carefully documented their ‘many serious mistakes and misrepresentations (and/or misunderstandings)’ that led us to describe their critique as ‘clearly imbalanced, imprudent and inaccurate’ (Davies & Read, 2019b), an assessment shared by a further commentator (Hengartner, 2019).

Jauhar and Hayes did, nevertheless, raise legitimate concerns about using online surveys (such as the one that generated the data for the current paper) to estimate incidences. Participants in such surveys are certainly not randomly selected or generalizable to all antidepressant users. It is possible, therefore, that they may over-represent dissatisfied or

disgruntled patients. We were able to reassure them, however, (Davies & Read, 2019b) that in the largest survey 83% believed the antidepressants had reduced their depression (Read et al., 2014). In the current survey this was the case for 63% (Read & Williams, 2018).

Jauhar & Hayes (2019), having corrected what they believed to be the errors in the Davies and Read review, proposed that a better estimate of the incidence of withdrawal effects among people who try to come off is 44%. This would still represent 3.2 million people in England alone. So researchers on both sides of a rather charged debate agree that about half (somewhere between 44% or 56%) of people experience withdrawal effects when they try to come off ADs.

The current paper reports further findings from an international survey about positive and negative effects of ADs (Read & Williams, 2018). The survey had found that withdrawal effects were reported by 59%, and addiction by 40% of 1,431 AD users from 38 countries. The current paper, analysing only responses from participants who had tried to come off or reduce their ADs, reports on the frequency of six specific types of withdrawal effects, on self-reported ease/difficulty of coming off, and on whether patients were told about withdrawal; plus analyses by demographics, treatment duration and drug type.

Very few studies have reported on how often people are informed about withdrawal effects when being prescribed the drugs (Read, Cartwright & Gibson, 2018; Read, Gee et al., 2018). This is only the second survey to report on ease/difficulty withdrawing (Read, Gee et al., 2018). This is the first large survey to report the incidence or severity of specific withdrawal effects. A recent analysis of 110 postings on a withdrawal website may be the next largest report on specific withdrawal effects (Stockman et al., 2018). RCTs tend to have artificially short treatment durations, small sample sizes, rarely report on withdrawal at all, let alone on specific withdrawal symptoms, and also tend not to analyse by demographics (Davies & Read, 2019a, 2019b). It is hoped that mapping the most common withdrawal

effects might assist in the identification of patients experiencing withdrawal, and that any links with demographic groupings might lead to extra caution in prescribing, and while withdrawing, with those groups.’

## **2. Method**

### *2.1. Instrument*

The AD sections of ‘The Experiences of Anti-depressant and Anti-psychotic Medication Survey’ (see Read & Williams, 2018) were based on the New Zealand ‘Views on Antidepressants’ questionnaire (Gibson, Cartwright & Read, 2016; Read, Cartwright & Gibson, 2014, 2018; Read et al., 2015). These sections generate quantitative data (yes/no and multiple-choice questions) and qualitative data (open-ended questions) about: the prescribing experience, positive and negative effects of ADs, beliefs about causes of depression, withdrawal experiences, and demographics. Questions were based on the research literature pertaining to each topic.

The questions generating the data which is the main focus of the current paper were:

‘Please rate the following side effects you may have experienced as a result of taking the anti-depressant’ – followed by a list of 14 effects including ‘Withdrawal Effects’ and ‘Addiction’ and the following response options: ‘Not at all’ ‘Mild’ ‘Moderate’ ‘Severe’.

When trying to withdraw from anti-depressants, did you experience an increase in the following: ‘Nausea’ ‘Brain Zaps’ ‘Dizziness’ ‘Anxiety/Panic’ ‘Irritability’ ‘Nightmares’ Other (please specify) – and the following options: ‘No increase’ ‘A slight increase’ ‘A big increase’

‘How easy was it for you to come off your medication?’ – ‘Very Difficult’ ‘Difficult’  
‘Somewhat Difficult’ ‘Somewhat Easy’ ‘Easy’ ‘Very Easy’.

‘Did the doctor inform you of possible side effects? Yes/No – If ‘Yes’ what side effects were mentioned?’

## *2.2. Participants*

Of the 2,346 who responded, 2,133 had taken ADs. Of these, 42 were deleted because they ticked ‘no’ when asked if they met the criteria: ‘I have been taking or have previously taken antidepressant medication continuously for at least one month for any reason’; ‘I am aged 18 or older’; and ‘I am not currently compulsorily detained in a psychiatric hospital’. Of the remaining 2,091, the 44 that responded to ‘What is the name of your current or most recent anti-depressant medication?’ with a drug other than antidepressants were deleted. There were 39 responses from the same Internet Protocol address as another response, indicating use of the same computer. Of these 39, 33 were deemed a repeat response (based on identical demographics or similar responses) and were omitted. Of the remaining 2,014, 497 completed insufficient questions in the AD sections, leaving 1,517. Of these, 499 had taken antipsychotics as well as ADs, and were excluded (to avoid potential confusion, or interactions, between withdrawal from the two types of drugs). Finally, 151 of the remaining 1018 ticked ‘No’ to the question ‘Have you ever reduced or tried to come off your anti-depressant medication?’ These 151 were deleted because withdrawal effects could not occur under those circumstances. This left 867.

## *2.3. Data Analysis*

Relationships between variables were analysed using chi-squares ( $\chi^2$ ) and spearman rank correlations ( $\rho$ ). Differences between means on continuous variables (e.g. age) were analysed with two-tailed t-tests. Because of the large number of analyses the significance level was set at  $p < .01$  rather than the traditional  $p < .05$ .

### **3. Results**

#### *3.1. Sample characteristics*

Respondents' were aged 18 to 77 years with an average of 45.8 (sd = 13.6); and 70.8% were women. IP addresses showed that the respondents lived in 31 countries, most commonly Australia (408; 47.1%) (from where the survey was conducted), the UK (152; 17.5%), and the USA (115; 13.3%). Seven other countries had more than 10 respondents: New Zealand (29), Germany (36), Denmark (21), Canada (20), Ireland (18), the Netherlands (11), and Sweden (11). Twenty one contributed up to eight participants: Albania, Algeria, Austria, Belgium, Bosnia, Bulgaria, Croatia, Faroe Islands, Finland, Greece, India, Italy, Lithuania, Norway, Poland, Portugal, Slovakia, Slovenia, South Africa, Spain and Switzerland.

When asked 'Do you think you were prescribed anti-depressant medication to treat depression?' most (84.2%) replied 'Yes'. More than two thirds (70.0%) thought the drugs reduced their depression, and 12.2% thought they made the depression worse. Similarly, 64.2% reported that Quality of Life was 'improved', and 18.3% thought it was made 'worse'.

Of the 759 who named their medication(s), the most commonly received SSRIs were fluoxetine (16.3%), citalopram (14.0%), sertraline (13.7%), paroxetine (9.0), and escitalopram (6.7%). Venlafaxine, an SSNRI, was cited by 7.2% and Tricyclic ADs by 7.9%; while 12.1% reported two or more ADs.

#### *3.2. Treatment duration*

More than half (59.1%) had taken ADs for ‘more than three years’; with 6.4% having taken them for ‘two to three years’, 10.3% for ‘one to two years’, 11.0% for ‘six to 12 months’, and 13.2% for between one and six months. Age was significantly correlated with treatment duration ( $\rho = .204$ ,  $n = 854$ ,  $p < .001$ ). Women had somewhat longer durations, with 62.2% on ADs for more than three years, compared to 52.2% of men. This difference did not meet the  $p < .01$  level set for this study ( $\rho = 11.25$ ,  $df = 5$ ,  $p = .047$ ).

Nearly half of the total sample (47.9%) had stopped taking ADs when they completed the survey. By analysing only the 452 who were still taking the drugs, duration of treatment could be ascertained in more detail than permitted by the five age groupings, by subtracting age at first use from current age. Of the 444 who provided current age and age at first use the average treatment duration was 14.3 years ( $sd = 9.1$ ). (58.7% had taken ADs ‘continuously’ and 41.2% ‘intermittently’). About two thirds (67.3%; 299) had been taking them for at least ten years; 28.8% (128) for at least 20 years, and 5.6% (25) for 30 years or more. Women had a significantly longer mean treatment duration (15.0) than men (12.4) ( $t = 2.63$ ,  $df = 439$ ,  $p = .009$ ). Age was strongly correlated to duration ( $r = 4.21$ ,  $n = 444$ ,  $p < .001$ ).

Extreme examples include a 61 year old Australia woman and a 58 year old New Zealand woman who had both been prescribed ADs as 14 year old girls and had been on them continuously for 47 and 44 years. A 68 year old man in the USA had taken ADs intermittently for 45 years, since the age of 23. A 73 year old Australian woman had taken ADs intermittently for 53 years, since the age of 20.

### 3.3. *Withdrawal effects*

Of the 803 responding to the question ‘Please rate the following side effects you may have experienced as a result of taking the anti-depressants’, 309 (38.5%) responded ‘not at all’ to

‘withdrawal effects’. Of the 494 (61.5%) reporting some degree of withdrawal effects, 31.2% reported them to be ‘mild’, 24.5% as ‘moderate’ and 44.3% as ‘severe’.

Experiencing some degree of withdrawal effects was strongly related to length of time taking ADs ( $X^2 = 23.03$ ,  $df = 5$ ,  $p < .001$ ). For example, 46.8% of those who had taken ADs for six months or less reported withdrawal effects, compared to 67.4% of those on ADs for more than three years. Similarly, amongst those with some degree of withdrawal effects, their severity was strongly correlated with treatment duration ( $\rho = .23$ ,  $n = 494$ ,  $p < .001$ ).

The mean age of people with some degree of withdrawal effects (43.7) was significantly younger than those who did not experience withdrawal (48.5) ( $t = 4.86$ ,  $df = 806.2$ ,  $p < .001$ ). Age was, however, unrelated to severity. Gender was unrelated to incidence or severity.

*3.3.1. Specific withdrawal effects.* Between 787 and 798 responded to questions about six specific withdrawal effects, worded as ‘When trying to withdraw from antidepressants did you experience an increase in ...?’ with possible responses of ‘no increase’, ‘a slight increase’ and ‘a big increase’. Of the 764 who responded to all six questions, most (79.2%) reported at least one withdrawal effects, 54.1% reported three or more and 15.8% reported all six. The mean number of effects was 2.83 ( $sd = 2.10$ ). The number of withdrawal effects was unrelated to gender but was negatively related to age ( $\rho = -.21$ ,  $n = 763$ ,  $p < .001$ ).

Table 1 shows that the six were experienced, to some degree, by between 65.6% (‘Anxiety/panic’) and 34.8% (Nausea). Women were significantly more likely than men to experience Dizziness ( $X^2 = 8.39$ ,  $df = 1$ ,  $p = .004$ ). The mean age of those experiencing four of the six withdrawal effects was significantly lower than those not experiencing them (see Table 1), with the largest difference being for Nausea (41.0 vs 47.8 years;  $t = 7.15$ ,  $df = 637.2$ ,  $p < .001$ ). Length of time taking ADs was strongly related to all six, five at the  $p < .001$  level; most strongly Anxiety/Panic ( $X^2 = 62.14$ ) and Irritability ( $X^2 = 60.95$ ).

## TABLES ONE & TWO ABOUT HERE

One or more ‘other’ withdrawal effects were identified by 193 people (see Table 2).

Some examples:

*Suicidality and self-harm.*

*I had body aches and pains, flu like symptoms, constant malaise.*

*Derealization, depersonalization, intrusive thoughts, cramps, nerve pain, exhaustion, vision problems, sexual problems, cognitive problems, constant fear, great grief, suicidal thoughts, high anxiety, trouble connecting to others, constant crying.*

*Severe diarrhea, severe exhaustion, severe headaches.*

*The electric shocks through my whole body from toes to fingertips to brain, for a few seconds every few seconds, all day even when lying down. They gradually stopped after about 4 weeks.*

*Permanant damage - brain zaps and sound sensitive, years after stopping.*

### 3.4. ‘Addiction to the medication’

Of the 803 responding to the side effects questions 320 (39.9%) reported some degree of ‘addiction to the medication’. Of these 320, 113 (35.3%) described the addiction as ‘mild’, 25.3% as ‘moderate’ and 39.4% as ‘severe’.

Experiencing some degree of addiction was strongly related to treatment duration ( $X^2 = 40.90$ ,  $df = 5$ ,  $p < .001$ ). For example, 25.7% of those who had taken ADs for six months or less reported addiction, compared to 48.1% of those on them for more than three years.

Treatment duration was also strongly correlated with *severity* of addiction ( $\rho = .30$ ,  $n = 310$ ,  $p < .001$ ).

Gender and age were unrelated to incidence or severity of addiction. Unsurprisingly, incidence of addiction was highly related to incidence of withdrawal ( $X^2 = 148.07$ ,  $df = 1$ ,  $p < .001$ ). Similarly, *severity* of addiction was highly related to *severity* of withdrawal ( $X^2 = 111.32$ ,  $df = 4$ ,  $p < .001$ ).

### 3.5 'How easy was it'?

Of the 797 who responded to 'How easy was it for you to come off your medication?' on a six point scale (1 = 'very difficult', 6 = 'very easy'), 10.9% ticked 'very easy', and 27.2% 'very difficult'. Overall, 45.4% found it 'easy' to some degree and 54.6% experienced some difficulty (see Table 3).

Difficulty coming off was not significantly related to age or gender. It was, unsurprisingly, strongly related to incidence and severity of both withdrawal effects and addiction, with all four relationships at the  $p < .001$  level. For example, 89.8% of those who found it 'very difficult' to come off experienced withdrawal effects, compared to 18.4% who found it 'very easy'. It was also strongly related to each of the six withdrawal effects, all at the  $p < .001$  level, with *rhos* ranging from 0.43 (Anxiety) to .50 (Dizziness).

## TABLES 3 & 4 ABOUT HERE

### 3.6. Drug types

The four most frequently cited SSRIs, the SSNRI venlafaxine, and tricyclics (combined) were compared. There were no significant differences in incidence of 'withdrawal effects' overall or 'addiction'. Paroxetine, however, produced reports of significantly greater *severity* of withdrawal effects, at the  $p < .001$  level than sertraline and tricyclics, and at the  $p < .01$  level compared to citalopram and fluoxetine. Each of the six specific withdrawal effects occurred significantly more frequently with paroxetine than with between one and four of the

other drug types (see Table 4). Brain zaps were reported more frequently with venlafaxine compared to sertraline and tricyclics.

### *3.7. Information*

Only 36.2% reported that they had been told anything about ‘any possible side effects’. When participants were asked what specific side effects they recalled being told about only six (0.7%) reported anything to do with withdrawal, dependence or addiction, including: ‘not to stop taking them all at once’, ‘they were habit forming and I could not stop taking abruptly’, and ‘need to go off gradually.’

When asked ‘Did the doctor tell you how long you should take the antidepressants for?’ 52.3% replied ‘no’. Gender and age were unrelated. Of those who were told anything, 6.6% were told to take them for three months or less, 35.5% were told between three and 12 months; 18.1% for more than a year, and 39.9% ticked ‘until you feel better’. Gender and age were unrelated to the recommended duration.

## **4. Discussion**

### *4.1. Treatment duration*

The long treatment durations reflect the large increases in duration noted earlier. A recent UK online survey of 752 AD users found that 36% had been taking them for at least five years, and 26% expected to be on them forever (Read, Gee, Diggle, & Butler, 2018).

### *4.2. Withdrawal symptoms*

The proportion of people experiencing some degree of withdrawal effects reported here (61.5%) is even higher than the 55% previously reported for this survey (Read & Williams, 2018), and the 55% found in a New Zealand survey with identical methods (Read, Cartwright, & Gibson, 2018), because the current analyses excluded participants who had

never tried to reduce or discontinue. These rates are also somewhat higher than traditional, drug company sponsored drug trials, which use artificially short treatment periods of 8 to 12 weeks (Davies & Read, 2019a). The weighted average of all studies to date, using a range of methodologies is 56% (Davies & Read, 2019a). The finding that younger people are more likely to experience withdrawal effects was not found in the New Zealand survey and has not been tested by drug trials, which tend to ignore demographics. Amongst those reporting withdrawal effects the percentage describing them as severe (44.3%) is similar to the percentage in the New Zealand survey (46%) and to two other surveys, by Groot & van Os (2018) - 51%, and Davies, Pauli and Montagu (2018) - 43%.

This is the first large survey to report the incidence or severity of specific withdrawal effects. A smaller but valuable analysis, of 110 postings on an antidepressant website (Stockman et al., 2018), found that 94% reported one or more ‘Psychological’ withdrawal effect, for example: ‘Brain fog’, anxiety, depression, feeling suicidal, irritable, feeling ‘lousy’, ‘emotional numbness’, and pessimism, (p. 178). Two thirds (66%) reported at least one ‘Neurological’ effect, for example: Dizziness, ‘brain zaps’, ‘whoosh in ears’, ringing ears, paraesthesia, ‘needles under skin’, sensitive to light, buzzing sound, and burning sensation. Less than half (43%) reported one or more of the following ‘Gastrointestinal’ effects: Nausea, bloated, diarrhoea, constipation, acid reflux, stomach cramps, appetite changes, sensitivity to food.

The six symptoms measured in the current study have been identified in drug trials but with smaller frequencies, due largely, again, to the atypically short treatment periods. The extent of the underestimation by drug trials is demonstrated by the fact that 38.1% of those on ADs for one to three months reported irritability when withdrawing, compared to 72.4% of those on them for the more typical duration of three years or more. The current findings, including more than 60% reporting anxiety/panic and irritability, need to be replicated with

equally large samples, but including some of the effects identified by the open request for ‘other’ withdrawal effects, such as suicidality, insomnia and sexual dysfunction.

#### *4.3 Addiction*

The issue of whether ADs should be considered addictive has polarised opinion. Many recipients report that they are addictive. The 40% rate of self-reported ‘addiction to the medication’ is slightly higher than the 37% previously reported from this survey when those who had never tried to come off were included (Read & Williams, 2018), but clearly higher than the 27% self-reported in the New Zealand survey (again including those who had never tried to come off). In both studies duration of treatment was strongly correlated with addiction. A review of studies of patient-centred perspectives found fear of addiction to be ‘the most frequently mentioned reason for a negative opinion of antidepressants’ (Gibson et al., 2014, p. 83). Among 493 AD users in Denmark, 56% agreed with ‘Your body can become addicted to antidepressants’ (Kessing et al. 2005). Of 192 people in the Netherlands who had been taking ADs for six months, 30% reported that ADs are ‘addictive’ (Hoencamp et al., 2002). It seems that somewhere between a quarter and a half of AD users experience ADs as addictive, with the proportion increasing with treatment duration.

Nevertheless, many of the researchers who find these high levels of self-reported addiction describe the patients’ experiences and views as ‘erroneous beliefs’ and ‘negative attitudes’ and worry that they may that impede medication compliance (e.g. Bogner et al., 2009; Hoencamp et al., 2002; Kessing et al., 2005). Similarly, the only reference to the issue in the American Psychiatric Association Practice (A.P.A.) Guideline for depression (2010) is ‘Common misperceptions about antidepressants (e.g. they are addictive) should be clarified’. (The authors listed over 80 instances of receiving payments from drug companies between them).

The Diagnostic and Statistical Manual for Mental Disorders (A.P.A., 2013) requires that two of eleven criteria are met for ‘substance dependence’. The current study, and the large New Zealand survey, suggest that ADs meet four of them: ‘Withdrawal manifesting as a characteristic syndrome’, ‘Wanting to cut down or quit but not being able to do it’, ‘Continued use despite persistent or recurring social or interpersonal problems caused or made worse by substance use’ and ‘Stopping or reducing important social, occupational, or recreational activities due to substance use.’

In 2012 the Nordic Cochrane Centre reviewed 45 papers on benzodiazepines and 31 papers on SSRIs and concluded that ‘Withdrawal reactions to SSRIs appear to be similar to those for benzodiazepines; referring to these reactions as part of a dependence syndrome in the case of benzodiazepines, but not selective serotonin re-uptake inhibitors, does not seem rational’ (Nielsen, Hansen, & Gotzsche, 2012).

If one includes physical cravings in one’s addiction criteria then ADs are not addictive. Similarly they do not, at first glance, have what the recent Public Health England report defines as the distinguishing characteristic of ‘addiction’, namely ‘a compulsive preoccupation to seek and take a substance despite consequences’ (Tayler et al., 2019, p 8). However, if the preoccupation includes a compulsion to put an end to the withdrawal effects then there is an argument that ADs do meet that particular criterion for addiction.

#### *4.4 Easy or difficult*

The range of responses regarding how easy it was to come off broadly parallels the finding of a large UK survey in which 20% found it ‘very easy’, 51% ‘fairly easy’; and 29% ‘not easy at all’ (Read, Gee, et al., 2018). The same survey also found that while 68% took less than three months to come off, 21% took between three and six months; 6% took between six and 12 months; and 5% took more than a year. Such distributions reveal important individual

differences. Even though duration of being on ADs is, in the current study, strongly predictive of how difficult it is, differences in withdrawal effects will still occur between people who have taken ADs for similar amounts of time. Therefore, there must be no ‘one size fits all’ approach to the time necessary to withdraw or how much support is needed.

#### *4.5. Drug types*

The findings regarding drug types confirm the findings of drug trials and the New Zealand survey (Read, Cartwright, & Gibson, 2018) that ADs with a shorter half-life, like paroxetine and venlafaxine, are even more likely to cause withdrawal effects than those with longer half-lives.

#### *4.6. Information*

The finding that only six people (0.7%) recalled being told anything about withdrawal effects is alarming. It is matched by the only other data on this important issue, from the New Zealand survey, in which nine out of 1,829 people (0.9%) recalled such information being imparted (Read, Cartwright, & Gibson, 2018). This breaches the ethical principle, binding on all health professionals, of ‘informed consent’.

#### *4.7 On a more positive note*

Alongside the disquieting findings about withdrawal effects and lack of information, it must be noted that a large majority of participants (70%) considered that antidepressants reduced their depressive symptoms, and improved their quality of life (64%). Findings that the majority of improved cases are the result of placebo effects (Jakobsen et al., 2017; Kirsch et al. 2008) cannot detract from the reality that most people in the sample felt better and believed this was a result of the drugs. Similarly it should also be underlined that 38.5% of

the sample did not experience withdrawal effects, and 19.2% reported only mild effects. Thus the majority (57.7%) did not experience moderate or severe withdrawal effects.

## **5. Limitations**

Although this is the second largest sample (and largest international sample) directly surveyed, it is a self-selected, convenience sample. Almost the entire sample lived in Europe, North America or Australasia. The over representation of women (70.8%) is not, however, a limitation because women are prescribed ADs approximately twice as often as men.

The excluded subgroups might present specific characteristics lowering the representativeness of the final sample. Those leaving the questionnaire without answering all the questions might have reduced attentional abilities or increased impulsivity; those also taking antipsychotic might present more severe depressive states or comorbidities; those not trying to reduce antidepressants might also have unknown specific characteristics

The high rates of reported withdrawal effects and addiction suggest the sample may be biased towards people who found ADs ineffective and had 'an axe to grind'. However, 70.0% reported that the ADs had reduced their depression.

The study relies on self-report, but so do most drug studies. Some of the reports, however, are for events many years ago. Some people may have been given more information about withdrawal than they could recall. In fact 42 participants wrote some variation of 'can't recall'. One 70 year old Australian man, wrote 'He was always good at discussing side effects of all medications he prescribed, however it is so long ago I can't recall what he said'.

When asked whether they had experienced 'withdrawal effects' 494 said they had, to some extent. However, when asked 'When trying to withdraw from antidepressants did you experience an increase in ...?', without explicitly describing the experiences as 'withdrawal

effects’, 605 reported at least one of the six experiences. It is possible, therefore, that a small minority of those reporting the most common experiences, ‘anxiety/panic’ and irritability’, while coming off the drugs did not interpret them as withdrawal effects, and/or that they were in fact not withdrawal effects. Since 521 reported ‘anxiety/panic’ and 499 reported ‘irritability’ the most this could apply to is 27 of those reporting the former (5.1%) and five of those reporting the latter (1.0%).

## **6. Conclusions**

The views of ‘experts-by-experience’ in general, and Patient-Reported Outcome Measures (PROMs) in particular, are now recognised as crucial to understanding whether mental health services are beneficial and safe (Gibson et al., 2014, 2016; Krägeloh, Czuba, Billington, Kersten, & Siegert, 2015). This survey confirms other surveys (Read, Cartwright, et al., 2014; 2018; R.C.P., 2012), and the recent systematic review (Davies & Read, 2019a), in finding that more than half of people experience withdrawal effects when trying to come off, or reduce, ADs, and shows that at least two specific effects, and some degree of difficulty coming off, are also experienced by more than half.

All these findings were fed into Public Health England’s inquiry into dependence on prescribed drugs (Taylor et al., 2019), and to the recently announced review of NICE guidelines for antidepressants (Davies et al., 2019; Hengartner, Davies & Read, 2019). In May 2019 The Royal College of Psychiatry published a new position statement, which included:

To ensure informed consent and shared decision-making, the use of antidepressants should always be underpinned by a discussion with the patient, and family/carer (as appropriate), about the potential level of benefits and harms, including withdrawal. . . . Discontinuation of antidepressants should involve the dosage being tapered or slowly decreased to reduce

the risk of distressing symptoms, which may occur over several months (R.C.P., 2019, pp. 1,2).

In September, 2019 Public Health England published its report (Taylor et al.) It found that: ‘Antidepressants are associated with withdrawal. Seventeen placebo-controlled trials (with 6,729 participants) show that withdrawal symptoms, such as insomnia, depression, suicidal ideation and physical symptoms, follow when patients stop taking medication’. (p 14). On the basis of these findings, and the Davies and Read (2019a) review, the report made vitally important recommendations in five areas for the drugs concerned, including antidepressants:

1. Increasing the availability and use of data on the prescribing of medicines that can cause dependence or withdrawal..
2. Enhancing clinical guidance and the likelihood it will be followed.
3. Improving information for patients and carers on prescribed medicines and other treatments, and increasing informed choice and shared decision making between clinicians and patients.
4. Improving the support available from the healthcare system for patients experiencing dependence on, or withdrawal from, prescribed medicines.
5. Further research on the prevention and treatment of dependence on, and withdrawal from, prescribed medicines. (p. 120).

We may finally be on the verge of GPs being provided with evidence-based information, and patients being offered appropriate advice about gradual tapering (Groot & van Os, 2018; Horowitz & Taylor, 2019) and being provided with long overdue withdrawal support services.

## Conflict of Interest

Professor John Read has no conflict of interests to declare.

## References

- Ambresin, G., Palmer, V., Densley, K., Dowrick, C., Gilchrist, G., & Gunn, J. (2015). What factors influence long-term antidepressant use in primary care? Findings from the Australian diamond cohort study. *Journal of Affective Disorders, 176*, 125–132.
- American Psychiatric Association (2010). *A.P.A. Practice Guideline for the Treatment of Patients with Major Depressive Disorder* (3rd ed.).  
[https://psychiatryonline.org/pb/assets/raw/sitewide/practice\\_guidelines/guidelines/mdd.pdf](https://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/mdd.pdf)
- American Psychiatric Association. *Diagnostic and statistical manual of mental disorders*. 5<sup>th</sup> ed. Washington D.C.: A.P.A.; 2013.
- Bogner, H., Cahill, E., Frauenhoffer, C., & Barg, F. (2009). Older primary care patient views regarding antidepressants: a mixed methods approach. *Journal of Mental Health, 18*, 57-64.
- Cruickshank, G., MacGillivray, S., & Bruce, D. (2008). Cross-sectional survey of patients in receipt of long-term repeat prescriptions for antidepressant drugs in primary care. *Mental Health in Family Medicine, 5*, 105-109.
- Davies, J., Pauli, G., & Montagu, L. (2018). *A survey of Antidepressant Withdrawal Reactions and their Management in Primary Care*. Report from the All Party Parliamentary Group for Prescribed Drug Dependence
- Davies, J., & Read, J. (2019a). A systematic review into the incidence, severity and duration of antidepressant withdrawal effects: Are guidelines evidence-based? *Addictive Behaviors, 97*, 111-121.
- Davies, J., & Read, J. (2019b). Authors' response to a critique by Jauhar and Hayes of 'A systematic review into the incidence, severity and duration of antidepressant withdrawal effects: Are guideline evidence-based?' *Addictive Behaviors, 97*, 127-130.

- Davies, J., Read, J., Hengartner, M., Cosci, F., Fava, G., Chouinard, G., ... Guy, A. (2019). Clinical guidelines on antidepressant withdrawal urgently need updating. *British Medical Journal*, *365*, 12238.
- Department of Health and Social Care (DHSC). (2018). Hansard: Prescriptions Drugs - Written Question – 128871. <https://www.parliament.uk/business>. (Accessed March 2019)
- Eveleigh, R. (2015). *Inappropriate long-term antidepressant use in primary care: A challenge to change*. (PhD thesis). Nijmegen: Radboud University.
- Fava, G., Gatti, A., Belaise, C., Guidi, J., & Offidani, E. (2015). Withdrawal symptoms after selective serotonin reuptake inhibitors discontinuation: A systematic review. *Psychotherapy and Psychosomatics*, *84*, 72-81.
- Fava, G., Benasi, G., Lucente, M., Offidani, E., Cosci, F., & Guidi, J. (2018). Withdrawal symptoms after serotonin-noradrenaline reuptake inhibitor discontinuation: Systematic review. *Psychotherapy and Psychosomatics*, *87*, 195-203.
- Gibson, K., Cartwright, C., & Read, J. (2016). 'In my life antidepressants have been....': A qualitative analysis of users' diverse experiences of antidepressants. *BMC Psychiatry*, *16*, 135.
- Gibson, L., Cartwright, C., & Read, J. (2014). Patient-centred perspectives on antidepressant use: A narrative review. *International Journal of Mental Health*, *43*, 81-99.
- Groot, P., & van Os, J. (2018). Antidepressant tapering strips to help people come off medication more safely. *Psychosis*, *10*, 142-145.
- Hengartner, M. (2019). Commentary on Jauhar and Hayes. *Addictive Behaviors*, *97*, 131.
- Hengartner, M., Davies, J., & Read, J. (2019). Antidepressant withdrawal – the tide is finally turning. *Epidemiology and Psychiatric Sciences*, doi.org/10.1017/S2045796019000465.
- Hoencamp, E., Stevens, A., & Haffmans, J. (2001). Patients' attitudes toward antidepressants. *Psychiatric Services*, *53*, 1180-1181.
- Horowitz, M., & Taylor, D. (2019). Tapering of SSRI treatment to mitigate withdrawal symptoms. *Lancet Psychiatry*, *6*, 538-546.
- Jakobsen, J., Katakam, K., Schou, A. [Hellmuth, S.](#), [Stallknecht, S.](#) [Leth-Møller, K.](#), [Iversen, M.](#), [Banke, M.](#), [Petersen I.](#) [Klingenberg, S.](#), [Krogh, J.](#), Ebert S., [Timm, A.](#), [Lindschou, J.](#), & [Gluud, C.](#) (2017). Selective serotonin reuptake inhibitors versus placebo in patients with major depressive disorder: A systematic review with meta-analysis and Trial Sequential Analysis. *BMC Psychiatry*, *17*, 58.

- Jauhar, S., & Hayes, J. (2019). The war on antidepressants: What we can, and can't conclude, from the systematic review of antidepressant withdrawal effects by Davies and Read. *Addictive Behaviors*, 97, 122-125.
- Johnson, C., Macdonald, H., Atkinson, P., Buchanan, A., Downes, N., & Dougall, N. (2012). Reviewing long-term antidepressants can reduce drug burden: A prospective observational cohort study. *British Journal of General Practice*, 62, e773–e779.
- Kessing, L., Hansen, H., Demyttenaere, K., & Bech, P. (2005). Depressive and bipolar disorders: patients' attitudes and beliefs towards depression and antidepressants. *Psychological Medicine*, 35, 1205-1213.
- Kirsch, I., Deacon, B., Huedo-Medina, T., [Scoboria, A.](#), [Moore, T.](#), & [Johnson, B.](#) (2008) Initial severity and antidepressant benefits: A meta-analysis of data submitted to the Food and Drug Administration. *PLoS Medicine*, 5, 260-268.
- Krägeloh, C., Czuba, K., Billington, R., Kersten, P., & Siegert, R. (2015). Using feedback from Patient-Reported Outcome Measures in mental health services: A scoping study and typology. *Psychiatric Services*, 66, 224-241.
- Mojtabai, R., & Olfson, M. (2014). National trends in long-term use of antidepressant medications: Results from the U.S. National Health and Nutrition Examination Survey. *Journal of Clinical Psychiatry*, 75, 169–177.
- Moore, M., Yuen, H., Dunn, N., Mullee, M., Maskell, J., & Kendrick T. (2009). Explaining the rise in antidepressant prescribing: A descriptive study using the general practice research database. *British Medical Journal*, 339, b3999.
- Munoz-Arroyo, R., Sutton, M., & Morrison, J. (2006). Exploring potential explanations for the increase in antidepressant prescribing in Scotland using secondary analyses of routine data. *British Journal of General Practice*, 56, 423-428.
- The National Institute for Health and Care Excellence (NICE) (2009). *Depression in adults: recognition and management*. <https://www.nice.org.uk/guidance/cg90/resources/depression-in-adults-recognition-and-management-pdf-975742638037>, (Accessed July 2018).
- Nielsen, M., Hansen, E., & Gotzsche, P. (2012). What is the difference between dependence and withdrawal reactions? A comparison of benzodiazepines and selective serotonin re-uptake inhibitors. *Addiction*, 107, 900-908.
- NHS Digital (2017). *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->

- thecommunity-statistics-for-england-2006-2016-pas. (Accessed July 2018).
- OECD (2017). *Antidepressant drugs consumption, 2000 and 2015 (or nearest year) in Pharmaceutical sector*. Paris. [https://doi.org/doi.org/10.1787/health\\_glance-2017-graph181-en](https://doi.org/doi.org/10.1787/health_glance-2017-graph181-en) (Accessed May 2019)
- OECD (2018). *Prescriptions Dispensed in the Community - Statistics for England, 2001-2017*. <https://digital.nhs.uk/data-and-information/publications/statistical/prescriptions-dispensed-in-the-community> (Accessed May 2019)
- Pratt, L., Brody, D., & G, Qu. (2017). *Antidepressant use among persons aged 12 and over: United States, 2011–2014. N.C.H.S. Data Brief, No. 283*. Washington DC: U.S. Department of Health and Human Services.
- Read, J., Cartwright, C., & Gibson, K. (2014). Adverse emotional and interpersonal effects reported by 1,829 New Zealanders while taking antidepressants. *Psychiatry Research, 216*, 67-73.
- Read, J., Cartwright, C., & Gibson, K. (2018). How many of 1,829 antidepressant users report withdrawal symptoms or addiction? *International Journal of Mental Health Nursing, 27*, 1805-1815.
- Read, J., Gee, A., Diggle, J., & Butler, H. (2018). Staying on, and coming off, antidepressants: The experiences of 752 UK adults. *Addictive Behaviors, 88*, 82-85.
- Read, J., Gibson, K., Cartwright, C., Shiels, C., Dowrick, C., & Gabbay M. (2015). The nonpharmacological correlates of self-reported efficacy of antidepressants. *Acta Psychiatrica Scandinavica, 131*, 434-445.
- Read, J., & Williams, J. (2018). Adverse effects of antidepressants reported by a large international cohort: Emotional blunting, suicidality, and withdrawal effects. *Current Drug Safety, 13*, 1-11.
- Royal College of Psychiatrists. (2012). *Coming off antidepressants*. London: R.C.P. [www.rcpsych.ac.uk/healthadvice/treatmentswellbeing/antidepressants/comingoffantidepressants.aspx](http://www.rcpsych.ac.uk/healthadvice/treatmentswellbeing/antidepressants/comingoffantidepressants.aspx). (Accessed Feb 2018).
- Royal College of Psychiatrists. (2019). *Position statement on antidepressants and depression. PS04/19*. [https://www.rcpsych.ac.uk/docs/default-source/improving-care/better-mh-policy/position-statements/ps04\\_19---antidepressants-and-depression.pdf?sfvrsn=ddea9473\\_5](https://www.rcpsych.ac.uk/docs/default-source/improving-care/better-mh-policy/position-statements/ps04_19---antidepressants-and-depression.pdf?sfvrsn=ddea9473_5) (Accessed Sept 2019)
- Schatzberg, A., Haddad, P., Kaplan, E., Lejoyeux, M., Rosenbaum, J., Young, A., & Zajecka, J. (1997). Serotonin reuptake inhibitor discontinuation syndrome: A hypothetical definition. *Journal of Clinical Psychiatry, 58*(Suppl. 7), 5-10.

Stockmann, T., Odegbare, D., Timimi, S., & Moncrieff, J. (2018). SSRI and SNRI withdrawal symptoms reported on an internet forum. *International Journal of Risk and Safety in Medicine*, 29, 175-180.

Taylor, S., Annand, F., Burkinshaw, P., Greaves, F., Kelleher, M., Knight, J., Perkins, C., Tran, A., White, M., & Marsden, J. (2019). *Dependence and withdrawal associated with some prescribed medicines: an evidence review*. London: Public Health England.

**Table 1**Specific withdrawal effects.<sup>1</sup>

	any	'slight increase'	'big increase'	women	younger	treatment duration
Anxiety/Panic	65.6%	31.7%	33.9%			***
Irritability	62.5%	31.8%	30.7%			***
Dizziness	43.9%	20.5%	23.4%	**	***	***
Brain Zaps	42.5%	18.0%	24.5%		***	***
Nightmares	36.7%	19.9%	16.8%		**	***
Nausea	34.8%	18.9%	15.9%		***	**

1: n from 787 to 798

\*\* &lt; .01

\*\*\* &lt; .001

**Table 2**

‘Other’ withdrawal effects mentioned by four or more participants.

Suicidal thoughts	19	Sweating	6
Insomnia	14	Visual disturbances	6
Pain/Aches	13	Crying	6
Sexual dysfunction	12	Twitches/tics	5
Anger/rage/aggressive	10	Spasms/cramps	5
Dissociation/depersonalisation	8	Body zaps	5
Diarrhea	8	Vertigo	5
Fatigue/exhaustion	8	Headaches	4
Akathisia/restless legs	7	‘Flu-like’ symptoms	4
Tremors/shakes	7	Sensitivity to light/sound	4
Difficulty thinking/concentrating	7	Tinnitus	4

**Table 3**

Level of difficulty experienced when coming off antidepressants

	Very Difficult	Difficult	Somewhat Difficult	Somewhat Easy	Easy	Very Easy		Some Difficulty
All (n = 797)	27.2%	13.2%	14.2%	20.6%	13.9%	10.9%		54.6%
Men (n = 228)	22.4%	12.3%	15.4%	23.7%	13.6%	12.7%		50.4%
Women (n = 562)	29.4%	13.5%	13.3%	19.2%	14.2%	10.3%		56.2%
Took ADs < 1 year (n = 199)	8.0%	5.5%	11.6%	28.6%	21.6%	24.6%		25.1%
Took ADS > 3 years *** (n = 462)	38.3%	16.9%	13.4%	17.3%	9.5%	4.5%		68.6%
Mean age (n = 796)	44.1	45.8	44.4	47.0	46.3	46.2		

\*\*\* p &lt; .001 treatment duration related to difficulty coming off

**Table 4**

Withdrawal effects, addiction and 'difficulty coming off, by drug types.

	Paroxetine n = 59	Venlafaxine n = 51	Fluoxetine n = 111	Escitalopram n = 48	Citalopram n = 100	Sertraline n = 102	Tricyclics n = 50
Withdrawal Effects	74.6%	<b>76.5%</b>	64.9%	64.6%	62.0%	55.9%	72.0%
Anxiety/ Panic	<b>89.5%</b> <sup>Cts</sup>	70.0%	72.7%	75.0%	64.3%	67.3%	66.0%
Irritability	<b>79.3%</b> <sup>t</sup>	76.0%	72.5%	72.9%	66.7%	62.7%	54.0%
Dizziness	<b>71.4%</b> <sup>STf</sup>	60.0%	46.8%	52.1%	52.0%	42.2%	38.8%
Brain Zaps	<b>69.0%</b> <sup>SCTf</sup>	64.0% <sup>st</sup>	46.2%	53.2%	41.8%	38.6%	36.7%
Nightmares	<b>60.0%</b> <sup>Sctf</sup>	46.0%	35.2%	43.8%	37.5%	26.5%	32.7%
Nausea	<b>57.9%</b> <sup>SFt</sup>	48.0%	30.8%	44.7%	42.3%	27.5%	28.0%
Addiction	<b>49.2%</b>	45.1%	41.4%	37.5%	33.0%	37.3%	46.0%
Some difficulty	<b>76.3%</b> <sup>SCTf</sup>	70.0%	62.7%	62.5%	55.6%	52.0%	52.0%

C &lt; .001 greater than citalopram; c &lt; .01 greater than citalopram

F &lt; .001 greater than fluoxetine; f &lt; .01 greater than fluoxetine

S &lt; .001 greater than sertraline; s &lt; .01 greater than sertraline

T &lt; .001 greater than tricyclics; t &lt; .01 greater than tricyclics