How many of 1,829 antidepressant users report withdrawal symptoms or addiction?

ABSTRACT: *More than 10% of adults are prescribed antidepressants annually in some countries. Recent increases in prescribing can be explained more by repeat prescriptions than new patients. This raises the question of whether antidepressants are addictive. 1,829 New Zealanders who had been prescribed antidepressants completed an online survey. 44% had been taking antidepressants for more than three years and were still taking them. Withdrawal effects when stopping medication were reported by 55%, and addiction by 27%. Paroxetine had particularly high rates of withdrawal symptoms. Only 1% of participants recalled being told about withdrawal effects when prescribed the drugs. Such high rates of withdrawal symptoms suggest that all concerned, including mental health nurses, need to help people considering antidepressants to understand that it can be difficult to withdraw from them. It will also be beneficial to closely monitor people already taking antidepressants and who are at risk of chronic usage.*

KEY WORDS: depression, antidepressants, withdrawal effects, addiction, discontinuation syndrome

INTRODUCTION

Prescription rates for antidepressants (ADs) are high and increasing (Ilyas & Moncrieff 2012). In 2012 one in eight adults in the USA were prescribed ADs (Kantor *et al.* 2015). In 2016, England had 64.7 million prescriptions for a population of 55.3 million. This was more than double the prescriptions in 2006. For four successive years ADs have had a larger annual increase than any other type of medication (NHS Digital 2017). In New Zealand, where the current study was conducted, and which has a similar mental health care system to the UK, the number of recipients per year increased by 35% between 2007 and 2012, from 304,530 to 412,631 (Pharmaceutical Management Agency [PHARMAC], personal communication 2013), in a population of 3.7 million adults. Thus one in nine adults, and approximately one in six women were being prescribed ADs every year. Since then the number of prescriptions has continued to increase at about 5% per year (PHARMAC, 2017).

It is difficult to justify these extraordinary and ever increasing prescription rates in terms of efficacy. Less than half of trials find ADs superior to placebo (Khan *et al.* 2002). Properly blinded and independent (non drug industry) studies are particularly unlikely to find any difference to placebo (Khan & Brown 2015; Moncrieff 2015). One meta-analysis found that 'the overall effect of new-generation antidepressant medications is below recommended criteria for clinical significance' (Kirsch *et al.* 2008), with greater benefit than for placebo found only for 'patients at the upper end of the very severely depressed category'. A more recent meta-analysis, of 131 randomised placebo-controlled trials, confirmed that the overall effect size does not reach the threshold for 'clinical significance' and concluded that 'The harmful effects of SSRIs versus placebo for major depressive disorder seem to outweigh any potential small beneficial effects' (Jakobsen *et al.* 2017).

Nor do the high rates seem to be explicable in terms of increased incidence or prevalence of depression, or changes in help-seeking behavior (Munoz-Arroyo *et al.* 2006). Attention

has therefore turned, instead, to increases in repeat prescriptions. For example, data on 189,851 patients of General Practitioners (GPs) in the UK revealed that a doubling of prescribing over eight years was explained not by increases in new prescriptions but a doubling of the number of prescriptions per patient (Moore *et al.* 2009).

In this context the issue of whether ADs are addictive has been increasingly discussed, albeit often avoiding the word itself. Drug company product information (e.g. Eli Lilly 2016; Glaxo Smith Kline 2014) uses terms such as 'withdrawal effects' and the novel term 'discontinuation syndrome', but never the word 'addiction'. The only use of the word in the 152 page American Psychiatric Association Practice Guideline for depression is 'Common misperceptions about antidepressants (e.g. they are addictive) should be clarified' (A.P.A. 2010). The authors had, between them, over 80 instances of receiving payments from drug companies in the preceding five years, including. In the UK the Royal College of Psychiatrists (RCP) (2015) states: 'We would like to reassure readers that despite some people having symptoms of withdrawal when stopping antidepressants, antidepressants are not addictive'.

Researchers at the Nordic Cochrane Centre disagree. Their 2012 review of 45 papers on benzodiazepine addiction and 31 papers on SSRI 'discontinuation syndrome' 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 *et al.* 2012). It must be acknowledged, however, that antidepressants are not associated with drug seeking behavior, or dose escalation to the same degree as benzodiazepines. Some go so far as to argue that non-medical use for pleasure is a requirement for classifying a substance as addictive.

One approach resolving this debate is to adopt a definition of addiction that best fits one's own conclusions. For example, those convinced that ADs *are* addictive, such as the Nordic Cochrane Group point to the presence of frequent, and often severe withdrawal effects as sufficient to meet criteria for addiction (Nielsen *et al.* 2016). Others, such as Professor Lars Vedel Kessing, in his rebuttal of the Nordic Cochrane Group, use more stringent criteria for addiction when making the case that ADs are *not* addictive: 'First, you lose control and the desire to take the drug becomes compulsive. . . . Next is the onset of tolerance. The dosage must be increased all the time to get the desired effect. . . .A strong urge to privately obtain more of the drug so it can be taken without the physicians knowledge. . . . Lastly, there will be a detrimental effect to the individual who will no longer be able to function' (Secher 2013). This seems slightly more stringent than the definition of 'substance use disorder' in the latest edition of the Diagnostic and Statistical Manual, which requires that just two of eleven criteria are met, including: 'taken in larger amounts or over a longer period than was intended' and 'persistent desire or unsuccessful effort to cut down or control use of the substance' (A.P.A. 2013).

Another approach, one which circumvents the experts' disagreements about definitions, is to allow people who have taken ADs to interpret the term 'addiction' as they wish. A 2004 review of studies of 'Patients' preferences in the treatment of depressive disorder in primary care' found that 'Antidepressants were often regarded as addictive' (van Schaik 2004). A 2014 review, of studies of 'Patient-centred perspectives on antidepressant use', concurred, reporting that 'the most frequently mentioned reason for a negative opinion of antidepressants is that they may be addictive' (Gibson *et al.* 2014).

Many researchers, however, seem to devalue the experience of patients, characterising patients' reports of addiction and withdrawal effects as negative and erroneous 'beliefs', 'fears', or 'attitudes'. For example, of 192 people in the Netherlands who had been taking

ADs for six months, 30% reported that ADs are 'addictive', with 30% also stating that 'a person who starts taking antidepressants can never stop using them' (Hoencamp *et al.* 2002). These findings were portrayed as 'negative attitudes toward antidepressants that contribute to noncompliance'. Of 29 older primary care patients taking ADs in the USA, seven (24%) spontaneously reported being addicted, in interviews (Bogner *et al.* 2009). This was presented as a 'negative attitude' that might 'impede adherence behaviors'. Another USA study, of 42 older patients with 'negative attitudes' towards their ADs, identified 'strong fears about addiction' as the first of four factors explaining the negative attitudes (Givens *et al*. 2006). Addiction was represented as a 'fear' not an fact, and as one of the 'most common negative attitudes', leading people 'to resist taking them'. Professor Kessing's Copenhagen research team[24] found that among 493 discharged inpatients administered the 'Antidepressant Compliance Questionnaire' 40.1% agreed with 'Your body can become immune to antidepressants', 56.8% agreed with 'When you have taken antidepressants over a long period of time it is difficult to stop taking them' and 56.4% agreed with 'Your body can become addicted to antidepressants'. All these were considered to be 'erroneous views' (Kessing *et al.* 2005). Even higher rates of 'negative beliefs', with 'implications for patient adherence', were found among 87 neurology clinic attenders in Scotland; 74% agreed that 'antidepressants are addictive' (Stone *et al.* 2004).

An analysis of 227 postings by AD users on depression websites found that 'a number of postings were devoted to the physical and mental side effects that occur when discontinuing anti-depressant use. … severe headaches, shaking, electric shock feelings in their hands and feet, sweating, anxiety, shortness of breath, mental confusion, and severe depression' (Pestello & Davis-Berman 2008). Examples included:

> ‘I am currently trying to wean myself off of Venlafaxine, which honestly is the most awful thing I have ever done. I have horrible dizzy spells and nausea whenever I lower my dose’.

> ‘It took me almost two years to get off Paroxetine and the side effects were horrendous. I even had to quit my job because I felt sick all the time. Even now that I am off of it, I still feel electric shocks in my brain’.

A survey by the Royal College of Psychiatrists (RCP) in the UK found that of 817 people who had stopped taking ADs, 62.7% experienced withdrawal symptoms (R.C.P. 2012). The survey did not ask about addiction. Another UK survey, of over 1,000 AD users, found that 37% had been taking antidepressants for more than five years, and 20% for more than 10 years (Read et al. 2017).

Objectives

The current study was not designed to definitively answer the question ‘Are antidepressants addictive or not’. Given the range of expert definitions of addiction alluded to above, this would be a problematic goal. Instead, the study sought to make a significant contribution to the estimation of rates of chronic usage, and of self-reported withdrawal symptoms and addiction, by directly asking the largest sample of AD users to date. These data are analysed in relation to length of AD usage, demographics, perceived efficacy of the ADs, type of AD and whether the prescriber was a GP or a psychiatrist. The study also aimed to ascertain how many people remember being told anything about addiction or withdrawal effects by the prescriber. It was hoped that the findings would be useful for prescribers and patients alike when thinking about prescribing or taking ADs, and about how long they should be taken.

METHODS

Instrument

The current study used the same questionnaire and data source as several previous papers, including one that reports a broader range of adverse effects (Read *et al.* 2014). The *Views and Experiences of Antidepressants in New Zealand* questionnaire (Read *et al.* 2014, 2015) has 47 questions, covering: demographics; depression symptoms and severity; prescribing process; AD usage and effectiveness; side-effects; benefits; alternative treatment options; and beliefs about causes of depression. The questionnaire consisted of multiple-choice questions and rating scales producing quantitative data, and open-ended questions eliciting qualitative data. The wording of the side effects sections was: 'Which, if any, of the following side effects do you think you experienced as a result of taking the anti-depressants?' followed by a list of 20 adverse effects (Read *et al.* 2014). This list includes: 'Addiction to the anti-depressants' and 'Withdrawal effects after stopping taking the anti-depressants', both followed by tick boxes for: 'not at all' (score = 0), 'mild' (1), 'moderate' (2), or 'severe' (3). Participants were also asked how long they had taken ADs and whether they were still taking them.

Recruitment

Following approval from the University of Auckland ethics committee, the questionnaire was posted online. A webpage advertising the study provided participant information and a link to the questionnaire. The study was publicised via media releases, TV and radio interviews with the researchers, and advertisements.

Participants

The criteria for participation included having been prescribed ADs in the last five years and being at least 18 years old. Of the 2,171 people commencing the survey, 295 completed less than a quarter. Their responses were excluded. Of the remaining 1,876, 45 cited medications other than ADs when asked which ADs they took. Of the remaining 1,831, the latter of each of two pairs of responses with identical Internet Protocol addresses (indicating use of the same computer) and similar responses, were rejected. This left 1,829 surveys. Not all participants responded to all questions.

Females made up 76.6% of the sample. The modal age group was 36-45 (24.2%); 16.3% were 18 to 25, and 15.9% were 56 or older. Most, 92.1%, identified as 'New Zealand/European'; 2.9% as Maori, 1.2% as Asian, 0.4% as Pacific Islander and 3.5% as 'Other'. Half (49.6%) had a university degree; 26.1% had a diploma or certificate after high school, 17.2% had completed high school, and 7.1% had not.

About half (52.6%) were first prescribed ADs between 2000 and 2009; with 25.9% reporting 2010 to 2013 (February); 16.1% 1990 to 1999, and 5.4% prior to 1990. Nearly all (97.4%) had taken the ADs when prescribed them. Of the 1715 (93.8%) who reported which AD they had been prescribed, the most common was Fluoxetine (22.4%), followed by Citalopram (20.3%) and Paroxetine (8.7%). Thirty nine percent had been prescribed multiple ADs. In 83.6% of cases the prescriber was a GP, and in 16.4% a psychiatrist.

On the basis of responses to a checklist of the DSM-IV symptoms for Major Depressive Episode (of which five are required) when first prescribed ADs, and (to assess for the DSM grief exclusion criterion) "In the *two months before* you were first prescribed antidepressants, had a loved one died?", 73.3% were estimated to have met criteria for Major Depressive Episode.

The majority (82.8%) responded 'yes' to the question 'Did the antidepressants reduce your depression?' The question 'While taking antidepressants my quality of life was….' elicited the following responses: 'greatly improved' - 49.2%, 'slightly improved' - 36.1%, 'unchanged' - 5.8%, slightly worse' - 4.4%. 'a lot worse' - 4.5% (Read et al., 2015).

Data analysis

Descriptive statistics are presented for self-reported addiction and withdrawal effects. A 'chronic usage' category was created for participants who had taken ADs for more than three years *and* were still taking them. Relationships between the three key variables (addiction, withdrawal effects, and chronic usage) and other variables were assessed using either Chi-squares (X^2) for categorical data or Spearman rank correlations (rho) for ranked, dimensional data. Analyses relating to different types of AD were based only on those drugs that had been taken exclusively by ten or more participants, plus comparisons to the group who had taken more than one type.

RESULTS

Self-reported withdrawal effects and addiction

Of the 1,367 participants who responded to the item *'Withdrawal effects after stopping taking the antidepressants'*, 45.1% responded 'not at all'. Thus, some degree of withdrawal effects was reported by 54.9%, with the following degrees of severity: 12.4% 'mild', 17.4% 'moderate' and 25.1% 'severe'. Fifteen participants wrote about withdrawal in the 'Other Side Effects' box. These are presented verbatim in Table 1.

Table 1 about here

Of the 1,521 who responded to the '*Addiction to the antidepressants'* item, 72.8% responded 'not at all'. Thus, some degree of addiction was reported by 27.4%, with the following degrees of severity: 11.8% 'mild', 9.4% 'moderate' and 6.2% 'severe'.

Reporting some degree of withdrawal effects was strongly related to reporting some degree of addiction ($X^2 = 218.9, < .001$). Most of those reporting some addiction (86.8%) reported some withdrawal effects; and 44.1% of those reporting withdrawal effects reported addiction. Using the dimensional scores (*extent* of withdrawal/addiction) also demonstrated a strong relationship (rho = 0.49, $p < .001$).

Validity

This strong relationship between ratings for withdrawal effects and addiction is evidence of the convergent validity of the measures of the two constructs, in that one would predict that the two constructs are strongly related. Evidence of divergent validity (albeit somewhat weaker because all adverse effects were related to each other) comes from the finding that withdrawal effects and addiction were more strongly correlated to each other (rho = 0.49) than with any other of the 18 other adverse effects measured. The next strongest correlation with withdrawal effects is 0.29 (agitation); and the next strongest with addiction is 0.26 (feeling aggressive). Furthermore, duration of being on antidepressants was positively correlated to only four of the 20 adverse effects and addiction (rho = .25, $p < .001$) and withdrawal effects (rho = 0.31, $p < .001$) were the most strongly correlated of the four.

Chronic usage

About half of the sample (51.7%) had taken ADs for three years or more. Over two thirds (69.1%) were still taking ADs when they participated in the study. More than four in ten

(43.7%) met both these criteria and were therefore categorised, for this study, as 'chronic usage'.

Chronic usage was strongly related to participants' reports of addiction, using either the dimensional data ($X^2 = 40.3$, $p < .001$), or the categorical data ($X^2 = 33.2$, $p < .001$). Yet only 35.1% of those classified as chronic usage reported addiction, while 21.7% of those *not* meeting chronic usage criteria reported addiction. Similarly, chronic usage was strongly related to reports of withdrawal symptoms, using both dimensional ($X^2 = 74.9$, $p < .001$) and categorical data ($X^2 = 36.6$, $p < .001$). Yet only 64.9% of those classified as chronic users reported withdrawal effects, as did 48.3% of those *not* meeting chronic usage criteria.

Table 2 shows that, as mentioned earlier, the number of months or years participants were on ADs was strongly related to both addiction and withdrawal effects. This is the case whether addiction is measured categorically ($X^2 = 90.6$, $< .001$) or as a dimension (rho = 0.25, $p < .001$); and, similarly, whether withdrawal effects are measured categorically ($X^2 = 117.9$, $< .001$) or as a dimension (rho = 0.31, $p < .001$).

Table 2 about here

Demographics

Age, ethnicity, income, sexual orientation, and being religious were all unrelated to self-reported withdrawal effects or addiction.

Gender was unrelated to withdrawal effects. Men, however, were more likely than women to report being addicted (32.5% vs 25.9%; $X^2 = 5.9$, $p = .015$), and to report a greater *level* of addiction ($X^2 = 18.7$, $p < .001$). Level of education was unrelated to withdrawal effects, but was negatively related to addiction ($X^2 = 12.7$, $p = .013$) and to *level* of addiction (rho = -.08, $p = .002$).

Chronic usage was unrelated to gender, ethnicity sexual orientation, education or being religious. Chronic usage was positively related to income ($X^2 = 20.3$, p = .002) and to age ($X^2 = 84.3$, p < .001).

Perceived efficacy of the antidepressants

Efficacy of the ADs was measured in terms of both self-reported depression reduction and increased Quality of Life. Neither addiction nor withdrawal effects were related to perceived depression reduction.

Withdrawal effects were negatively related to Quality of Life whether the effects were measured categorically ($X^2 = 18.57$, p = .001), or as a dimension (rho = .08, p = .002). For example, worsening of Quality of Life was reported by 16.2% of participants experiencing 'severe' withdrawal effects but only 7.2% of those reporting no withdrawal effects. Addiction was also related to reduced Quality of Life while taking ADs, whether measured categorically ($X^2 = 10.5$, p = .032), or as a dimension (rho = .07, p = .009). For example, worsening of Quality of Life was reported by 21.7% of participants who reported 'severe' addiction, but only 7.9% of those reporting no addiction.

Chronic usage was positively related to both reduction in depression ($X^2 = 63.5$, p < .001) and improvement in Quality of Life ($X^2 = 88.6$, p < .001) while taking ADs.

Drug type

Table 3 shows that among the seven drug types with samples larger than 10 people who took only that drug type, the frequency of reported withdrawal effects ranged from 18.2% (Sertraline) to 75.9% (Paroxetine). The frequency of addiction ranged from 0% (Sertraline) to 45.8% (Paroxetine). Even when reports of only a 'mild' level are excluded the highest frequencies remain at 64.8% for withdrawal effects and 33.3% for addiction (both

Paroxetine). Of those who had received more than one AD, 68.3% reported withdrawal effects and 34.7% reported addiction; remaining at 55.1% and 20.2% respectively after excluding mild cases.

Table 3 also shows the considerable variation in chronic usage according to type of AD, from 57.3% (multiple ADs), 55.7% (tricyclics) and 51.8 (Paroxetine) to 10.0% (Escitalopram).

Table 3 about here

Prescriber

Of participants first prescribed ADs by a psychiatrist 33.6% reported addiction, compared to 26.2% of those prescribed to by a GP ($X^2 = 8.3$, $p < .041$). Similarly, 64.2% of those prescribed ADs by a psychiatrist reported withdrawal effects, compared to 53.2% of those prescribed to by a GP ($X^2 = 8.3$, $p < .041$). Of those first prescribed ADs by a psychiatrist 60.3% had been on ADs for at least three years and were still taking them (chronic usage), compared to 40.1% if the prescriber was a GP ($X^2 = 38.9$, $p < .001$).

Table 4 about here

Information from prescriber

Only 17 (0.9%) recalled being told about difficulty coming off, or specifically about 'withdrawal' effects (3), 'addiction' (3), 'dependence' (1) or 'discontinuation syndrome' (1) (see Table 4). Nine of these 17 recollections involved advice to not come off 'suddenly' or 'too quickly'. Another respondent was told 'Not to miss a dose as it may cause some dizziness'. Three others were just told not to stop taking them, without a reason. So the most

liberal interpretation is that there were 21 recollections (1.1%), direct or indirect, of being told anything about withdrawal or addiction.

Three respondents recalled having been told that ADs were *not* addictive. For example:

> 'I was assured that Paroxetine was not addictive. However, I have had major problems with discontinuation syndrome so am still on it today. ….. GSK {Glaxo Smith Klein} has subsequently been rapped over the knuckles by the FDA for playing down discontinuation syndrome. …. I feel like I am harnessed to a beast.'

Another respondent wrote:

> 'The information I got was very limited - there was no suggestion of coming back to make sure they worked - just given a prescription for 6 months supply, no information about coming off them and no counseling services offered. This period was a dreadful time for me.'

Being told about withdrawal or addiction, or the need to come off slowly, was not related to any demographic variables. None of the psychiatrists told their patients about withdrawal effects, addiction or the need to come off slowly, compared to 21 of the GPs (1.4%) (X^2 = 4.2, p = .041).

Being told about withdrawal effects, addiction or the need to come off slowly did not increase the probability of reporting addiction, but was significantly related to reporting withdrawal effects (X^2 = 8.1, p = .033). Of those who were given some information 84.2% reported withdrawal effects, compared to 54.5% who were told nothing.

DISCUSSION

This study was the largest direct-to-user survey asking about withdrawal effects and the only large scale study to ask users about addiction. The study found that 54.9% reported withdrawal effects when they stopped taking them. This is broadly similar to the 62.7% in the 2012, RCP survey. In the current study the figure rose to 66.9% among those who had taken ADs for more than three years. One in four (25.1%) categorised these effects as 'severe', by far the highest proportion of the 20 adverse effects assessed by the survey (Read et al. 2014). The finding that paroxetine had particularly high rates of withdrawal replicates previous findings (R.C.P. 2012; Tonks 2002) (and thereby provides further validation of the data of the current study).

The 2012 RCP survey of over 800 antidepressant users, which found that withdrawal symptoms were experienced by 63%, also found that the symptoms '…. generally lasted for up to 6 weeks'. Furthermore, 'A quarter of our group reported anxiety lasting more than 12 weeks'. This is inconsistent with the recent public assertion, by the President of the RCP and its Chair of Psychopharmacology, that 'We know that in the vast majority of patients, any unpleasant symptoms experienced on discontinuing antidepressants have resolved within two weeks of stopping treatment' (Burns & Baldwin 2018). Furthermore, a recent review (Fava *et al.* 2015) concluded that withdrawal symptoms 'typically occur within a few days from drug discontinuation and last a few weeks. However, many variations are possible, including late onset and/or longer persistence of disturbances.' The review found two studies documenting the persistence of withdrawal symptoms one year after coming off paroxetine, and, also found that 'Only in a few cases did symptoms spontaneously remit in about 2 weeks'.

One in four (27.4%) overall, and one in three (36.8%) of those taking ADs for over three years, responded in the affirmative to a question about addiction to ADs. This is consistent with the 24% (Bogner *et al.* 2009) and 30% (Hoencamp *et al.* 2002) findings of two small studies cited earlier, but far smaller than the 56% finding from the larger Copenhagen study

(Kessing *et al.* 2005). It might reasonably be concluded that between a quarter and a half of AD recipients experience them as addictive, with the percentage increasing the longer one stays on the drugs. Using our 27% finding would mean that over eight million of the 30 million adults in USA receiving ADs believe them to be addictive. Dismissing this finding as an 'erroneous' belief seems unwarranted.

A worrying finding is that very few (1.1%) of this large sample recall being told anything about withdrawal or addiction, and that this was the case for none of those prescribed ADs by a psychiatrist. It is probable, however, that more than 21 people were told about addiction or withdrawal effects. Indeed, many acknowledged that they could not recall all the adverse effects discussed. The 1.1%, however, can be contrasted with the adverse effects about which patients most frequently recalled being informed: nausea (16.8%), and weight/appetite changes (10.7%) (Read *et al*. 2014).

Limitations

Although this sample was the largest ever to be directly asked about withdrawal and addiction it was a self-selected, convenience, online, sample. Maori, Pacific Islanders and Asian people, who make up 15%, 7% and 12% of the population respectively (StatsNZ 2017) are all under-represented, as are older and poorer people were under-represented. It is possible that dissatisfied people are more likely to complete an online survey about a treatment. Although this seems unlikely in this case, as 83% believed that the ADs had reduced their depression, it is still possible that people who have had problems are over-represented. By definition, people who are long-term users are over-represented, as many short-term users would no longer qualify.

The data relies on self-report, as do most 'objective' measures. Memory of events several years ago, however, may be less than reliable. Reports of addiction by people taking a drug

may not accord with assessments of researchers or clinicians; but, as we saw earlier, experts' opinions on what constitutes addiction vary considerably. Similarly self-reports of 'withdrawal symptoms' by patients may not correspond with expert definitions of the construct.

The lower Quality of Life experienced by those reporting withdrawal effects or addiction should be interpreted cautiously. It is not clear whether the relationships are causal. Furthermore, the direction of causality, if any, would be unclear.

The study design is not able to determine whether the increased probability of reporting withdrawal effects among those who were given some information about withdrawal by their GP represents a 'self fulfilling prophecy' (i.e. the effects were imagined or misinterpretations of other symptoms) or an increased willingness/ability to identify withdrawal effects accurately.

It would have been desirable to have gathered data on dosage and speed of withdrawal as both are likely to have been related to probability and severity of withdrawal symptoms.

CONCLUSION

All concerned need to be wary of drug company claims on this issue (e.g. Eli Lilly 2016; Glaxo Smith Kline 2016; Tonks 2002), including on the internet (de Wattignar & Read 2009; Read & Cain 2013). In light of the difficulty millions of people are experiencing when trying to stop, or reduce their ADs, patients, and the general public, need to be educated about the existence, and difficulty, of withdrawal symptoms.

RELEVANCE FOR CLINICAL PRACTICE

Mental health professionals - including mental health nurses, as well as managers, policy makers, professional organisations and drug companies, need to respond ethically to the

findings of this and the previous studies by making sure that potential AD recipients are fully informed of the chances of withdrawal effects, which may be mild but which some recipients describe as 'severe'. Such information might lead to some people deciding to pursue alternative evidence-based options before, or instead of, trying ADs. Those who choose to take them regardless of this information might give more thought to how long they might stay on them. Being more informed about possible withdrawal effects would also forewarn them about the need for ADs to be tapered and discontinued slowly, especially if the patient has been taking a high dose of an antidepressant for years, and ideally under medical supervision and with the support of friends and family (Hall 2012). New Zealand nurses only gained prescribing rights in 2015 (Ministry of Health, 2016), but with or without prescribing rights nurses can play an important role in ensuring their patients are fully informed when making choices (Desplenter *et al.* 2013) and in supporting people who choose to withdraw.

The ethical principle of 'informed choice' also requires that potential AD recipients be offered non-pharmacological alternatives (Read et al. 2016). ADs are often prescribed inappropriately. A recent study, which found that 69% of AD recipients had never met DSM criteria for Major Depressive Disorder, concluded that **'**antidepressants are commonly used in the absence of clear evidence-based indications' (Weichers *et al*. 2014; p. 40). Of the half a million US Veterans prescribed ADs outside psychiatric services in 2010, half (51%) had no psychiatric diagnosis (Taganayaki *et al.* 2015). Of the sample in the current study self-reported severity of depression in the 'year before taking antidepressants' was: 'severe' - 42.7%, 'moderate' - 37.8%, 'mild' - 11.8%, 'not at all' - 7.6% (Read *et al.* 2015). Thus the majority of prescriptions were for levels of depression severity at which ADs are no more effective than placebos (Khan & Brown 2015; Kirsch *et al.* 2008; Moncrieff 2015). Although 73.3% met DSM criteria for Major Depressive Disorder, this was the case for only 59.4% of those over 55 years old (Read *et al.* 2016), who seem to be the target of disproportionate

levels of inappropriate prescribing of ADs (Mojtabai & Olfsen 2011; Snowden *et al.* 2011; Weichers *et al.* 2014).

Although there are differing views on how long people should take ADs, another implication is that people should probably not be prescribed ADs indefinitely, and should be reviewed regularly, probably monthly. We have previously reported that of the approximately half of the current sample (46.1%) who recall being told how long to stay on the ADS, only 6% were told less than 3 months, and 25% were told 'more than a year'**.** Psychiatrists recommended taking them for longer than GPs (after controlling for depression level). The 2012 survey of over 1,000 UK AD users (Read *et al*. 2017) found that 71% had never had their GP or psychiatrist raise the possibility of coming off, including 66% of those who had been on them for either five or ten years. More than a third (37%) expected to be on their medication 'for ever'.

Acknowledgements

We thank all those who took the time to complete the survey

Declaration of Interests

The authors report no conflicts of interest.

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TABLE 1: *Verbatim personal accounts of withdrawing*

I felt a bit of nausea, dizziness and unsteadiness 2 or 3 times when I missed taking the anti-depressants for more than 2 days.
When I reduced the dose - from 1 tablet to half a tablet - I had vivid nightmares. This has also happened if I forget to take them.
Tried to go off them but aside affects very acute so still on them
Electric shocks in brain when coming off them
Inability to find reduction / stopping management
I cannot stop Paroxetine, even by slow titration as I feel physically awful
Tried few times to stop, very bad withdrawal but also panic attacks became very severe so still on them now
I get terrible ""brain zaps"" when withdrawing, even if I forget to take the meds for a day or two
washout periods when changing medication were really awful to go through
I felt a bit of nausea, dizziness and unsteadiness 2 or 3 times during the prescribed period, which was when I missed taking the anit-depressants for more than 2 days
Protracted withdrawal
If I forgot to take the pills for a day, apt to get a migraine
Just reducing the dosage now...severe withdrawal effects
I forgot to take my Citalopram for two days and woke up one morning with severe dizziness. It was so extreme that I fell over when I tried to get out of bed and I threw up
it took me 2 months of hell to come off the antidepressants. Was massively harder than I expected. Had severe depression, fatigue, massive anger tendencies - which is not a normal part of my nature

TABLE 2: *Relationships of self-reported withdrawal effects and addiction to length of time on antidepressants*

		‘How long have you taken antidepressants?’					
	Overall	< 3 months	3 - 6 months	6 - 12 months	1 - 2 years	2 - 3 years	> 3 years
Withdrawal Effects (n = 1,367)	54.9%	28.0%	28.3%	40.4%	48.2%	62.9%	66.9%
(moderate/ severe)	(42.5%)	(17.0%)	(19.2%)	(24.4%)	(31.1%)	(48.3%)	(56.2%)
Addiction (n = 1,521)	27.4%	8.8%	10.6%	16.0%	19.0%	33.1%	36.8%
(moderate/ severe)	(15.6%)	(3.6%)	(2.7%)	(5.7%)	(7.9%)	(19.0%)	(23.3%)

TABLE 3: *Frequency (and 'moderate' or 'severe' percentages) of self-reported addiction and withdrawal effects, and frequency meeting criteria for 'Chronic Usage', by drug type*

	Parox-etine	**Venla-faxine**	**Cital-opram**	**Fluox-etine**	**Escita-lopram**	**Sertr-aline**	**Tricyclics**	**Multiple ADs**
sample sizes[1]	108-137	27-35	247-337	273-346	15-20	11-16	55-70	559-560
Withdrawal effects (mod/severe)[2]	75.9% (64.8%)	70.4% (62.7%)	46.6% (34.9%)	35.5% (22.7%)	33.3% (26.7%)	18.2% (18.2%)	50.9% (41.8%)	68.3% (55.1%)
Addiction (mod/severe)	45.8% (33.3%)	25.0% (10.7%)	20.1% (9.2%)	15.8% (7.9%)	5.9% (5.9%)	0% (0%)	36.1% (26.3%)	34.7% (20.2%)
Chronic Usage[3]	51.8%	45.7%	27.6%	39.8%	10.0%	12.5%	55.7%	57.3%

1 sample sizes varied within each drug type across the three variables

2 i.e. excluding 'mild' cases

3 taken ADs for 3 years and still taking them

TABLE 4: *Seventeen patients' recollections of being told about withdrawal or addiction by prescriber*

withdrawal effects if stopped abruptly
about withdrawal symptoms I may feel worse than before if stop taking them
withdrawls if stopped suddenly
they would be addictive and I would need to be weened off them carefully and slowly
she did talk about the risk of addiction. Said it wasn't that likely
she was very thorough and honest and said that prolonged use could cause addiction and to not come off them too quickly or go cold turkey or that could cause bad side effects
dependence
advised to continuously take the meds, and not stop suddenly, due to discontinuation syndrome
problems if I stopped taking the pills 'cold turkey'
dizziness if I tried to come off them too quickly
mainly discussed what could happen if I stopped taking them suddenly
paroxetine- high withdrawel symptoms
coming off them = dangerous
nausea if I came off them
coming off them would be difficult
that they were not easy to come off once you had been on them for some time
not to suddenly stop taking them