



Adverse emotional and interpersonal effects reported by 1829 New Zealanders while taking antidepressants



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ABSTRACT

In the context of rapidly increasing antidepressant use internationally, and recent reviews raising concerns about efficacy and adverse effects, this study aimed to survey the largest sample of AD recipients to date. An online questionnaire about experiences with, and beliefs about, antidepressants was completed by 1829 adults who had been prescribed antidepressants in the last five years (53% were first prescribed them between 2000 and 2009, and 52% reported taking them for more than three years). Eight of the 20 adverse effects studied were reported by over half the participants; most frequently Sexual Difficulties (62%) and Feeling Emotionally Numb (60%). Percentages for other effects included: Feeling Not Like Myself – 52%, Reduction In Positive Feelings – 42%, Caring Less About Others – 39%, Suicidality – 39% and Withdrawal Effects – 55%. Total Adverse Effect scores were related to younger age, lower education and income, and type of antidepressant, but not to level of depression prior to taking antidepressants. The adverse effects of antidepressants may be more frequent than previously reported, and include emotional and interpersonal effects.

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1. Introduction

In England, between 1998 and 2010, prescriptions for antidepressants [ADs] increased by 10% annually (Ilyas and Moncrieff, 2012). By 2005 one in 10 people over the age of six in the U.S.A. were being prescribed ADs annually (Olfson and Marcus, 2009). In New Zealand the number of annual prescriptions rose by 37% between 2006/07 and 2011/12, while the number of recipients increased by 35% from 304,530 to 412,631 [PHARMAC, personal communication, 2012], in a population of 4.4 million, of whom 3.7 million are aged 16 or older. Thus one in nine adults, and one in six women are prescribed ADs every year.

The adverse effects most commonly studied and reported, by researchers (Moret et al., 2009; Uher et al., 2009) and drug companies (Ely Lilly, 2012) are physical symptoms such as diarrhea, dry mouth, dyspepsia, impotence, insomnia, nausea, sweating and tremors. A study of 811 AD recipients (Uher et al., 2009) produced rates for Nortriptyline from 3% (diarrhea) to 72% (dry mouth) and for Escitalopram from 3% (disorientation) to 23% (dry mouth). Like many other studies, this study did not measure psychological or interpersonal effects, fear of addiction,

withdrawal effects, or suicidality. This is unfortunate since the purpose of the study was to develop the 'Antidepressant Side-Effect Checklist' for researchers and doctors. The items included in the checklist, were 'compiled from a review of the literature' (p. 203) – with just four studies cited, none of which were surveys of the first-hand experience of AD recipients, which have identified psychological and interpersonal effects (Gibson et al., 2014). Similarly, the 'Patient-Rated Inventory of Side Effects (PRISE)' measures eight types, all 'biological systems' (Adkins et al., 2012).

An online UK survey of nearly 1500 AD users (MIND, 2012) found that over half experienced adverse effects, with 44% reporting that ADs affected their sex lives, 27% their ability to work or study, and 21% their relationships with family or friends. An analysis of 468 comments about fluoxetine and venlafaxine on a patient-oriented website found that the most common 'psycho-active' effects were sedative-type effects, subjectively impaired cognition, activation effects, reduced libido, emotional blunting and emotional instability (Goldberg and Moncrieff, 2011).

A 2013 review of studies of the subjective experiences of people who receive ADs (Gibson et al., 2014) identified multiple adverse effects in the psychological, emotional and interpersonal domains that have received little attention in previous studies, or measures, of adverse effects. These included a reduction of positive and negative emotions, emotional detachment, a belief that ADs prevent natural

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sadness, personality changes, harmful effects on relationships, fear of addiction, and suicidality (Givens et al., 2006; Liebert and Gavey, 2008; Pestello and Davis-Berman, 2008; Price et al., 2009). The review concluded that AD recipients have complex and ambivalent perspectives, which can change over time. The review found, however, that the overall attitude of most AD recipients is negative, not only because of adverse effects (Pestello and Davis-Berman, 2008; Van Geffen et al., 2009), but because of stigma (Sirey et al., 2001) and failure to address social and psychological issues (Honcamp et al., 2002). The review also found, nevertheless, that many people continue taking ADs, partly because of lack of availability of preferred alternative treatments such as psychotherapy (Backenstrass et al., 2006; Lowe et al., 2006) and, most consistently, because of a belief that they are addictive and the related fear of withdrawal effects (Bogner et al., 2009; Kessing et al., 2005; Stone et al., 2004).

1.1. Aims of the study

A questionnaire was designed to explore the subjective experiences of AD recipients, by asking the largest sample to date about their experiences with, and attitudes and beliefs about, depression and ADs. This paper reports participants' experiences of 20 biological, emotional and interpersonal adverse effects.

2. Method

2.1. Instrument

The questionnaire had 47 questions, in eight sections: demographics; the prescribing process; information about AD usage and perceptions of their effectiveness; side-effects; benefits; experiences of alternative treatment options; and beliefs about the causes of depression. The questionnaire consisted of multiple-choice questions and rating scales producing quantitative data and open-ended questions. The criteria for participation included having been prescribed ADs in the last five years and being 18 years of age or over.

2.2. Recruitment

Following ethics approval from the University of Auckland, the anonymous questionnaire was placed online. A google webpage advertising the study was

established (www.viewsonantidepressants.co.nz). This webpage provided participant information and a link to the online questionnaire. The study was publicized in the New Zealand media via media releases, interviews with the researchers and advertisements.

2.3. Participants

Of the 2171 people who started the survey, 295 stopped before the end of the second section (question 19 of 47); their responses were not analyzed. Of the remaining 1876, 45 cited medications other than ADs in response to questions about which ADs they had been prescribed. Of the remaining 1831, the latter of each of two pairs of responses with the same Internet Protocol address (indicating use of the same computer) and similar responses, were discarded. This left 1829 surveys for analysis. The number of responses to each question varied as not all participants responded to all questions.

Females constituted 76.6% of the sample. The modal age group was 36–45 (24.2%); 16.3% were 18–25, and 15.9% were 56 or older. A large majority, 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'. The majority, 89.1%, identified as heterosexual; 2.2% as gay, 2.9% as lesbian and 5.7% as bisexual.

In terms of education, 49.6% had a university degree; 26.1% gained a diploma or certificate after high school, 17.2% completed high school, and 7.1% did not complete high school. (In 2006, 14.2% of adult New Zealanders had an undergraduate degree or higher and 22.4 percent had no formal qualification (Education Counts, 2006)).

Annual income (in NZ dollars) ranged from less than \$10,000 (15.0%) to more than \$100,000 (7.7%). The modal income was \$40,000–\$59,999 (22.1%). (The median income of the NZ population in 2012 was \$29,000 (Statistics New Zealand, 2012a, 2012b)).

About half (52.6%) reported first being prescribed ADs between 2000 and 2009; with 25.9% reporting 2010–2013 (February); 16.1% 1990–1999, and 5.4% prior to 1990. Nearly all (97.4%) had taken the ADs when prescribed them, and 69.1% were still taking ADs. Approximately half (51.7%) had taken them for more than three years, and 7.8% for less than three months. In 83.6% of cases the prescriber was a GP, and in 16.4% a psychiatrist. 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%), Paroxetine (8.7%), Tricyclics (4.5%) and Venlafaxine (2.2%). Thirty nine percent reported that they had been prescribed multiple ADs.

The majority (82.8%) reported that the ADs had reduced their depression. Participants reported the following levels of depression in the year before taking ADs: 'severe' – 42.7%, 'moderate' – 37.8%, 'mild' – 11.8%, and 'not at all' – 7.6%. While taking ADs the rates were: 'severe' – 10.5%, 'moderate' – 23.1%, 'mild' – 45.2%, and 'not at all' – 21.2%. The question 'While taking antidepressants my quality of life was...' elicited the following response rates: 'greatly improved' – 49.2%, 'slightly improved' – 36.1%, 'unchanged' – 5.8%, 'slightly worse' – 4.4%, 'a lot worse' – 4.5%.

Table 1

Percentages of participants reporting each of 20 adverse effects, analyzed by gender, age and treatment duration (more than three years vs. three years or less).

	<i>n</i>	% Any	% Severe	% moderate/severe	Gender	Age	Treatment duration
Sexual difficulties	1587	62.3	14.1	39.1	M**		> 3 yr**
Feeling emotionally numb	1603	60.4	13.5	35.5		Y***	
Failure to reach orgasm	1569	59.5	18.5	40.7	M**		
Drowsiness	1582	57.8	8.6	30.8		Y***	
Dry mouth	1609	57.6	9.7	28.7			> 3 yr**
Weight gain	1593	56.4	12.2	35.0	F*		> 3 yrs
Withdrawal effects	1367	54.9	25.0	42.5			> 3 yr***
Feeling not like myself	1576	52.4	11.0	29.0		Y***	≤ 3 yr*
Headaches	1567	47.0	5.1	22.3		Y***	
Agitation	1557	46.9	7.0	23.6		Y***	
Dizziness	1567	45.2	4.8	18.8		Y***	
Reduction in positive feelings	1560	41.7	8.0	20.6	M*		
Nausea	1554	39.4	4.6	16.3		Y***	
Suicidality	1555	38.9	7.8	18.2		Y***	> 3 yr*
Caring less about others	1556	38.8	4.9	15.9	M***		
Tremors	1556	31.3	4.5	13.7			
Feeling aggressive	1557	28.0	4.9	12.9	M*		
Addiction	1521	27.4	6.2	15.6			> 3 yr***
Diarrhea	1523	20.0	1.4	6.7			
Weight loss	1480	15.1	2.2	6.7			

Age: Pearson correlations (Y=younger age).

Gender and treatment duration: *t*-test independent means.

* < 0.01.

** < 0.001.

*** < 0.0001.

2.4. Data analysis

Descriptive data for the 1829 participants were calculated for the following question: 'Please rate the following side effects that you may have experienced as a result of taking the anti-depressants' – which was followed by 20 possible effects (see Table 1) plus 'other – please specify', and four possible responses: 'not at all', 'mild', 'moderate' and 'severe'. A Total Adverse Effects (TAE) score was calculated by adding the scores (0=not at all, to 3=severe) for the 20 items. Statistical analyses used either independent means *t*-tests or Spearman *rho* correlation coefficients. Because of the large number of analyses, only results at the $p < 0.01$ are reported, to reduce the probability of type I errors (false positives).

3. Results

3.1. Specific adverse effects

The number of participants responding to the questions about each of the 20 adverse effects varied. By far the lowest (1367) was for Withdrawal Effects, presumably because some participants had been on ADs continuously and had no experience of withdrawal.

Eight of the 20 effects were reported by more than half of the participants (see Table 1). The most frequent were Sexual Difficulties (62%), Feeling Emotionally Numb (60%) and Failure to Reach Orgasm (59%). The percentages reporting the other three effects of particular interest in this study were: Feeling Not Like Myself – 52%, Reduction In Positive Feelings – 42% and Caring Less About Others – 39%. Five effects were experienced at a 'moderate' or 'severe' level by a third or more of participants (see Table 1), most frequently Withdrawal Effects (42%) and Failure to Reach Orgasm (41%). The same five effects were rated as 'severe' by 10% or more of participants. For example, Feeling Emotionally Numb was rated as 'moderate' or 'severe' by 35% and as 'severe' by 13%.

All adverse effects were significantly related to Suicidality (all $p < 0.001$ level), with the most strongly related being: Reduction in Positive Feelings ($\rho = 0.50$), Feeling Not Like Myself (0.49), Feeling Aggressive (0.46), Agitation (0.47), Feeling Emotionally Numb (0.44) and Caring Less About Others (0.40).

In the 'other' box that followed the 20 adverse effects, 584 participants reported 87 effects. Table 2 lists the 22 of these effects reported by five or more people. Sixty three of these reports were in the sleep domain, with 29 reporting insomnia, seven disturbed sleep, 18 unusually vivid or frightening dreams, and nine reporting night sweats. Nineteen reported memory or other cognitive difficulties. Eighteen used terms like 'zombie' 'detached' 'fuzzy' or 'foggy' to describe their experiences: 'I was in lala land – it was like I wasn't in the real world – just looking into it from somewhere'; 'now am a zombie I think. Got very little feeling at all'; 'detached from self and reality'.

Seventeen described increased or new anxiety, including five panic attacks. Thirteen reported 'electric shocks', mostly in the head [9], described as 'brain zaps' or 'brain flashes, like a sudden flick in my brain' or 'severe feeling of 'spasm' in my head – sort of like my brain is jumping'.

Table 2
'Other' self-reported adverse effects.

Insomnia	29	Nightmares	8
'Fuzzy'/'zombie'	18	Jaw grinding	8
Sweating	18	Blurred vision	8
Constipation	15	Disturbed/restless sleep	7
Anxiety	12	Heart palpitations	7
Difficulty thinking	10	Fatigue/exhaustion	6
Strange/vivid dreams	10	Stiff muscles/joints	6
'Brain zaps'	9	Mania	6
Excessive yawning	9	Panic attacks	5
Memory loss	9	Decreased motivation	5
Night sweats	9	Decreased appetite	5

3.2. Total Adverse Effects scores

The mean score on the Total Adverse Effects (TAE) scale (range 0–60) was 14.24 (S.D.=10.39). The mean TAE score for men (15.30) was not significantly greater than that for women (13.91). TAE was negatively correlated with age ($\rho = -0.15$, $p < 0.001$). The mean for 18–25 year olds (16.51) was greater than the mean for the 56–65 age group (10.12) ($t = 5.63$, d.f. 230.5, $p < 0.001$). The specific effects that were reported to a significantly greater extent by younger participants included: Feeling Emotionally Numb, Feeling Not Like Myself and Suicidality (see Table 1). Over half the 18–25 age group (55.3%) experienced Suicidality as a result of the ADS, 13.6% to a 'severe' extent. TAE was also negatively correlated with income ($\rho = -0.11$, $p < 0.001$) and education ($\rho = -0.09$, $p < 0.01$).

TAE was positively correlated with duration of treatment ($\rho = 0.08$, $p < 0.01$), with the mean TAE score for those taking ADs for more than three years (15.29) being significantly greater than the mean (13.28) for those taking them for three years or less ($t = 5.63$, d.f. 1100.2, $p < 0.001$). (See Table 1 for differences on specific adverse effects).

TAE was negatively correlated with the perceived quality of the relationship with the prescriber ($\rho = -0.26$, $p < 0.01$). The 35.8% of participants who reported that the prescriber had not informed them about side-effects produced a higher mean TAE (16.73) than those who stated that they had been informed (13.12) ($t = 5.43$, d.f. 643.5, $p < 0.001$). TAE was positively correlated with the length of time since first prescribed ADs ($\rho = 0.09$, $p < 0.01$).

Analyses in relation to the different types of ADs produced reasonably consistent results regardless of whether the independent variable was defined in terms of being on only one type of drug, or the drug taken for the longest period (Table 3). Venlafaxine, Paroxetine and the Tricyclics produced higher TAE means than the other types of ADs (although the *n*'s for Sertraline and Escitalopram were low).

Table 4 presents frequencies (any and 'severe') for the five most commonly prescribed types of ADs, in relation to the four effects of particular interest, plus the two relating to sexual function (because of their high overall frequency), suicidality, and withdrawal effects (because this is also an effect which has received relatively little attention). The percentages are based on groups of participants who received only one type of AD.

3.3. Adverse effects as reason for stopping medication

Of the 459 participants who were not currently taking ADs and responded to the question why, 218 (47.5%) ticked the 'they had unpleasant side effects' box.

Table 3
Total Adverse Effects scores by medication type.

	<i>n</i>	Only drug used	<i>n</i>	Drug used longest
Venlafaxine	21	16.81 ^a	136	18.90 ^d
Paroxetine	83	15.78 ^b	141	16.36 ^e
Citalopram	207	11.09	317	12.97
Fluoxetine	230	10.31	296	11.71
Sertraline	11	8.36	26	14.31
Escitalopram	14	6.79	22	10.55
Tricyclics	37	13.70 ^c	64	16.44 ^f

^a Greater than fluoxetine ($p < 0.01$), sertraline ($p < 0.01$), citalopram ($p < 0.01$) and escitalopram ($p < 0.01$).

^b Greater than fluoxetine ($p < 0.001$), sertraline ($p < 0.001$), citalopram ($p < 0.001$) and escitalopram ($p < 0.01$).

^c Greater than sertraline ($p < 0.01$).

^d Greater than fluoxetine ($p < 0.001$), citalopram ($p < 0.001$) and escitalopram ($p < 0.001$).

^e Greater than fluoxetine ($p < 0.001$) and citalopram ($p < 0.001$).

^f Greater than fluoxetine ($p < 0.01$).

Table 4

Frequency (and 'severe' percentages) of eight adverse effects by drug type.

	Paroxetine	Venlafaxine	Citalopram	Fluoxetine	Tricyclics
Feeling emotionally numb	69% (13%)	67% (13%)	54% (9%)	49% (10%)	49% (12%)
Feeling not like myself	57% (11%)	59% (15%)	43% (8%)	39% (7%)	48% (14%)
Reduction in positive feelings	46% (7%)	50% (4%)	20% (3%)	28% (4%)	39% (11%)
Caring less about others	41% (4%)	41% (3%)	32% (1%)	31% (5%)	32% (8%)
Sexual difficulties	70% (13%)	63% (17%)	55% (11%)	54% (12%)	56% (8%)
Failure to reach orgasm	65% (15%)	57% (23%)	55% (15%)	50% (13%)	41% (14%)
Suicidality	29% (7%)	37% (4%)	26% (1%)	33% (5%)	32% (5%)
Withdrawal effects	76% (47%)	70% (41%)	47% (15%)	35% (12%)	51% (27%)

Table 5

Frequency of adverse effects about which participants were informed by prescribers (20 or more).

Nausea	308	Anxiety	67
Weight/appetite changes	195	Increased depression	60
Sexual dysfunction	160	Nightmares/dreams	40
Dry mouth	155	Agitation	24
Sleepiness/drowsiness	147	Constipation	23
Insomnia	123	Addiction/withdrawal	21
Headaches	112	'Spacey'/'Fuzzy'	21
Suicidality	84	Tremors	20
Dizziness	79		

3.4. Information given by prescribers

In response to the question 'Did the doctor inform you about possible side effects?' 64.2% responded 'yes'. The most common responses to the subsequent question, 'If yes, what side effects can you recall being mentioned' (answered by 682 participants), are presented in Table 5.

Only three people recalled being told anything about feeling emotionally numb or a reduction in positive feelings – e.g., 'that the peaks of pleasant emotions may not seem as intense' and 'that some people felt it prevented them feeling the real highs – it dampened good and bad emotions'. None were told anything about feeling less like themselves or about possible effects on relationships with other people (other than sexual dysfunction).

3.5. Level of depression

Self-reported level of depression 'while taking antidepressants' was positively correlated with TAE ($\rho=0.46$, $p<0.001$), with all 20 adverse effects correlated at the $p<0.001$ level. TAE was not, however, significantly related to level of depression during 'the year before taking anti-depressants' ($\rho=0.015$, $p=0.87$). Only one of the 20 specific adverse effects was correlated with level of depression prior to taking ADs (Failure to Reach Orgasm; $\rho=0.76$, $p<0.005$). The effect most strongly correlated with depression while taking ADs was Suicidality ($\rho=0.49$, $p<0.001$); but Suicidality was only related to level of depression prior to taking ADs at the $p<0.05$ level ($\rho=0.05$, $p=0.04$). Feeling Not Like Myself was positively correlated with level of depression while taking ADs ($\rho=0.47$, $p<0.001$) but was negatively correlated with level of depression prior to taking ADs ($\rho=-0.09$, $p<0.001$). Reduction in Positive Feelings was also positively correlated with depression while taking ADs ($\rho=0.45$, $p<0.001$) but negatively correlated with level of depression prior to taking them ($\rho=-0.08$, $p<0.01$).

The 82.8% of participants who responded 'yes' to 'Did the antidepressant reduce your depression?' reported fewer adverse effects (mean TAE=12.50) than those responding 'no' (22.71) ($t=10.87$, d.f. 237.7, $p<0.001$). Similarly, perceived improvement in quality of life while taking the ADs was negatively correlated with TAE scores ($\rho=-0.45$, $p<0.001$).

4. Discussion

4.1. 'Closing down'

Our findings, from the largest sample to date, suggest that it may be important to follow up results from smaller, qualitative studies, with large-scale surveys. All four of the emotional or interpersonal effects identified in previous qualitative studies (Gibson et al., in press; Goldberg and Moncrieff, 2011; MIND, 2012) were reported to be very common: Feeling Emotionally Numb (60%), Feeling Not Like Myself (52%), Reduction In Positive Feelings (42%), Caring Less About Others (39%). Between 16% and 35% experienced these four effects as either 'moderate' or 'severe'. Furthermore, all four effects were strongly associated with the belief that suicidality was experienced 'as a result' of the ADs, as was Agitation. This is consistent with a study that found suicidality associated with the adverse effects 'emotional blunting' and 'emotional instability' (Goldberg and Moncrieff, 2011).

Younger people were more likely to experience Feeling Emotionally Numb and Feeling Not Like Myself, and men were more likely to experience Reduction In Positive Feelings and Caring Less About Others.

This diminished capacity to experience feelings, positive or negative, and to care about other people, might be characterized as a sort of 'closing down', a withdrawal from the emotional and interpersonal world. This might be considered an exacerbation of the problems for which ADs are prescribed in the first place. These effects may also reduce the probability of using other pathways to recovery.

4.2. Sexuality

The very high rates of Sexual Difficulties in general (62%) and, more specifically, Failure to Reach Orgasm (59%), which have also been found in other studies (MIND, 2012; Williams et al., 2006), are alarming, especially since 39% and 41%, respectively, experienced these as either 'moderate' or 'severe'. Reduced sexual functioning can be viewed as either a result, or cause, of depression, or both – in a reciprocal cycle. That a treatment designed to treat depression might be creating this effect so pervasively is of concern because sex can be a source of personal happiness and interpersonal closeness. This further 'closing down' raises the issue of whether the drugs are, to some extent, locking some people into a world where sources of, or the capacity to experience, pleasure and happiness are reduced, thereby perpetuating the perceived need to continue taking the medication. One participant wrote:

'Loss of sexual appetite and this worried me I thought to myself god I really don't want to lose the one thing that still gives me enjoyment!'

4.3. Suicidality and aggression

In light of recent concerns about the possibility that ADs can increase suicidality (Makris et al., 2013; Nassir et al., 2013) and

aggression, it is important to note that 39% reported Suicidality, and 28% Feeling Aggressive, 'as a result of' the ADs. The Suicidality finding is similar to a recent study that found that 204 of 706 AD recipients (35%) experienced 'treatment-increasing suicidal ideation' (Perroud et al., 2012).

In the current study, Suicidality was correlated with younger age, with 56% of the 18–25 age group reporting this effect, 14% at the 'severe' level. This is consistent with previous findings that young people are more at risk of suicide on ADs than adults (Hammad et al., 2006).

4.4. Withdrawal effects and fear of addiction

Some previous studies have suggested that the belief that one is addicted, and a fear of withdrawal effects, are common and may be a primary reason for continuing to take the medication (Bogner et al., 2009; Gibson et al., *in press*; Kessing et al., 2005; Stone et al., 2004). Because ADs are not generally considered biologically addictive this widespread fear of addiction is sometimes dismissed as unwarranted (Kessing et al., 2005). In the current study 27% reported Addiction (6% 'severe') and 55% Withdrawal Effects (25% 'severe'). Whereas the wording of the former item might have generated responses indicative of a fear of being or becoming addicted, the latter item seems sufficiently explicit to assume that respondents were reporting actual effects. Several participants described these effects in response to the item about 'other' adverse effects. For example:

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.

Electric shocks in brain when coming off them.

I get terrible "brain zaps" when withdrawing, even if I forget to take the meds for a day or two.

Tried few times to stop, very bad withdrawal but also panic attacks became very severe so still on them now.

Just reducing the dosage now...severe withdrawal effects.

The fear of the consequences of coming off, and therefore being psychologically addicted, is, for some based on fear of, or actual experience of the return of depressive symptoms; for example: 'I'm scared to come off the anti-depressants in case the problems return'; and 'Many times I have tried to wean myself off them but when I do I start getting very weepy.' Nevertheless it seems that, for some people, there are also additional, quite real withdrawal effects (Belaise et al., 2012), and that these can contribute to a decision to go back on the medication. Only 21 participants recalled being informed of these effects by the prescriber. One participant wrote:

I was assured that Paroxetine was not addictive. However, I have had major problems with discontinuation syndrome so am still on it today. I am not happy about that but accept that the medication was new at the time and the GP was going on available information from GSK {Glaxo Smith Klein}. GSK has subsequently been rapped over the knuckles by the FDA for playing down discontinuation syndrome and other side effects. I feel like I am harnessed to a beast.

'Discontinuation effects' have been identified by traditional research, especially nausea, irritability, anxiety and aches; paroxetine has been found to be particularly associated with withdrawal

effects (Hime and Okamura, 2006). In the current study this was the case for both Paroxetine and Venlafaxine (see Table 4).

4.5. Causality

Our findings contribute to the important debate about whether some or all of the adverse effects of ADs are partially or totally caused by depression rather than by the drugs. This important issue is difficult to resolve because some 'symptoms', such as appetite change and insomnia are included in measures of both depression and adverse effects, thereby inflating any correlation between the two (Uher et al., 2009).

The developers of the 'Antidepressant Side-Effect Checklist' found that many adverse effects were commonly reported prior to study commencement and implied that these could not, therefore, be considered adverse effects (Uher et al., 2009). However, their 'average participant was in her second episode of moderately severe depression', and would likely, therefore already have been on ADs for some time. Indeed, they found that 44% already had contraindications to one of the two ADs used in their study. In another study using the same sample the researchers acknowledge that some of their participants were already on 'other antidepressants' (Perroud et al., 2012).

The current study, with a much larger sample, explicitly asked participants about their level of depression *prior* to taking any ADs. The finding that there was no significant relationship between level of depression prior to taking ADs and Total Adverse Effects scores is informative. If adverse events are, as often suggested, caused by depression rather than by ADs the correlation between the two should exist prior to taking ADs. The most parsimonious explanation of our findings would seem to be, therefore, that the adverse effects are caused by the ADs not the depression.

The correlation between adverse effects and level of depression while taking ADs is not easy to interpret with any degree of certainty. The hypothesis that the direction of causality, if any, is from depression to adverse effects is not supported by the absence of correlation with level of depression prior to taking ADs. The alternative hypothesis, that the ADs are causing the adverse effects, however, cannot be definitively proved by a correlation. A third possible explanation is that people who experiences ADs as helpful pay less attention to, and/or are less distressed by, the adverse effects. This hypothesis receives support from the findings that those who believed the ADs reduced their depression, and those who reported improved quality of life while taking ADs, reported significantly fewer adverse events. This third hypothesis is also indirectly supported by the absence of a correlation between depression and adverse effects prior to taking ADs. A fourth possible interpretation of correlations between depression and adverse effect is that some of the adverse effects might be depressing. The specific adverse effects most highly correlated with level of depression while taking ADs included Reduction in Positive Feelings, Feeling Emotionally Numb and Feeling Not Like Myself (all at the $p < 0.001$ level).

4.6. Being informed

The finding that 36% had not been told about adverse effects by the prescriber is consistent with a 41% finding among 107 patients of British GPs (Byng et al., 2007). The recent survey of nearly 1500 AD recipients in the UK found that 45% thought they had not been given enough information about the medication they were prescribed (MIND, 2012), although the percentage was lower among those prescribed ADs more recently. The current study also found that recency of first prescription was related to being told about adverse effects ($\rho = 0.10$, $p < 0.001$).

4.7. Implications

Recent research has raised concerns about the efficacy of ADs, compared to psychological treatments (Dobson et al., 2008) or placebo (Pigott et al., 2010). A meta-analysis which included previously unpublished drug company studies (Kirsch et al., 2008) found that 'the overall effect of new-generation antidepressant medications is below recommended criteria for clinical significance' with no significant benefit compared to placebo for all but 'patients at the upper end of the very severely depressed category'. Therefore, it seems important to have a complete picture of the drugs' adverse effects to weigh against these disappointing efficacy findings when calculating cost-benefit analysis.

Our findings, based on direct questioning of the largest sample of AD recipients to date, indicate that the adverse effects of ADs are many and varied and are experienced by very high percentages of AD recipients. This needs to be more widely recognized. Among the most frequent are effects which could be risk factors for depression, such as loss of sexual functioning and emotional numbing, and also include effects that are indicative of the problem which the drugs are intended to treat, including reduced ability to feel positive emotions, and reduced interest in other people. Our findings are broadly consistent with those of a recent review (Moret et al., 2009, p. 967):

Following long-term treatment with the SSRIs, some serious adverse events may occur. Some of them can be difficult to recognize because they can resemble residual symptoms of depression. The most serious can be life threatening. They all have a negative influence on the patient's quality of life.

It seems important to respond to subjective experiences of patients impartially. A Danish survey of 493 AD recipients (Kessing et al., 2005) found that 43% reported that ADs 'can alter your personality', 56% that 'your body can become addicted', 42% that 'when taking antidepressants you have less control over your thoughts and feelings' and 81% that 'as long as you are taking antidepressants you do not really know if they are actually necessary'. All of these responses, however, were categorized by the researchers as reduced 'Perceived Autonomy', and were dismissed as 'incorrect' and 'erroneous'.

One obvious implication of responding to patients' subjective experiences respectfully (Schofield et al., 2011) would be to include items commonly experienced and reported by AD recipients in future checklists for researchers and clinicians.

While the current findings concur with those of a similar, British study (MIND, 2012), in that the percentage of people being told about adverse effects has increased over time, about a third are not told (or don't recall being told). Very few, it seems, are told about the more subtle, but pervasive and potentially demoralizing, effects on one's ability to feel positive emotions, or to feel anything at all, or about the potential effects on their relationships with other people. The ethical principle of informed choice suggests that this needs to change. The finding that adverse effects were higher in participants not told about adverse effects should help allay clinicians' concerns that they may promote such effects through creating expectation (the nocebo effect).

4.8. Limitations

This self-selected, convenience sample, despite being the largest ever surveyed, was not, in some regards, representative of the New Zealand population. Maori, Pacific Islanders, men, older people, and poorer and less educated people were all under-represented. For example, while 13.7% of the population are 65 or older (Statistics New Zealand, 2012), only 3.6% of our sample were

over 65. The overrepresentation of women (76.6%) is not of great concern because women are prescribed ADs at approximately twice the rate as men internationally. Although an internet sample may be biased towards the more wealthy and better educated, 80% of New Zealand households have internet access (Statistics New Zealand, 2013). Furthermore, given that TAE scores were significantly related to lower education and income, the underrepresentation of these groups would have served to underestimate the prevalence of adverse effects. The over representation of younger people, however, would have operated in the opposite direction.

The very high frequencies of adverse effects raise the issue of whether recipients who were dissatisfied with their medication were more likely to participate. This seems very unlikely, however, given that the majority (82.8%) reported that they believed the drugs had reduced their depression, a rate far higher than most conventional efficacy studies of ADs. If the survey had attracted a disproportionate number of unsatisfied people one might have expected a much higher rate reporting a reduced quality of life while on ADs (8.9%). Thus the sample appears to be biased towards people who had a positive response to ADs.

The study relies entirely on self-report. Conventional studies using established check-lists [4] also rely on self-report. Self-report of adverse effects in the present has been found to be reliable [4]. A more appropriate concern, however, is that some of our data is retrospective and therefore subject to the fallibilities of memory of experiences from weeks to several years in the past. The majority (69%), however, were still taking the ADs at the time of completing the questionnaire.

Although the wording of the question preceding the list of possible adverse effects explicitly included the phrase 'as a result of taking the anti-depressants', it remains possible, as for most other studies, that some of the adverse effects experienced, were not actually caused, or were only partially caused, by the medication.

Some of the participants may have been prescribed ADs for conditions other than depression. However the reason for being prescribed ADs is not directly relevant to the perceived adverse effects of ADs, and the majority (92%) reported that they had experienced depression in the year prior to their first AD prescription.

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