Psychiatry Research xxx (xxxx) xxx

Contents lists available at ScienceDirect

Psychiatry Research

journal homepage: www.elsevier.com/locate/psychres

Antidepressants withdrawal effects and duration of use: a survey of patients enrolled in primary care psychotherapy services☆

Mark A. Horowitz [a,b,c,*], Joshua E.J. Buckman [d,e], Rob Saunders [d], Elisa Aguirre [f], James Davies [g], Joanna Moncrieff [a,c]

[a] Research and Development Department, North East London NHS Foundation Trust (NELFT), Goodmayes Hospital, Ilford, UK
[b] Institute of Pharmaceutical Sciences, King's College London, 57 Waterloo Road London, UK
[c] Division of Psychiatry, University College London, 149 Tottenham Court Road, London, UK, (Honorary for MAH)
[d] CORE Data Lab, Centre for Outcomes Research and Effectiveness (CORE), Research Department of Clinical, Educational & Health Psychology, University College London, 1-19 Torrington Place, London, UK
[e] Camden and Islington NHS Talking Therapies for anxiety and depression services, North London NHS Foundation Trust, St Pancras Hospital, London, UK
[f] Universidad Europea Madrid (UEM), Calle Tajo, 28670, Villaviciosa de Odon, Madrid, Spain
[g] Department of Psychology, University of Roehampton, London, UK

ARTICLE INFO

Keywords:
Antidepressant withdrawal
Discontinuation
Brain zaps
Protracted antidepressant withdrawal
PAWS

ABSTRACT

Background: Previous studies of antidepressant withdrawal have been limited by short duration of drug exposure or self-selected samples. Our study aimed to estimate withdrawal effects in routine clinical practice.
Methods: Participants from NHS primary care psychological treatment services who had ever tried to stop an antidepressant were surveyed. Regression models were constructed to examine the association between personal and medication characteristics, and withdrawal.
Results: Respondents(n = 310) were mostly female(78 %), white(75 %), with an average age of 38.79(SD 12.4). The response rate was 18 % of eligible patients. 62 % reported antidepressants had been helpful. Withdrawal symptoms of some degree were reported by 79 %. 45 % reported severe or moderately severe symptoms. 43 % met the most stringent definition of a withdrawal syndrome, reporting 4 or more 'non-emotional' withdrawal symptoms. 38 % of participants reported being unable to stop their antidepressant when they tried to do so. 20 % reported withdrawal symptoms lasting more than three months and 10 % for more than a year. In fully adjusted models those using antidepressants for over 24-months prior to stopping were more likely to experience a withdrawal syndrome (OR(95 %CI)=10.41(2.88;37.67)), report severe withdrawal effects (OR(95 %CI) = 5.16 (2.75;9.70)), report longer lasting symptoms (Beta(95 %CI)=18.11(3.85;32.38), and be less likely to be able to stop (OR(95 %CI)=27.55(10.29;73.81), than those using for less than six-months.
Conclusion: Antidepressant withdrawal symptoms were common, and severe and prolonged for a substantial proportion of users. Longer duration of use was associated with greater likelihood of severe and protracted symptoms and being less likely to be able to stop. A limitation of this study is the low rate of response.

1. Introduction

Problematic withdrawal effects from SSRIs were first reported in the 1990s, a few years after their release onto the market (Fava et al., 2015). Following short term exposure (mostly 6–12 weeks) to antidepressants studies sponsored by industry reported that "discontinuation effects" were mostly mild and self-limited (Baldwin et al., 2007; Schatzberg et al., 2006, 1997), which became incorporated into influential guidelines (Horowitz and Taylor, 2024; Iacobucci, 2019). In the last few years antidepressant withdrawal symptoms have been recognised as more common, and, potentially, more severe and long-lasting than previously supposed (Davies and Read, 2019; Gastaldon et al., 2022; Horowitz et al., 2023; Horowitz and Taylor, 2022, 2019). This has prompted updates to the NICE guidelines on depression (Iacobucci, 2019; NICE, 2022a) and a position statement from the Royal College of Psychiatrists (Royal College of Psychiatrists, 2019). However, there

☆ This position is honorary for MAH

* Corresponding author at: Division of Psychiatry, University College London, 149 Tottenham Court Road, London, UK.
E-mail address: m.horowitz@ucl.ac.uk (M.A. Horowitz).

https://doi.org/10.1016/j.psychres.2025.116497
Received 3 December 2024; Received in revised form 12 April 2025; Accepted 12 April 2025
Available online 18 April 2025

remains uncertainty about the incidence, severity and duration of withdrawal symptoms.

A recent systematic review concluded that about one in six people experience withdrawal effects from antidepressants, and one in 35 experience severe withdrawal effects (Henssler et al., 2024). However, this review risks under-estimating incidence and severity of withdrawal effects because most studies included were not designed to assess withdrawal effects and relied on spontaneous reporting, which is likely to under-estimate rates compared with systematic evaluation (Moncrieff et al., n.d.; Read and Davies, 2024). Furthermore, the studies captured mostly examined short term use: 36 out of 79 included patients exposed to antidepressants for <12 weeks and the weighted average duration of use of patients was 25 weeks (Henssler et al., 2024). This is in sharp contrast to use in the wider population: for example, in the UK half of all patients on antidepressants have been taking them for >12-months (Public Health England, 2019), and 70 % of patients in the USA have used them for more than two years (Mojtabai and Olfson, 2014).

Other studies have used online surveys to investigate withdrawal symptoms in longer term users and have found half of the participants report withdrawal effects, with half of these reporting severe effects (Davies and Read, 2019; Moncrieff et al., 2024; Read et al., 2019; Read et al., 2023). However, such surveys draw on undefined populations and tend to capture self-selected samples increasing the likelihood of selection bias by over-representing the experience of those with worse than average withdrawal effects (Jauhar et al., 2019). Notably, studies find that duration of exposure to antidepressants appears to influence incidence, severity and perhaps duration of withdrawal effects, perhaps explaining discrepancies between different studies and systematic reviews which have examined patients following differing durations of antidepressant exposure (Horowitz et al., 2023). Notably, a relationship between duration of use and increased risk of withdrawal effects is a common principle across psychotropic medications likely related to the degree of homeostatic adaptation to the drug during exposure (NICE, 2022b).

There remains uncertainty about the nature and frequency of withdrawal effects in long-term users of antidepressants. Therefore, we aimed to estimate the incidence, severity and duration of antidepressant withdrawal effects experienced by patients in routine clinical care (in a free primary care therapy service), and identify moderators of withdrawal effects, including duration of prior use of antidepressants.

2. Methods

A cross-sectional survey was distributed to patients of UK-based NHS psychological therapies services. It was piloted and feedback was sought from experts-by-experience and expert clinicians. A study protocol and analysis were pre-registered after data were collected, but before analyses were undertaken (https://osf.io/ta6sw). Ethical approval was obtained (20/PR/0423) ("WISE USE (antidepressant) survey," n.d.). The study is reported in accordance with Consensus-Based Checklist for Reporting of Survey Studies (CROSS) (Sharma et al., 2021) (Supp material).

2.1. Participants and procedure

Participants were patients of four NHS Talking Therapies for anxiety and depression (TTad) services operated by North East London NHS Foundation Trust (NELFT). Details of these services are provided elsewhere (Saunders et al., 2020). Briefly, patients of these services are either referred by a health professional (typically a GP) or self-referred. The service provides therapy for depression and anxiety disorders. Following assessment by a clinician in the TTad service, diagnoses are determined using ICD-10 diagnostic criteria and a 'problem descriptor' is agreed with the patient and recorded in the electronic patient record. This is the agreed focus of treatment in the TTad service, and is the variable used for diagnoses in this study and many other studies of TTad service users (Saunders et al., 2020).

Patients who had consented to be approached for research (about 50 % of all patients in the services), and met eligibility criteria for the study (aged 18 or above, and had ever used an antidepressant medication) were contacted by a researcher to enrol in the study. Patients who consented were then sent the online survey between February-2021 and December-2022. The one-off survey, was hosted on REDCap and took approximately 30 min to complete, with a £5 voucher for compensation. This paper reports the experiences of the subgroup of respondents who reported that they had ever tried to stop their antidepressant.

2.2. Measures

The survey (see Appendices) contained questions on antidepressant use and discontinuation, including a modified and shortened version of the Discontinuation-Emergent Signs and Symptoms (DESS) checklist (Rosenbaum et al., 1998) to assess withdrawal symptoms. We included 20 items from the original DESS, selected after consultation with experts and experts-by-experience regarding the most common symptoms with two additional items ('brain zaps' and depersonalisation/derealisation) added, following a similar approach recently used (Lewis, 2016). We extracted sociodemographic characteristics, primary presenting problem (diagnosis), and PHQ-9 and GAD-7 scores, which are routinely collected at entry to the therapy service, from participants' electronic health records.

2.3. Sample size determination

We estimated a sample of 300 participants would be necessary to measure incidence of withdrawal syndrome with ±6 % precision (using estimates from a previous systematic review) (Davies and Read, 2019). We planned recruitment to last seven months but it took 22 months to recruit all the participants.

2.4. Outcomes

The primary outcomes were the incidence of withdrawal effects, their severity, their duration, and the proportion of people who were able to stop their antidepressant when trying to do so. There is no established manner to determine the presence of an antidepressant withdrawal syndrome. Many studies have defined withdrawal as four or more symptoms on the 43-item DESS (Rosenbaum et al., 1998); others have used a smaller number of symptoms (Oehrberg et al., 1995; Sir et al., 2005; Zajecka et al., 1998). We pre-specified our primary definition of withdrawal as reporting symptoms of any severity on a question about the overall severity of withdrawal or discontinuation symptoms. We explored a number of alternative definitions of withdrawal as secondary outcomes:

- reporting at least two, three, or four symptoms of any severity on the modified DESS (using at least three as our main secondary outcome);
- reporting at least one, two, three or four individual symptoms on a 'non-emotional' sub-scale of the DESS encompassing 10 symptoms which have the clearest difference from symptoms of anxiety disorders or depression (Table S1)), in order to delineate withdrawal effects less prone to confounding with relapse.
- reporting at least one, two, three, or four or more individual withdrawal symptoms of a moderate or severe degree on the modified DESS.

2.5. Analyses

Analyses were conducted in Stata version 18 (StataCorp, 2023). Univariable regression models were fitted to explore associations between potential risk factors and the incidence, severity and duration of a withdrawal syndrome and ability to stop, using an ordinal link function

for ordered outcome variables and logistic link function for binary outcomes. The models were then adjusted for the following pre-specified potential confounding factors: sociodemographics (including gender, ethnicity, age, and employment status), mental health diagnosis (based on ICD-10 codes), the antidepressant taken, duration of antidepressant medication use before attempting to stop, PHQ-9 and GAD-7 scores at entry to the therapy services, and whether or not the participant was taking other medication for their mental health in addition to the antidepressant.

2.6. Sensitivity analyses and missing data

Pre-planned sensitivity analyses were conducted repeating analyses above with alternative versions of several outcome variables. A binary categorical severity variable was explored (no or mild symptoms versus moderate or severe). Further sensitivity analyses were conducted to compare the analyses above for the four main outcomes with analyses using multiple imputation with chained equations (conducted using mi impute in Stata) to create 50 imputed datasets.

2.7. Deviation from protocol

In analysing overall withdrawal severity, the original self-reported categories of severity were retained rather than binarised because this provided more information. As there were few people taking many specific antidepressants, they were divided into high risk for withdrawal symptoms (venlafaxine, duloxetine and paroxetine) and low risk (all others) according to a recent analysis (Gastaldon et al., 2022). As there were relatively few respondents who tapered over long periods, tapering period was binarised into up to and more than four weeks, following long-standing NICE guidance (National Institute for Health and Care Excellence, 2009), and common clinical practice (Read et al., 2023).

3. Results

3.1. Recruitment

Of the patients in the therapy services who had consented to be contacted about research 3023 were potentially eligible for this study and 316 declined the study following telephone contact (Fig. 1). We sent surveys to 2707 who agreed to receive it by phone or did not answer three phone calls. We received 497 usable (valid, non-duplicated ID number, taken an antidepressant, 3 or more questions answered) responses (18.4 %). The 310 respondents who had ever tried to stop antidepressant treatment were used for analyses (Fig. 1). These respondents were 77.9 % female, mostly white (75.1 %) with a mean age of 38.8 years. See Table 1 for further characteristics of the sample. 62.0 % of respondents reported that antidepressants had improved or much improved their symptoms.

3.2. Comparisons to wider service population

Compared to all users of the therapy service over the same time period, those that completed the survey were more likely to be female (77.92 % vs 65.59 %, $p < 0.001$), were less likely to be unemployed (24.58 % vs 31.58 %, $p = 0.009$), were more likely to identify as of White British ethnicity (63.23 % vs 55.19 %, $p = 0.005$), and had a slightly lower mean age (36.99(12.33) vs 38.62(14.32), $p = 0.046$). They had similar average PHQ-9 scores pre-treatment (16.16(5.78) vs 15.83 (6.27), $p = 0.36$) and slightly higher GAD-7 scores (14.63(4.80) vs 14.02 (5.14), $p = 0.037$).

3.3. Characteristics of withdrawal

Of the 310 respondents who had ever tried to stop an antidepressant, 37.9 % reported having been unable to do so despite trying one or multiple times, 8.3 % were currently in the process of trying to do so, and 53.8 % reported having been able to stop (Table 2). Many participants described the process of stopping their antidepressant as 'difficult' (37.4 %) or 'very difficult' (15.3 %). 43.3 % of respondents had tried to stop their antidepressant more than once, with 7.7 % having tried more than four times. Participants who were unable to stop their antidepressant were more likely to report severe withdrawal symptoms (rho=0.41, $p < 0.0001$).

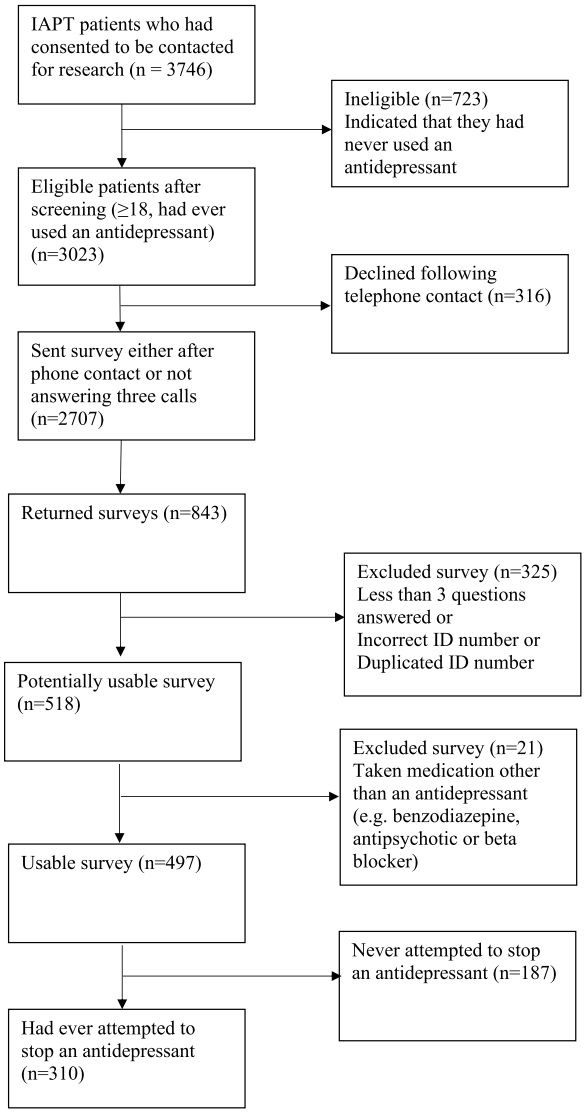

Fig. 1. – Flow diagram of recruitment to survey.

When asked about the withdrawal experience overall, 222(79.3 %) participants reported withdrawal symptoms of at least mild severity. 45.0 % rated the symptoms as moderate (30.4 %) or severe (14.6 %). Incidence varied between 42.6–85.8 % with secondary outcome definitions of withdrawal (Table 2). 56.4 % had at least four moderate or severe symptoms of withdrawal. 76 % had at least one 'non-emotional' withdrawal symptom and 42.6 % met the most stringent definition of 4 or more 'non-emotional' withdrawal symptoms. Of ten 'non-emotional' withdrawal symptoms three were reported by >50 % of respondents: headache, derealisation/depersonalisation and dizziness/lightheadedness (Table 3).

Symptoms were predominantly reported to last less than four weeks (58.5 %), but 19.7 % reported their symptoms lasted >3 months, and 9.5 % more than a year (Table 2).

Table 1
– Sociodemographic and medication characteristics of respondents who had tried to stop their antidepressant at some point.

Characteristic	Sub-types	N (%) or Mean (SD)	Number with complete data (N)
Gender	Male	68 (22.1 %)	308
	Female	240 (77.9 %)	
Duration of use before stopping	< 6 months	126 (42.3 %)	298
	7–24 months	101 (33.9 %)	
	>24 months	71 (23.8 %)	
Age		38.79 (12.35)	308
Ethnicity	White	232 (75.1 %)	310
	Asian or Asian British	28 (9.1 %)	
	Black, Black British, Caribbean or African	25 (8.1 %)	
	Mixed or multiple ethnic groups	19 (6.1 %)	
	Other ethnic group	4 (1.3 %)	
	Not specified	1 (0.3 %)	
Employment status	In employment	227 (75.4 %)	301
	Not in employment (student, carer, retired, unemployed)	74 (24.6 %)	
Presenting problem	Depressive disorder	158 (51.0 %)	310
	Anxiety disorder	133 (42.9 %)	
	Other	19 (6.1 %)	
PHQ-9 Score		16.50 (5.45)	309
GAD-7 Score		14.60 (4.80)	308
Prescribed antidepressant name	Amitriptyline	5 (1.6 %)	307
	Citalopram	110 (35.8 %)	
	Duloxetine**	4 (1.3 %)	
	Escitalopram	11 (3.6 %)	
	Fluoxetine	36 (11.7 %)	
	Lofepramine	1 (0.3 %)	
	Mirtazapine	21 (6.8 %)	
	Nortriptyline	1 (0.3 %)	
	Paroxetine**	4 (1.3 %)	
	Sertraline	100 (32.6 %)	
	Trazodone	2 (0.7 %)	
	Venlafaxine**	10 (3.3 %)	
	Other	2 (0.7 %)	
Concomitant medication	None	257 (83.4 %)	308
	At least one	51 (16.6 %)	
Which concomitant medication	Benzodiazepine	7 (13.7 %)	51
	Z-drug	6 (11.8 %)	
	Other antidepressant***	11 (21.6 %)	
	gabapentin (Neurontin) oid	3 (5.9 %)	
	Antipsychotic	1 (2.0 %)	
	Mood stabiliser	1 (2.0 %)	
	Multiple drugs	6 (11.8 %)	
	Not specified	3 (5.9 %)	
	Other drugs (e.g. beta blocker or antihistamine)	11 (21.6 %)	
	Not a medication used for psychiatric reasons (e.g. NSAID, OCP)	2 (3.9 %)	
Number of attempts to stop antidepressants	Once	169 (56.7 %)	298
	2 to 4 times	106 (35.6 %)	
	>4 times	23 (7.7 %)	
Did antidepressants improve or worsen the symptoms for which they were originally prescribed?	Much improved	90 (33.6 %)	268
	A bit improved	76 (28.4 %)	
	No change	26 (9.7 %)	
	A bit worsened	15 (5.6 %)	
	Much worsened	22 (8.2 %)	
	Not sure	39 (14.6 %)	

Values add up to >100 % in some cases because values were rounded to 1 decimal point.
*Talking Therapy services note down 'presenting problem'. ICD-10 codes from F30–39 were classified as depressive disorders, those from F40–49 were classified as anxiety disorders, and all others as 'other.'.
**High risk antidepressants according to analysis by Gastaldon et al. (2022), with cut-off of a reporting odds ratio of 10.
***If a respondent was on more than one antidepressant, the primary antidepressant was defined as the one they commenced first.

3.4. Characteristics associated with withdrawal outcomes

3.4.1. Incidence of withdrawal syndrome

The duration of antidepressant use prior to discontinuing the medication was strongly associated with the odds of experiencing a withdrawal syndrome in adjusted and unadjusted analyses (Table 4). For respondents who had used antidepressants for <6 months, 64.3 % experienced withdrawal effects of any severity, compared with 86.0 % and 95.7 % for 7–24 months, and >24 months respectively.

In the adjusted analysis the odds of experiencing withdrawal effects for those who used antidepressants between 7 and 24 months compared to 6 months or less was 2.83(95 %CI 1.29;6.18), and for those who had used antidepressants for >24 months the odds ratio was 10.41 (2.88;37.67)].

After adjusting for confounding factors there was no evidence of associations between sociodemographic variables, duration or method of tapering, PHQ-9 score, GAD-7 score, or the type of antidepressant, with the likelihood, or severity of withdrawal symptoms (see Table 4 and sections below). Sensitivity analyses (Tables S2–6) using alternative definitions of incidence, and severity of withdrawal and repeating the analyses over imputed datasets produced similar results.

3.4.2. Severity of withdrawal

There was evidence of a gradient between a longer duration of prior antidepressant use and the severity of withdrawal symptoms. Respondents who had used antidepressants for 0–6 months predominantly reported none or mild withdrawal symptoms (73.1 %), only 7.0 % reported severe withdrawal effects (Fig. 2a). For respondents using for 24-

Table 2
The process of stopping and characteristics of withdrawal symptoms.

Category	Response	Number (proportion)
Status of cessation (n = 301)		
	Successfully stopped medication	162 (53.8 %)
	Unable to stop despite trying to	114 (37.9 %)
	Currently tapering	25 (8.3 %)
Difficulty of stopping (n = 294)		
	Very easy	26 (8.8 %)
	Easy	113 (38.4 %)
	Difficult	110 (37.4 %)
	Very difficult	45 (15.3 %)
Severity of withdrawal symptoms (n = 280)		
	None	58 (20.7 %)
	Mild	96 (34.3 %)
	Moderate	85 (30.4 %)
	Severe	41 (14.6 %)
Any self-defined withdrawal symptoms (n = 280)*	Question "Overall, how severe were the withdrawal or discontinuation symptoms you experienced on stopping your antidepressant?"	
	No (Responding "No symptoms")	58 (20.7)
	Yes (Responding "Mild", "Moderate" or "Severe")	222 (79.3)
Any modified DESS symptoms (n = 310)		
	2 or more of any withdrawal symptoms	266 (85.8)
	3 or more of any withdrawal symptoms**	256 (82.6)
	4 or more of any withdrawal symptoms	244 (78.7)
Moderate or severe modified DESS symptoms (n = 310)		
	1 or more moderate or severe withdrawal symptoms	231 (74.5)
	2 or more moderate or severe withdrawal symptoms	211 (68.1)
	3 or more moderate or severe withdrawal symptoms	195 (62.9)
	4 or more moderate or severe withdrawal symptoms	175 (56.4)
'Non-emotional' withdrawal symptoms (n = 310)		
	1 or more non-emotional withdrawal symptoms	234 (75.5)
	2 or more non-emotional withdrawal symptoms	196 (63.2)
	3 or more non-emotional withdrawal symptoms	156 (50.3)
	4 or more non-emotional withdrawal symptoms	132 (42.6)
Duration of withdrawal symptoms (n = 253)		
	1 week or less	44 (17.4 %)
	1 to 4 weeks	104 (41.1 %)
	1–3 months	55 (21.7 %)
	4–6 months	13 (5.1 %)
	6–12 months	13 (5.1 %)
	1–3 years	9 (3.6 %)
	>3 years	15 (5.9 %)
Tapering approach (n = 275)		
	Stopped suddenly	103 (37.5)
	1 day to 1 week	39 (14.2)
	1 to 4 weeks	74 (26.9)
	1 to 3 months	46 (16.7)
	4 to 12 months	9 (3.3)
	More than one year	4 (1.5)
Method for reducing dose (more than one answer possible) (n = 308)		
	Skipping doses	145 (47.1)
	Stopping abruptly (in one day)	119 (38.6)
	Pill splitting	81 (26.3)
	Making a liquid mixture	2 (0.6)
	Bead-counting	1 (0.3)
	Weighing beads	0 (0)
	Weighing powder	1 (0.3)
	Weighing shavings or chunks	1 (0.3)
	Using a compounding pharmacy	0 (0)
	Manufacturer's liquid	2 (0.6)
	Tapering strips	0 (0)
	Other	14 (4.5)

* Primary outcome pre-specified in the protocol.
** Main secondary outcome pre-specified in the protocol.

months or more, 63.7 % reported moderate or severe withdrawal effects, with 24.6 % reporting severe withdrawal effects.

Adjusting for confounding variables, the odds of rating withdrawal as 'severe' after 7–24 months of use was 2.90(1.66;5.06) compared to use of 0–6 months and it was 5.16(2.75;9.70) after >24 months of use.

3.4.3. Duration of withdrawal

The duration of prior use of antidepressants was also associated with the duration of withdrawal symptoms. Of respondents who had used antidepressants for <6 months only 27.4 % reported withdrawal symptoms that lasted more than four weeks and 10.5 % reported symptoms for >3 months, with 7.4 % reporting symptoms for >12 months. For respondents that had used antidepressants for >24 months the respective figures were 53.6 % (more than four weeks), 30.4 % (>3 months) and 11.6 % (>12 months) (Fig. 2b).

After adjusting for confounders, longer duration of prior use was associated with an increase in weeks of withdrawal. Higher PHQ-9 scores at baseline were also associated with fewer weeks of withdrawal symptoms on average and conversely, higher GAD-7 scores were associated with a greater number of weeks of withdrawal symptoms. No other variables were associated with duration of withdrawal symptoms.

3.4.4. Being able to stop or not

Longer duration of use and higher risk antidepressant was associated with greater chance of not being able to stop: of respondents using antidepressants for <6 months 23.2 % were unable to stop the medication; this was 39.8 % and 79.4 % for 7–24 and 24-plus months' use respectively (Fig. 2c). Of respondents taking 'high risk' antidepressants 82.4 % reported being unable to stop, while 38.6 % taking 'low risk' antidepressants were unable to stop them.

After adjusting for confounders, longer prior use of antidepressants was associated with a five times greater odds of not being able to stop the medication despite trying (OR(95 %C) = 5.02(3.09;8.16) per-category increase). The odds of not being able to stop antidepressants were more than eight times higher for those taking a 'high risk' medication (those with the highest risk of withdrawal effects) compared to a 'low risk' one (OR(95 %CI) = 8.40(1.50–47.24)). Skipping doses was also associated with greater odds of not being able to stop relative to all other stopping techniques. No other variables were associated with ability to stop antidepressants.

3.4.5. Severity of symptoms and duration of use

To explore whether the relationship between indices of withdrawal and duration of use was explained by the severity of the underlying condition, we examined the correlation between mean PHQ-9 and GAD-7 scores, and duration of antidepressant use prior to stopping. Correlations were small and not statistically significant (for PHQ-9, r =

Table 3
Incidence and severity (by category) of 22 withdrawal symptoms. Symptoms are arranged in order of incidence from most common (any severity) to least common.

		Frequency N (%)				
Modified DESS item	n	Any increase	No increase	Mild increase	Moderate increase	Severe increase
Anxiety or nervousness	285	229 (80.4)	56 (19.6)	65 (22.8)	90 (31.6)	74 (26.0)
Worsened mood	285	221 (77.5)	64 (22.5)	79 (27.7)	75 (26.3)	67 (23.5)
Agitation	284	199 (70.1)	85 (29.9)	84 (29.6)	66 (23.2)	49 (17.3)
Tearfulness	285	198 (69.5)	87 (30.5)	71 (24.9)	67 (23.5)	60 (21.1)
Fatigue	284	195 (68.7)	89 (31.3)	80 (28.2)	63 (22.2)	52 (18.3)
Insomnia	287	193 (67.3)	94 (32.8)	61 (21.3)	62 (21.6)	70 (24.4)
Mood swings	282	185 (65.6)	97 (34.4)	67 (23.8)	57 (20.2)	61 (21.6)
Irritability	281	180 (64.0)	101 (35.9)	81 (28.8)	57 (20.3)	42 (14.9)
Confusion or trouble concentrating	285	175 (61.4)	110 (38.6)	80 (28.1)	55 (19.3)	40 (14.0)
Angry outbursts	286	158 (55.3)	128 (44.8)	58 (20.3)	54 (18.9)	46 (16.1)
Headache*	285	153 (53.6)	132 (46.3)	79 (27.7)	54 (18.9)	20 (7.0)
Forgetfulness	286	151 (52.7)	135 (47.2)	73 (25.5)	45 (15.7)	33 (11.5)
Depersonalisation or derealisation*	285	149 (52.3)	136 (47.7)	68 (23.9)	40 (14.0)	41 (14.4)
Dizziness*	287	148 (51.6)	139 (48.4)	70 (24.4)	55 (19.2)	23 (8.0)
Nightmares*	284	126 (44.4)	158 (55.6)	57 (20.1)	38 (13.4)	31 (10.9)
Elevated mood	279	87 (31.3)	192 (68.8)	49 (17.6)	25 (9.0)	13 (4.7)
Unsteady gait *	280	84 (30.0)	196 (70.0)	49 (17.5)	24 (8.6)	11 (3.9)
Vertigo*	282	80 (28.3)	202 (71.6)	39 (13.8)	28 (9.9)	13 (4.6)
Electric sensations*	283	79 (27.9)	204 (72.1)	31 (11.0)	23 (8.1)	25 (8.8)
Muscle cramps*	283	76 (26.8)	207 (73.1)	40 (14.1)	30 (10.6)	6 (2.1)
Nausea or vomiting*	283	74 (26.1)	209 (73.9)	59 (20.8)	9 (3.2)	6 (2.1)
Diarrhoea*	281	68 (24.2)	213 (75.8)	44 (15.7)	20 (7.1)	4 (1.4)

* 10 'non-emotional' symptoms that do not overlap with symptoms of anxiety and depression.

−0.0584, $p = 0.3159$; for GAD-7 $r = 0.0002$, $p = 0.9971$). There were also no associations when the analyses were conducted using mood scores arranged as categorical data (see Appendices, Section 4).

4. Discussion

We conducted a survey of patients' experiences of antidepressant withdrawal effects in a population enrolled in NHS psychological therapy services. Overall, around 80 % reported experiencing withdrawal symptoms of any severity when trying to stop, with around a third (30.4 %) reporting mild symptoms, a third (34.2 %) reporting moderate symptoms and one in seven (14.6 %) reporting severe symptoms. Almost 40 % had not been able to stop their antidepressant despite trying to do so. Difficulty stopping correlated strongly with experiencing more severe withdrawal effects. Most people experienced withdrawal symptoms that resolved within 4 weeks (58.5 %) but for one-fifth (19.7 %) they persisted for >3-months and for one-tenth it was >12-months. The figures suggest some degree of withdrawal is common, with just under half experiencing moderate or severe symptoms.

The duration of antidepressant use before trying to stop was strongly associated with all withdrawal outcomes. For brief use (≤6 months) withdrawal symptoms were mostly mild and brief, with three-quarters (76.8 %) reporting no or mild symptoms, and three-quarters (72.6 %) reporting brief symptoms of less than four weeks. Only one in four (23.2 %) of such patients were unable to stop. For long term users (>24 months), most (63.7 %) reported moderate or severe withdrawal effects, with one-quarter (24.6 %) reporting severe withdrawal effects. Almost one-third (30.4 %) of long-term users reported symptoms that lasted for more than three months. Four-fifths (79.4 %) of these patients were unable to stop their antidepressant. The relationship between long-term use and withdrawal severity is likely related to a greater degree of neuroadaptation after long-term exposure, as dictated by the law of homeostasis, creating circumstances for a greater degree of withdrawal on cessation (Fava and Cosci, 2019; Horowitz et al., 2023). This relationship was not explained by the severity of the underlying condition as evaluated with measures taken at entry to the therapy service.

Few other factors were associated with withdrawal in our data. Being on a high-risk antidepressant was associated with not being able to stop the antidepressant, but the number of people on such antidepressants was small. High-risk antidepressants were not associated with other indicators of withdrawal. This may be because most (80 %) of these patients returned to their medication, minimising the severity and duration of their symptoms or because there were too few such patients to detect a signal. Diagnosis and baseline depression and anxiety scores were for the most part not associated with measures of withdrawal.

Respondents were similar to other users of the services that they were recruited from in terms of levels of depression and anxiety symptoms pre-treatment, although respondents were more likely to be female, ethnically white, and employed. Compared to the population of people prescribed antidepressants in England, our sample were younger (36.99 vs 51.69 and, more likely to be female (77.92 % vs 65.60 %), but were similar in terms of antidepressants prescribed (although fewer were prescribed amitriptyline)(NHS Digital, 2023).

Previous studies and reviews find varying rates of withdrawal (Davies and Read, 2019; Henssler et al., 2024; Zhang et al., 2024). We found that the incidence depends on the definition of withdrawal that is used and that the centrality of duration of use may help to explain previously conflicting findings. Although the recently reported meta-analysis by Henssler et al. (2024) reported lower rates of withdrawal than found in the present study, this meta-analysis has been criticised for its non-systematic evaluation of withdrawal effects (relying largely on spontaneous reporting) and for inclusion of many studies involving short periods of treatment (Moncrieff et al., n.d.; Read and Davies, 2024).

In discontinuation studies conducted after short-term regulatory trials (<6 month exposure) withdrawal symptoms are mostly mild and short-lived, as captured in the Henssler review (Henssler et al., 2024). In this review the incidence of severe withdrawal effects was only 3 %, and although this is possibly an under-estimate due to being based mostly on spontaneously reported adverse events (Henssler et al., 2024), it is not dis-similar to the 7 % value we found in respondents in the current study who had taken antidepressants for <6 months.

Other analyses also appear to show that longer use is associated with higher incidence, severity, and perhaps duration of withdrawal effects as found in our data (Horowitz et al., 2023) From survey data, about a third of patients treated with antidepressants for 6 months reported withdrawal effects, with about a fifth reporting moderate or severe withdrawal symptoms (Horowitz et al., 2023). For patients who had taken antidepressants for >3 years, three-fifths reported withdrawal effects and half of these reported moderate or severe symptoms (Horowitz

Table 4
Associations between baseline characteristics and withdrawal outcomes.

	Unadjusted Estimates		Adjusted Estimates *	
	OR	95 %CI	AOR	95 %CI
Incidence of withdrawal syndrome (binary outcome)				
Gender				
Female	0.61	0.28 – 1.32	0.40	0.15 – 1.07
Male	1.00		1.00	
Employment status				
Unemployed	0.98	0.49 – 1.93	0.85	0.37 – 1.95
Employed	1.00		1.00	
Ethnicity				
White	1.00		1.00	
Other	1.14	0.56 – 2.32	1.48	0.64 – 3.44
Age				
Per 1 year increase	1.00	0.98 – 1.03	1.01	0.97 – 1.04
Taking concomitant medication				
Yes	2.29	0.77 – 6.75	1.53	0.46 – 5.05
No	1.00		1.00	
Diagnosis				
Depressive disorder	1.00		1.00	
Anxiety disorder	1.32	0.72 – 2.42	1.52	0.70 – 3.30
Other	2.45	0.54 – 11.20	7.65	0.87 – 67.31
PHQ-9 score				
Per 1 point increase	0.98	0.92 – 1.03	1.00	0.92 – 1.08
GAD-7 score				
Per 1 point increase	0.98	0.92 – 1.04	0.96	0.88 – 1.06
Duration of prior use				
Per category increase	***3.46***	***2.11 – 5.67***	***3.08***	***1.80 – 5.27***
< 6 months	1.00		1.00	
7–24 months	***3.41***	***1.69 – 6.86***	***2.83***	***1.29 – 6.18***
>24 months	***12.19***	***3.60 - 41.22***	***10.41***	***2.88 - 37.67***
Tapering duration				
≤ 4 week	1.00		1.00	
> 4 week	2.24	0.96 - 5.24	00.91	0.30 – 2.71
Method of tapering				
Skipping doses**	***1.86***	***1.03 – 3.35***	1.94	0.97 – 3.89
Stopping abruptly**	0.97	0.54 – 1.74	1.74	0.78 – 3.91
Pill splitting**	1.97	0.96 – 4.02	1.18	0.50 – 2.78
Other stopping technique**	1.05	0.34 – 3.27	0.71	0.19 – 2.68
Antidepressant risk category				
Low risk	1.00		1.00	
High risk	4.13	0.53 – 31.94	1.43	0.16 – 12.73
	Unadjusted Estimates		**Adjusted Estimates** *	
	OR	95 %CI	AOR	95 %CI
Severity of withdrawal syndrome				
Gender				
Female	0.77	0.38 – 1.17	0.67	0.39 – 1.18
Male	1.00		1.00	
Employment status				
Unemployed	1.03	0.52 – 1.55	0.87	0.50 – 1.51
Employed	1.00		1.00	
Ethnicity				
White	1.00		1.00	
Other	1.00	0.50 – 1.51	1.20	0.70 – 2.08
Age				
Per 1 year increase	1.00	0.98 – 1.02	1.00	0.98 – 1.02
Taking concomitant medication				
Yes	1.44	0.56 – 2.32	1.03	0.54 – 1.97
No	1.00		1.00	
Diagnosis				
Depressive disorder	1.00		1.00	
Anxiety disorder	1.20	0.77 – 1.87	1.33	0.79 – 2.24
Other	1.24	0.54 – 2.86	1.44	0.52 – 3.95
PHQ-9 score				
Per 1 point increase	0.99	0.96 – 1.03	1.01	0.95 – 1.06
GAD-7 score				
Per 1 point increase	1.00	0.95 – 1.04	0.99	0.93 – 1.05
Duration of prior use				
Per category increase	***2.40***	***1.80 – 3.19***	***2.31***	***1.68 – 3.16***
< 6 months	1.00		1.00	
7–24 months	***3.29***	***1.96 – 5.53***	***2.90***	***1.66 – 5.06***
>24 months	***5.51***	***3.10 – 9.77***	***5.16***	***2.75 – 9.70***
Tapering duration				
≤ 4 week	1.00		1.00	

(*continued on next page*)

Table 4 (*continued*)

	Unadjusted Estimates		Adjusted Estimates *	
	OR	95 %CI	AOR	95 %CI
> 4 week	1.24	0.75 – 2.06	0.60	0.32 – 1.13
Method of tapering				
Skipping doses**	1.15	0.66 – 1.63	1.09	0.69 – 1.73
Stopping abruptly**	1.07	0.61 – 1.53	1.43	0.80 – 2.55
Pill splitting**	1.54	0.82 – 2.26	1.05	0.60 – 1.81
Other stopping technique**	1.14	0.20 – 2.08	0.86	0.36 – 2.06
Antidepressant risk category				
Low risk	1.00		1.00	
High risk	***2.95***	***1.17 – 7.39***	1.66	0.62 – 4.44
	Unadjusted Estimates		**Adjusted Estimates** *	
	OR	95 %CI	OR	95 %CI
Not able to stop				
Gender				
Female	0.62	0.35 – 1.10	0.65	0.30 – 1.43
Male	1.00		1.00	
Employment status				
Unemployed	1.52	0.87 – 2.66	1.71	0.78 – 3.77
Employed	1.00		1.00	
Ethnicity				
White	1.00			
Other	0.90	0.50 – 1.61	1.35	0.61 – 2.95
Age				
Per 1 year increase	***1.02***	***1.00 –1.04***	1.01	0.99 – 1.04
Taking concomitant medication				
Yes	1.29	0.60 – 2.76	1.11	0.42 – 2.94
No	1.00		1.00	
Diagnosis				
Depressive disorder	1.00		1.00	
Anxiety disorder	0.82	0.50 – 1.36	0.89	0.43 – 1.82
Other	1.51	0.55 – 4.15	3.61	0.90 – 14.58
PHQ-9 score				
Per 1 point increase	1.02	0.97 – 1.06	1.07	0.99 – 1.16
GAD-7 score				
Per 1 point increase	0.99	0.94 – 1.04	0.92	0.85 – 1.00
Duration of prior use				
Per category increase	***3.37***	***2.35 – 4.83***	***5.02***	***3.09 – 8.16***
< 6 months	1.00		1.00	
7–24 months	***2.19***	***1.19 – 4.00***	***2.77***	***1.27 – 6.02***
>24 months	***12.72***	***6.00 – 26.97***	***27.55***	***10.29 – 73.81***
Tapering duration				
≤ 4 week	1.00		1.00	
> 4 week	1.59	0.85 – 2.93	0.63	0.25 – 1.57
Method of tapering				
Skipping doses**	***1.65***	***1.02 – 2.67***	***2.08***	***1.05 – 4.10***
Stopping abruptly**	0.74	0.45 – 1.21	0.45	0.20 – 1.01
Pill splitting**	0.94	0.55 – 1.63	0.60	0.26 – 1.37
Other stopping technique**	1.45	0.53 – 3.99	1.19	0.31 – 4.61
Antidepressant risk category				
Low risk	1.00		1.00	
High risk	***7.42***	***2.08 – 26.47***	***8.40***	***1.50 – 47.24***
	Unadjusted Estimates		**Adjusted Estimates** *	
	Beta	95 %CI	aBeta	95 %CI
Duration of withdrawal				
Gender				
Female	8.98	−3.74 – 21.71	9.26	−0.389 – 22.41
Male	1.00		1.00	
Employment status				
Unemployed	4.38	−7.50 – 16.27	5.41	−7.58 – 18.41
Employed	1.00		1.00	
Ethnicity				
White	1.00		1.00	
Other	4.56	−7.66 – 16.79	7.76	−5.07 – 20.59
Age				
Per 1 year increase	−0.16	−0.58 – 0.27	−0.27	−0.74 - 0.21
Taking concomitant medication				
Yes	−4.35	−19.18 – 10.49	−2.99	−18.47 – 12.48
No	1.00		1.00	
Diagnosis				
Depressive disorder	1.00		1.00	
Anxiety disorder	−1.97	−12.72 – 8.79	−9.17	−21.29 – 2.96
Other	−13.13	−34.90 – 8.65	−19.24	−43.12 – 4.64

(*continued on next page*)

Table 4 (*continued*)

	Unadjusted Estimates		Adjusted Estimates *	
	Beta	95 %CI	aBeta	95 %CI
PHQ-9 score				
Per 1 point increase	−0.72	−1.65 – 0.22	***−1.73***	***−3.02 – −0.44***
GAD-7 score				
Per 1 point increase	0.33	−0.74 – 1.40	***1.67***	***0.22 – 3.13***
Duration of prior use				
Per category increase	7.97	1.53 – 14.41	***9.12***	***2.02 – 16.22***
< 6 months	1.00		1.00	
7–24 months	9.33	−2.80 – 21.46	10.42	−2.55 – 23.40
>24 months	15.78	2.82 – 28.74	***18.11***	***3.85 – 32.38***
Tapering duration				
≤ 4 week	1.00		1.00	
> 4 week	8.73	−3.62 – 21.07	6.59	−8.08 – 21.25
Method of tapering				
Skipping doses**	4.08	−6.29 – 14.46	3.65	−7.34 – 14.65
Stopping abruptly**	7.27	−3.19 – 17.74	9.43	−4.23 – 23.10
Pill splitting**	0.52	−10.64 – 11.69	−1.26	−14.06 – 11.54
Other stopping technique**	−2.15	−21.23 – 17.03	−3.37	−23.71 – 16.96
Antidepressant risk category				
Low risk	1.00		1.00	
High risk	−8.92	−30.15 – 12.32	−10.04	−32.87 – 12.79

* Adjusted for: Duration of Prior ADM use, Tapering Duration, Antidepressant risk of withdrawal syndrome, PHQ-9 Score, GAD-7 Score, Age, Sex, Employment Status, Concomitant Medication, and Diagnosis.

** High risk antidepressants according to analysis by Gastaldon et al. (2022)[1], with cut-off of a reporting odds ratio of 10; see Table 1.

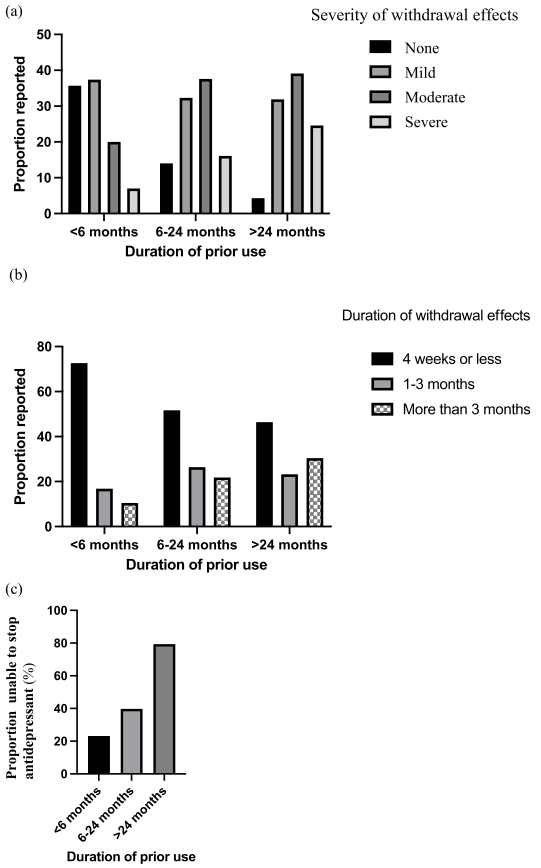

Fig. 2. The role of duration of prior use in severity and duration of withdrawal effects

a) The relationship between duration of prior use (in 3 categories) and severity of withdrawal effects (in 4 categories). b) The relationship between duration of prior use (in 3 categories) and duration of withdrawal symptoms (in 3 categories). c) The relationship between duration of prior use (in 3 categories) and proportion unable to stop medication.

et al., 2023), broadly consistent with the current findings. In a carefully conducted (and double-blinded) trial after 11 months on average of use, 66 % of participants stopping paroxetine reported 4 or more withdrawal symptoms on the DESS, and 60 % of sertraline users, not dissimilar to the findings in the present study (Rosenbaum et al., 1998). In a double-blind RCT of patients who had been taking antidepressants for >2 years, withdrawal symptoms were increased for, on average, 9 months after stopping (Lewis et al., 2021), somewhat longer than the equivalent group in our study of whom 30 % reported symptoms of longer than 3 months.

Slower tapering showed no association with incidence of withdrawal in adjusted analyses. Given most analyses associate slower tapering with less withdrawal (Gøtzsche and Demasi, 2023; Groot and van Os, 2021), this may be due to a floor effect where almost all tapering was performed relatively quickly in our sample (<3 months), meaning there was not gradual enough tapering to see any mitigating effect of gradual tapering. There may also be a degree of reverse causation where people who experienced withdrawal effects slowed down their taper or it may be the case that people who had used antidepressants for longer pre-emptively decided or were advised to taper more slowly. Many patients stopped their drugs abruptly (37.5 % of respondents) and it is difficult to know whether this was based on their own decision or doctors' advice. This may be quicker than current practice, although studies find that patients are often given advice to stop over a few weeks or less (Read et al., 2023) and it is important to have information about the consequences of abrupt withdrawal.

4.1. Strengths and limitations

A strength of this study is that it examined withdrawal effects in a sample recruited from primary care settings better representing those withdrawing in routine clinical practice than previous surveys or randomised trials, and whose duration of use closely reflects national trends (Johnson et al., 2012; Public Health England, 2019) - 44.0 % of the current sample took antidepressants for >12 months, compared with 50 % of English antidepressant users (Public Health England, 2019).

The low response rate (18.3 % of those sent the survey) makes it possible that the survey may have been answered by people with a worse than average experience of withdrawal (which may have motivated them to participate). However, respondents did not have to have attempted to stop an antidepressant to participate as the survey

examined general experiences of using the drugs. The participant information sheet did not particularly highlight withdrawal which was only one component of the survey (see Appendix). It should also be noted that the TTad group that respondents were derived from is well characterised and more similar to the wider population of antidepressant users than in industry trials upon which previous estimated have been based. Our sample was more likely to be female, white and educated than other patients in these services, as is typical for study samples (Kennedy-Martin et al., 2015), although their baseline symptom scores were similar. We were unable to capture all clinical and sociodemographic variables, including psychiatric comorbidities. In the therapy service clinicians make a determination of the 'main presenting problem' (often anxiety or depression) with the service user and this may under-estimate the degree of co-morbidity.

As this was a retrospective survey responses were susceptible to recall bias and withdrawal severity may be prone to distortion in retrospect. There may be a selection bias towards people who have not responded to antidepressants and have therefore sought therapy, although GPs can prescribe antidepressants and refer to therapy at the same time. However, three-fifths of respondents reported that their antidepressants had improved their symptoms. Our method of sampling might under-estimate withdrawal effects because patients who returned to their medication (40 %) might have experienced only brief withdrawal effects. Previous surveys have been criticised for using unstructured reporting of symptoms (Jauhar et al., 2019), but we used a structured approach based on the widely-used DESS. However, as we used an abbreviated version of the DESS it is possible that we have missed some symptoms. Overall, a limitation to the measurement of withdrawal effects in general is the lack of objective measures, with assessment relying on self-report of subjective symptoms. We also did not have data on medication adherence, although it seems unlikely that people would misrepresent this significantly when answering a voluntary survey.

There is the risk that participants may attribute symptoms of relapse to withdrawal effects as there is an overlap between the symptoms of both conditions. However, it seems more likely the opposite would occur based on prior research (Read et al., 2018) and due to a general lack of awareness of withdrawal effects. To minimise mis-attribution we used a modified version of the standard DESS instrument that included key symptoms of withdrawal and also examined stringent definitions of withdrawal. For example, 42.6 % of participants met even the most stringent criteria of 4 or more 'non-emotional' symptoms (including headache, dizziness and nightmares). Although these 'non-emotional' symptoms might occur occasionally in people with anxiety and depressive disorders a previous analysis has found that these symptoms are much more common following antidepressant withdrawal (Moncrieff et al., 2024), emphasising their discriminatory nature.

The number of people who had used antidepressants for $>$ 24 months was relatively small ($N = 71$), and this may have impacted analyses of duration of use. However the relationship between duration of use and effect on withdrawal characteristics was strong and robust throughout multiple sensitivity analyses.

Respondents may also have misattributed ongoing mental health symptoms or incidental symptoms to withdrawal. To mitigate against this the survey specified that symptoms should be "either new onset or an increase" after stopping their antidepressant, so that these were not just reporting ongoing background symptoms. Furthermore, GAD-7 and PHQ-9 scores were not associated with any aspect of withdrawal (aside from a small difference in the mean number of weeks with withdrawal symptoms, in opposite directions), suggesting that mood state was not strongly associated with reported withdrawal experiences. They were also not associated with duration of prior treatment, suggesting that the severity of the underlying condition does not confound the apparent relationship between duration of use and risk and severity of withdrawal symptoms. However, depression and anxiety symptoms were measured at entry to the therapy service and not at the initiation of antidepressant treatment .

There is also a risk of 'nocebo' withdrawal effects which are symptoms that arise from patients' expectations of negative outcome when stopping medications. Our study did not include a group ceasing placebo so we were unable to evaluate the role of nocebo effects in this study which may inflate rates of withdrawal detected. Nocebo withdrawal effect have been found to vary from about 12 % to 17 % in studies, although they are likely to be less severe than physiological withdrawal symptoms (Henssler et al., 2024; Horowitz et al., 2023). Some physical withdrawal symptoms are common occurrences and may be associated with emotional disorders, but other symptoms, not usually associated with emotional disorders, were still commonly endorsed in our survey. For example, 28 % of our sample experience brain zaps, 27 % experienced muscle cramps, 27 % experienced nausea or vomiting, 24 % diarrhoea, and 30 % an unsteady gait.

5. Conclusion

Among a sample of primary care psychological therapy patients who had tried to stop an antidepressant, withdrawal experiences were common. The duration of prior use of antidepressants was identified as a risk factor for incidence, severity and duration of withdrawal symptoms, and ability to stop the medication. Few other characteristics were independently associated with withdrawal outcomes. Brief users ($\leq$6 months) reported mostly mild and brief symptoms. Longer term users ($>$24 months), reported mostly moderate or severe withdrawal effects (one-quarter severe). Almost one-third of long-term users reported symptoms that lasted for more than three months and four-fifths of these patients were unable to stop their antidepressant when they attempted to do so. Guidelines should be updated accordingly and patients informed of these risks when considering commencing, deciding on whether to continue and when stopping antidepressant treatment (Cooper et al., 2023; Read et al., 2023a, b). The increasing withdrawal risks with longer use provides one rationale to minimise long-term antidepressant prescribing in the population (Horowitz and Wilcock, 2022).

Ethical approval

Ethical approval was obtained through the London City and East Research Ethics Committee of the NHS Health Research Authority (20/PR/0423) ("WISE USE (antidepressant) survey," n.d.).

Funding

This study was funded by online crowdfunding and a seed grant from the University of Roehampton. The study was portfolio-adopted by the NIHR-funded Research and Development department at NELFT. These contributors had no say in the final form of the study or publication.

Contributions to study

MAH conceived and designed the study, wrote the ethics proposal, contributed to the protocol and wrote the first draft of the manuscript. JB and RS contributed to the protocol, preformed statistical analyses and substantially revised the manuscript. EA contributed to the protocol and revision of the manuscript. JD contributed to revision of the manuscript. JM supervised the project, contributed to the protocol and substantially revised the manuscript.

CRediT authorship contribution statement

Mark A. Horowitz: Writing – review & editing, Writing – original draft, Project administration, Methodology, Funding acquisition, Data curation, Conceptualization. **Joshua E.J. Buckman:** Writing – review & editing, Software, Methodology, Formal analysis. **Rob Saunders:** Writing – review & editing, Software, Methodology, Formal analysis,

Data curation. **Elisa Aguirre:** Writing – review & editing, Resources, Project administration. **James Davies:** Writing – review & editing, Funding acquisition. **Joanna Moncrieff:** Writing – review & editing, Supervision, Project administration, Methodology, Formal analysis, Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Mark Horowitz reports a relationship with Australian Government Medical Research Future Fund that includes: funding grants. Mark Horowitz reports a relationship with National Health and Medical Research Council that includes: funding grants. Mark Horowitz reports a relationship with various hospitals and universities that includes: speaking and lecture fees. Mark Horowitz reports a relationship with Outro Health that includes: consulting or advisory and equity or stocks. Joanna Moncrieff reports a relationship with various universities and hospitals that includes: speaking and lecture fees. Joanna Moncrieff reports a relationship with National Institute for Health and Care Research that includes: funding grants. Joanna Moncrieff reports a relationship with National Health and Medical Research Council that includes: funding grants. Joanna Moncrieff reports a relationship with Australian Government Medical Research Future Fund that includes: funding grants. Rob Saunders reports a relationship with Royal College of Psychiatrists that includes: funding grants. Rob Saunders reports a relationship with National Institute for Health and Care Research that includes: funding grants. Josh Buckman reports a relationship with National Institute for Health and Care Research that includes: funding grants. Joshua Buckman reports a relationship with Royal College of Psychiatrists that includes: funding grants. Joshua Buckman reports a relationship with UK Research and Innovation Medical Research Council that includes: funding grants. Royalties for books about psychiatric drugs - JM. Unpaid chairperson for the Critical Psychiatry Network -JM. Royalties from Wiley Blackwell for the Maudsley Deprescribing Guidelines: Antidepressants, Benzodiazepines, Gabapentinoids and Z-drugs -MAH. RS's institution has been compensated for consulting work he has conducted for NHS England regarding the Talking Therapies dataset, outside the present work - RS. JD reports being a practising psychotherapist and secretariat member of the previous All-Party Parliamentary Group for Prescribed Drug Dependence - JD. Royalties on authored and edited books -JD. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.psychres.2025.116497.

References

Baldwin, D.S., Montgomery, S.A., Nil, R., Lader, M., 2007. Discontinuation symptoms in depression and anxiety disorders. Int. J. Neuropsychopharmacol. 10, 73–84. https://doi.org/10.1017/S1461145705006358.

Cooper, R.E., Ashman, M., Lomani, J., Moncrieff, J., Guy, A., Davies, J., Morant, N., Horowitz, M., 2023. Stabilise-reduce, stabilise-reduce": a survey of the common practices of deprescribing services and recommendations for future services. PLoS One 18, e0282988. https://doi.org/10.1371/journal.pone.0282988.

Davies, J., Read, J., 2019. A systematic review into the incidence, severity and duration of antidepressant withdrawal effects: are guidelines evidence-based? Addict. Behav. 97, 111–121. https://doi.org/10.1016/j.addbeh.2018.08.027.

Fava, G.A., Cosci, F., 2019. Understanding and managing withdrawal syndromes after discontinuation of antidepressant drugs. J Clin Psychiatry. https://doi.org/10.4088/jcp.19com12794.

Fava, G.A., Gatti, A., Belaise, C., Guidi, J., Offidani, E., 2015. Withdrawal symptoms after selective serotonin reuptake inhibitor discontinuation: a systematic review. Psychother. Psychosom. 84, 72–81. https://doi.org/10.1159/000370338.

Gastaldon, C., Schoretsanitis, G., Arzenton, E., Raschi, E., Papola, D., Ostuzzi, G., Moretti, U., Seifritz, E., Kane, J.M., Trifirò, G., Barbui, C., 2022. Withdrawal syndrome following discontinuation of 28 antidepressants: pharmacovigilance analysis of 31,688 reports from the WHO Spontaneous Reporting Database. Drug Saf 45, 1539–1549. https://doi.org/10.1007/s40264-022-01246-4.

Gøtzsche, P.C., Demasi, M., 2023. Interventions to help patients withdraw from depression drugs: systematic review. medRxiv. https://doi.org/10.1101/2023.03.13.23287182.

Groot, P.C., van Os, J., 2021. Successful use of tapering strips for hyperbolic reduction of antidepressant dose: a cohort study. Ther Adv Psychopharmacol 11. https://doi.org/10.1177/20451253211039327, 20451253211039330.

Henssler, J., Schmidt, Y., Schmidt, U., Schwarzer, G., Bschor, T., Baethge, C., 2024. Incidence of antidepressant discontinuation symptoms: a systematic review and meta-analysis. Lancet Psychiatry 11, 526–535. https://doi.org/10.1016/S2215-0366(24)00133-0.

Horowitz, M., Taylor, D., 2024. The Maudsley Deprescribing Guidelines in Psychiatry: antidepressants, Benzodiazepines, Gabapentinoids and Z-drugs.

Horowitz, M., Wilcock, M., 2022. Newer generation antidepressants and withdrawal effects: reconsidering the role of antidepressants and helping patients to stop. Drug Ther. Bull. 60, 7–12. https://doi.org/10.1136/dtb.2020.000080.

Horowitz, M.A., Framer, A., Hengartner, M.P., Sørensen, A., Taylor, D., 2023. Estimating risk of antidepressant withdrawal from a review of published data. CNS Drugs 37, 143–157. https://doi.org/10.1007/s40263-022-00960-y.

Horowitz, M.A., Taylor, D., 2022. Distinguishing relapse from antidepressant withdrawal: clinical practice and antidepressant discontinuation studies. BJPsych Advances 28, 297–311. https://doi.org/10.1192/bja.2021.62.

Horowitz, M.A., Taylor, D., 2019. Tapering of SSRI treatment to mitigate withdrawal symptoms. The Lancet Psychiatry 6, 538–546. https://doi.org/10.1016/S2215-0366(19)30032-X.

Iacobucci, G., 2019. NICE updates antidepressant guidelines to reflect severity and length of withdrawal symptoms. BMJ 367, l6103. https://doi.org/10.1136/bmj.l6103.

Jauhar, S., Hayes, J., Goodwin, G.M., Baldwin, D.S., Cowen, P.J., Nutt, D.J., 2019. Antidepressants, withdrawal, and addiction; where are we now? J. Psychopharmacol. 33, 655–659. https://doi.org/10.1177/0269881119845799.

Johnson, C.F., Macdonald, H.J., Atkinson, P., Buchanan, A.I., Downes, N., Dougall, N., 2012. Reviewing long-term antidepressants can reduce drug burden: a prospective observational cohort study. Br. J. Gen. Pract. 62, e773–e779. https://doi.org/10.3399/bjgp12X658304.

Kennedy-Martin, T., Curtis, S., Faries, D., Robinson, S., Johnston, J., 2015. A literature review on the representativeness of randomized controlled trial samples and implications for the external validity of trial results. Trials 16, 495. https://doi.org/10.1186/s13063-015-1023-4.

Lewis, G., 2016. Antidepressant to prevent relapse in depression (ANTLER) protocol.

Lewis, Gemma, Marston, L., Duffy, L., Freemantle, N., Gilbody, S., Hunter, R., Kendrick, T., Kessler, D., Mangin, D., King, M., Lanham, P., Moore, M., Nazareth, I., Wiles, N., Bacon, F., Bird, M., Brabyn, S., Burns, A., Clarke, C.S., Hunt, A., Pervin, J., Lewis, Glyn, 2021. Maintenance or discontinuation of antidepressants in primary care. N. Engl. J. Med. 385, 1257–1267. https://doi.org/10.1056/NEJMoa2106356.

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. J. Clin. Psychiatry 75, 169–177. https://doi.org/10.4088/JCP.13m08443.

Moncrieff, J., Hobday, H., Sørensen, A., Read, J., Plöderl, M., Hengartner, M.P., Kamp, C. B., Jakobsen, J.C., Juul, S., Davies, J., Horowitz., M., n.d. Evidence on antidepressant withdrawal: a critique and re-analysis of a recent systematic review.

Moncrieff, J., Read, J., Horowitz, M.A., 2024. The nature and impact of antidepressant withdrawal symptoms and proposal of the discriminatory antidepressant withdrawal Symptoms Scale (DAWSS). Journal of Affective Disorders Reports 16, 100765. https://doi.org/10.1016/j.jadr.2024.100765.

National Institute for Health and Care Excellence, 2009. Depression in adults: Recognition and management. (NICE Guideline 90). NICE, London.

NHS Digital, 2023. Medicines Used in Mental Health England 2022/23 [WWW Document]. NHS Business Services Authority. URL. https://nhsbsa-opendata.s3.eu-west-2.amazonaws.com/mumh/mumh_annual_2223_v001.html (accessed 11.8.23).

NICE, 2022a. Depression in adults: treatment and management | guidance | NICE [WWW Document]. URL. https://www.nice.org.uk/guidance/ng222 (accessed 7.16.22).

NICE, 2022b. Medicines associated with dependence or withdrawal symptoms: safe prescribing and withdrawal management for adults | guidance | NICE [WWW Document]. URL. https://www.nice.org.uk/guidance/ng215/chapter/Recommendations (accessed 6.27.22).

Oehrberg, S., Christiansen, P.E., Behnke, K., Borup, A.L., Severin, B., Soegaard, J., Calberg, H., Judge, R., Ohrstrom, J.K., Manniche, P.M., 1995. Paroxetine in the treatment of panic disorder. A randomised, double-blind, placebo-controlled study. Br. J. Psychiatry 167, 36–42.

Public Health England, 2019. Dependence and withdrawal associated with some prescribed medicines. An evidence review [WWW Document]. URL. https://www.gov.uk/government/publications/prescribed-medicines-review-report (accessed 5.25.21).

Read, J., Cartwright, C., Gibson, K., 2018. How many of 1829 antidepressant users report withdrawal effects or addiction? Int. J. Ment. Health Nurs. 27, 1805–1815. https://doi.org/10.1111/inm.12488.

Read, J., Davies, J., 2024. Incidence of antidepressant withdrawal symptoms. Lancet Psychiatry. https://doi.org/10.1016/S2215-0366(24)00273-6.

Read, J., Gee, A., Diggle, J., Butler, H., 2019. Staying on, and coming off, antidepressants: the experiences of 752 UK adults. Addict. Behav. 88, 82–85. https://doi.org/10.1016/j.addbeh.2018.08.021.

Read, J., Lewis, S., Horowitz, M., Moncrieff, J., 2023a. The need for antidepressant withdrawal support services: recommendations from 708 patients. Psychiatry Res.

Read, J., Moncrieff, J., Horowitz, M.A., 2023b. Designing withdrawal support services for antidepressant users: patients' views on existing services and what they really need. J. Psychiatr. Res. 161, 298–306. https://doi.org/10.1016/j.jpsychires.2023.03.013.

Rosenbaum, J.F., Fava, M., Hoog, S.L., Ascroft, R.C., Krebs, W.B., 1998. Selective serotonin reuptake inhibitor discontinuation syndrome: a randomized clinical trial. Biol. Psychiatry 44, 77–87. https://doi.org/10.1016/S0006-3223(98)00126-7.

Saunders, R., Cape, J., Leibowitz, J., Aguirre, E., Jena, R., Cirkovic, M., Wheatley, J., Main, N., Pilling, S., Buckman, J.E.J., 2020. Improvement in IAPT outcomes over time: are they driven by changes in clinical practice? The Cognitive Behaviour Therapist 13, 1–15. https://doi.org/10.1017/s1754470x20000173.

Schatzberg, A.F., Blier, P., Delgado, P.L., Fava, M., Haddad, P.M., Shelton, R.C., 2006. Antidepressant discontinuation syndrome: consensus panel recommendations for clinical management and additional research. J. Clin. Psychiatry 67 (Suppl 4), 27–30.

Schatzberg, A.F., Haddad, P., Kaplan, E.M., Lejoyeux, M., Rosenbaum, J.F., Young, A.H., Zajecka, J., 1997. Serotonin reuptake inhibitor discontinuation syndrome: a hypothetical definition. Discontinuation consensus panel. J. Clin. Psychiatry 58 (Suppl 7), 5–10.

Sharma, A., Minh Duc, N.T., Luu Lam Thang, T., Nam, N.H., Ng, S.J., Abbas, K.S., Huy, N. T., Marušić, A., Paul, C.L., Kwok, J., Karbwang, J., de Waure, C., Drummond, F.J., Kizawa, Y., Taal, E., Vermeulen, J., Lee, G.H.M., Gyedu, A., To, K.G., Verra, M.L., Jacqz-Aigrain, É.M., Leclercq, W.K.G., Salminen, S.T., Sherbourne, C.D., Mintzes, B., Lozano, S., Tran, U.S., Matsui, M., Karamouzian, M., 2021. A consensus-based checklist for reporting of survey studies (CROSS). J. Gen. Intern. Med. 36, 3179–3187. https://doi.org/10.1007/s11606-021-06737-1.

Sir, A., D'Souza, R.F., Uguz, S., George, T., Vahip, S., Hopwood, M., Martin, A.J., Lam, W., Burt, T., 2005. Randomized trial of sertraline versus venlafaxine XR in major depression: efficacy and discontinuation symptoms. J. Clin. Psychiatry 66, 1312–1320. https://doi.org/10.4088/JCP.v66n1015.

Royal College of Psychiatrists, 2019. Position statement on antidepressants and depression. www.rcpsych.ac.uk/docs/default-source/improving-care/better-mh-policy/position-statements/ps04_19—antidepressants-and-depression.pdf.

StataCorp, 2023. Stata Statistical Software: release 18. Stata Statistical Software. https://doi.org/10.2307/2234838.

WISE USE (antidepressant) survey [WWW Document], n.d. Health Research Authority. URL https://www.hra.nhs.uk/planning-and-improving-research/application-summaries/research-summaries/wise-use-antidepressant-survey/ (accessed 5.14.23).

Zajecka, J., Fawcett, J., Amsterdam, J., Quitkin, F., Reimherr, F., Rosenbaum, J., Michelson, D., Beasley, C., 1998. Safety of abrupt discontinuation of fluoxetine: a randomized, placebo-controlled study. J. Clin. Psychopharmacol. 18, 193–197.

Zhang, M.-M., Tan, X., Zheng, Y.-B., Zeng, N., Li, Z., Horowitz, M.A., Feng, X.-Z., Wang, K., Li, Z.-Y., Zhu, W.-L., Zhou, X., Xie, P., Zhang, X., Wang, Y., Shi, J., Bao, Y.-P., Lu, L., Li, S.-X., 2024. Incidence and risk factors of antidepressant withdrawal symptoms: a meta-analysis and systematic review. Mol. Psychiatry 1–12.