

Barriers to discontinuing antidepressants in patients with depressive and anxiety disorders: a review of the literature and clinical recommendations

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Abstract: Use of antidepressants has recently increased, mainly caused by the increase of long-term users. Although evidence-based indications for long-term use are lacking, it is assumed that long-term use is unnecessary or undesirable in some patients. Perceived barriers to discontinuing antidepressants contribute to unnecessary or undesirable long-term use. Identifying barriers prior to, during and following discontinuation may enable strategies to overcome them.

This narrative review summarises relevant qualitative and quantitative articles on perceived barriers to discontinuing antidepressants and provides recommendations for clinical practice. We can conclude that implications for clinical practice are diverse and the most important barriers experienced by patients and physicians include the fear of relapse or recurrence, insufficient evaluation and monitoring, withdrawal symptoms, and actual relapse or recurrence.

Keywords: antidepressants, anxiety disorder, barrier, depressive disorder, discontinuation, long-term outcome, prognosis, recurrence, relapse

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Introduction

All around the world, use of antidepressants has risen tremendously in recent decades.^{1–3} This rise is not due to more patients using antidepressants, but rather to the same number of patients using antidepressants for longer time periods.^{2,4} When comparing antidepressant use in previous decades to more recent times, it becomes apparent that the median duration of antidepressant use has increased,^{3,5,6} and that the proportion of long-term users has risen.^{2,4,7} For example, in the UK, approximately 90% of prescriptions were for chronic or intermittent use,⁴ and in the US, two thirds of patients used antidepressants for over 2 years.²

In line with this increase in long-term antidepressant use, policy makers have called for the rational prescribing of medication to improve mental health care.¹ Antidepressants, especially selective serotonin reuptake inhibitors, are prescribed predominantly

for depressive and anxiety disorders.^{8–10} With these disorders, relapse or recurrence is common,^{11,12} and optimising long-term treatment to improve long-term prognosis is therefore certainly a rational strategy. However, an accurate and specified definition of the rational use of antidepressants following the initial treatment phase is lacking.

To date, it is unknown which patients have to continue antidepressants and which patients can discontinue.^{13,14} In the same vein, the optimum duration of antidepressant treatment is unknown.^{13,15} This is due to randomised discontinuation studies typically having a limited duration of treatment prior to discontinuation. In addition, observational studies with longer treatment durations often include chronic patients and thus might lead to bias favouring continuation treatment.¹⁶ Moreover, randomized discontinuation studies discontinue antidepressants within a limited time period.

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Consequently, discontinuation symptoms may occur more often, which may be difficult to differentiate from relapses.¹⁷

Due to this lack of evidence with regard to long-term strategies, guidelines rely on consensus. In general, guidelines recommend long-term use for patients with recurrent depressive episodes.¹⁸ However, guidelines for depressive and anxiety disorders vary regarding the recommended durations of treatment, definitions of recurrence, and on whether characteristics such as severity, residual symptoms, comorbidity, age or family history should be viewed as determining factors for long-term treatment.^{18,19}

Given the uncertainties surrounding optimal long-term strategies, it is important to realise that it is unknown to what extent the increased long-term use of antidepressants reflects inadequate *versus* appropriate care.^{4,20,21} Simply labelling long-term use as inappropriate reflects opinions rather than science and may stigmatise patients who are on long-term medication. Some research findings indeed indicate that long-term use is not simply the result of neglecting patients on long-term antidepressants, but is preserved for those with more severe^{6,21,22} or more recurrent illnesses.^{5,21}

However, it is assumed that in a proportion of patients, long-term antidepressant use is neither necessary nor wanted. Patients and physicians often encounter barriers to discontinuation.²³ Resolving these barriers may help in discontinuing antidepressant use. In this article, we add to existing literature by looking at barriers prior to discontinuation, during discontinuation and following discontinuation from a broad perspective, using both quantitative and qualitative data.

We searched the database PubMed for relevant literature for this narrative review, focusing on qualitative and quantitative studies on long-term use of antidepressants and discontinuation of antidepressants in patients with anxiety or depressive disorders.

We thereby take into account factors related to patients, type of antidepressants, course of anxiety or depressive disorders, physicians, and the health-care system. Subsequently, recommendations to facilitate discontinuation of antidepressants are presented that may be useful in clinical practice.

Barriers prior to discontinuation

Patients and physicians experience various barriers prior to discontinuation. First, it appears that regular evaluation of long-term antidepressant use is often lacking. In qualitative research, patients reported a lack of monitoring, with their physicians providing repeat prescriptions without a doctor's appointment.²⁴ This view is corroborated by a study using a primary care database. In this study, it appeared that in one fifth of patients who had been using antidepressants for 2 years, antidepressant use had not been reviewed in this period, even though all patients had visited their general practitioners (GPs) during that time.¹⁰ In addition, from a general practice study, it appeared that with longer durations of antidepressant use, the number of evaluations decreased.^{25,26} Qualitative research shows that patients expect their physicians to initiate this evaluation,^{23,24,27} whereas GPs expect patients to address the subject.⁸ This difference of opinion about who should initiate an evaluation may hamper regular evaluations. Additionally, interviews with physicians indicate that experiencing insufficient knowledge regarding discontinuation prevented these physicians from addressing discontinuation.²⁸

When patients and their physicians do discuss possible discontinuation, various barriers become apparent. Some patients, and to a lesser extent also physicians, incorrectly assume that anxiety and depression have a biochemical cause and that antidepressants are required to counter a deficiency in serotonin.^{23,29} Some patients also view these disorders as long-term conditions that, per definition, require long-term treatment.²³ GPs may think that discontinuation is not indicated in the case of a major life event.²⁴ A main barrier for both patients and physicians prior to discontinuation is the fear that they may become imbalanced after discontinuing medication, that withdrawal symptoms may occur, or that the disorder may recur.^{23,27,29–32} Often these fears are driven by previous experiences when attempts to discontinue antidepressants had failed.²⁹ To reduce risks of adverse consequences, physicians and patients may show reluctance in discontinuing.²⁸

Qualitative research further shows that sufficient supportive guidance of discontinuation is an issue of concern for both physicians and patients. Patients fear stopping without such guidance, tend to think that sufficient guidance is unavailable,^{30,33} and for some, this fear leads to continuing

antidepressants.³⁰ Physicians seem to differ in their view regarding whether they are equipped to guide antidepressant discontinuation. Whereas some physicians mention a lack of knowledge, missing policies on the long-term management of antidepressants, and report not having enough time to guide patients with discontinuation, other physicians consider themselves suitably equipped for guidance.²⁴ Where physicians feel comfortable with guiding the discontinuation process, their own patients may not agree.²⁴

Finally, patients' uncertainties about stopping are further fuelled by a lack of continuity in health care and health-care professionals, who sometimes disagree about discontinuing antidepressants.^{28,30}

Barriers during discontinuation

It appears that the intention or an advice to discontinue antidepressants does not always lead to the discontinuation actually being initiated. In addition, once started, discontinuation does not always succeed. A randomised controlled trial in primary care³³ focused on patients who took antidepressants for more than 9 months and who did not have an indication for continuation treatment according to clinical guidelines.³⁴ Patients and their GPs received a recommendation to discontinue antidepressants. It appeared that only half of the patients and GPs agreed to try, while only 6% actually discontinued and did not restart within a year. This proportion did not differ significantly from the proportion of patients with successful discontinuation in the control group who had not received any recommendation to discontinue. A barrier to start and to actually discontinue is also reflected in a randomised controlled trial by Scholten *et al.*³⁵ This included 71 remitted anxiety disorder patients who had decided to discontinue antidepressants. Of these 71 patients, 25% never started discontinuation and 38% started discontinuation but either did not complete the discontinuation process, or increased the dose following a decrease or following total discontinuation.³⁵

In a general practice study, 15,689 patients who were treated long-term with antidepressants were reviewed. This resulted in the policy to stop medication in 7% of the cases, and to reduce the dose in 12.8%. At three-month follow up, however, 24% of those who had stopped their antidepressants had restarted, while 13% of those who tapered down had increased the dose again.⁹ It is

possible that this process of discontinuation is hampered by patients' fear of relapse. Patients may notice that their equilibrium is disturbed by withdrawal symptoms which may be interpreted as relapse or recurrence of the disorder, or by actual relapse or recurrence.

Patients may experience withdrawal symptoms when an antidepressant is being tapered or stopped. As mentioned before, qualitative research showed that a fear of withdrawal symptoms^{23,27,29–32} may be a barrier to even starting discontinuation of antidepressants. During discontinuation, occurrence of withdrawal symptoms may hamper discontinuation. When withdrawal symptoms are severe or longlasting and require an intervention, reversing the dose reduction will relieve withdrawal symptoms,³⁶ thereby contributing to unwanted long-term use.

Withdrawal symptoms are diverse, varying from mild flu-like symptoms and moderate neuromuscular symptoms (ataxia, tremor and rigidity) to more severe symptoms such as suicidality, confusion and psychosis.³⁷ The prevailing view that withdrawal symptoms start 1–10 days after reducing the dose and usually disappear spontaneously in 2–3 weeks³⁸ has recently been challenged,³⁹ by reporting that the onset of withdrawal symptoms may occur up to 6 weeks after tapering the antidepressants and may not always remit spontaneously in 2–3 weeks.¹⁷ In the latter case, the withdrawal symptoms may become chronic and a new syndrome may develop, often referred to as 'persistent post-withdrawal syndrome'.³⁶ Thus, withdrawal symptoms may be severe and may persist for more than 1 year.⁴⁰ Beforehand, it is unknown which patients will experience withdrawal symptoms, although it is assumed that a higher dose, a higher blood level, a shorter half-life of the antidepressant and more abrupt tapering influence early onset and severity of withdrawal symptoms.⁴⁰

Quantifying the occurrence of withdrawal symptoms is difficult for various reasons. Despite recent attempts to classify withdrawal symptoms,⁴⁰ an evidence-based standard definition is lacking, resulting in definitions varying across studies. Consequently, withdrawal instruments that disregard severity report higher occurrence rates; moreover, as withdrawal symptoms are time dependent, the timing of the assessment substantially impacts the occurrence rate. Also, the duration that patients have been on antidepressants

might impact discontinuation rates. It is therefore not surprising that there is an ongoing debate on incidence rates and severity of withdrawal symptoms. Discontinuation studies did not systematically examine withdrawal symptoms.¹⁵ Based on methodologically diverse studies, the incidence of withdrawal symptoms in antidepressants was estimated to be 55%.¹⁷ Another review challenged these data, pointing to the heterogeneity of the studies included, which question the appropriateness of meta-analysing them.⁴¹ This latter review reported withdrawal proportions per antidepressant, for example 28.4–32.7% withdrawal symptoms when tapering paroxetine, the antidepressant causing most withdrawal symptoms. These authors also reviewed the proportion of 1.9–12.2% withdrawal rates found during the tapering of placebo pills and subsequently suggested that a ‘nocebo’ effect must be taken into account when tapering antidepressants.

Withdrawal syndromes may be confused with relapse or recurrence of the index disorder.⁴² As a result, the relapse or recurrences following discontinuation would have been overestimated, resulting in the estimate of the protective effect of maintenance medication being too optimistic.^{13,15,43} This phenomenon of misclassifying withdrawal as a relapse or recurrence appeared present in discontinuation studies of antipsychotics and stimulants, but is understudied with regard to discontinuation of antidepressants.⁴⁴ As a result, the magnitude of misclassification when discontinuing antidepressants needs verification. Whereas the occurrence of early ‘relapses’ suggests misclassification,⁴⁵ several randomised antidepressant discontinuation studies conducted sensitivity analyses by considering early relapse or recurrences and relapse or recurrences of short duration, and reported that conclusions remained similar (see, for example, the work by Batelaan *et al.*¹⁵).

As the issues described above have substantial implications for patients wishing to discontinue antidepressants, further research should systematically examine occurrence and severity of withdrawal symptoms over time, and should examine how to disentangle withdrawal and relapse or recurrence.

Barriers following discontinuation

As mentioned above, fear of relapse or recurrence following discontinuation is common in many patients, and also frequently mentioned by their

physicians. Recurrence has been examined in multiple studies in patients with a depressive or anxiety disorder who responded to antidepressants. In these studies, remitted patients were randomised to either continuing the antidepressant or switching to a placebo. Recurrence rates between these groups were subsequently compared. Examining recurrence rates in depression, Geddes *et al.*¹³ meta-analysed 31 studies, including a total of 4410 patients. The recurrence rate was 41% in patients who discontinued antidepressants *versus* 18% in patients who continued. Continuing antidepressants significantly reduced the odds of recurrence by around two thirds. A meta-analysis on anxiety disorders summarising 28 studies with a total of 5233 patients reported highly comparable results.¹⁵ Recurrence rates were 36.4% for the discontinuation group *versus* 16.4% for the continuation group. With treatment durations up to 1 year, discontinuation significantly increased the odds of relapse or recurrence, as compared with continuation (odds ratio 3.11). Most patients have a recurrence in the first months after discontinuation.⁴⁶ Although recurrence rates following discontinuation reflect that relapse or recurrence is substantial and therefore that the fear of relapse is realistic, it should be noted that the majority of patients can discontinue antidepressants without experiencing relapse or recurrence. Whether recurrence rates differ across settings is unknown.

Rather than recurrence percentages on a group level, for individual patients it is crucial to weigh their own risk of relapse or recurrence following discontinuation. Individuals with a higher *a priori* risk for relapse or recurrence (i.e. those with prior episodes or those with residual symptoms) have more to gain from the protective effects of antidepressants than those with a lower *a priori* risk for relapse or recurrence. Predictors of relapse or recurrence specifically related to discontinuation, i.e. separate from the naturalistic course, have received little attention and have not led to individualised recommendations.¹⁴

Where a relapse or recurrence occurs following discontinuation of antidepressants, the effectiveness of the antidepressant after reinstating this antidepressant is crucial. However, it appears that in a substantial minority of patients (16.5%), response to the antidepressant is insufficient when reinstated.³¹ Although it seems rational to weigh this aspect when discussing antidepressant discontinuation, to our knowledge neither

Table 1. Clinical implications to overcome barriers to discontinuation of antidepressants.**Starting treatment**

- (1) Consider psychological treatment first, even in severe patients, using a stepped-care approach
- (2) Give psycho-education about the working mechanism, side effects, expected recovery process
- (3) Discuss duration of treatment after remission and probabilities of maintaining remission or relapse after discontinuation

Prior to discontinuation

- (1) Weigh risks and benefits of discontinuation *versus* continuation
- (2) Explore fears, expectations and attributions of patients towards antidepressant discontinuation and taper methods
- (3) Discuss probabilities of maintaining remission or relapse after discontinuation again
- (4) Provide psycho-education about possibility of withdrawal symptoms when tapering antidepressants
- (5) Prepare discontinuation carefully:
 - (a) Agreement with patient on timing of follow-up consultations and monitoring of symptoms
 - (b) Determine an individualised dose-reduction programme: consider 'hyperbolic' dose reduction; consider substituting antidepressant with short half-life to one with long half-life; consider CBT or MBCT to facilitate discontinuation or to reduce relapse risks
 - (c) Ascertain that a relapse prevention plan is available

During discontinuation

- (1) Taper stepwise: agreement with patient on number of steps and time interval between tapering steps
- (2) Monitor withdrawal symptoms
- (3) In case of severe withdrawal symptoms: consider reversing the dose reduction and smaller steps in a later attempt

Following discontinuation

- (1) Monitor relapse in regular consultations
- (2) Stimulate self-monitoring in patients by using their relapse prevention plan
- (3) Ascertain that patients have access to rapid and appropriate health care in case of relapse
- (4) Consider psychological treatment in case of relapse

CBT, cognitive behavioural therapy; MBCT, mindfulness-based cognitive therapy.

patients nor physicians reported this aspect as a barrier to discontinuing treatment, which might be due to the ignorance of both patients and physicians regarding this topic.

Clinical recommendations to overcome barriers (Table 1)

Starting treatment

To prevent unwanted long-term use, caution should be exercised when starting pharmacological treatment. Psychological treatment may be an alternative evidence-based first-line treatment option for both anxiety and depressive disorders.⁴⁷ Although clinicians may believe that medication is indicated for 'severe' or 'comorbid' patients, the literature suggests that psychotherapy may also be effective in the treatment of more severe patients.^{48,49} Commencing treatment with psychological interventions, and reserving antidepressants for recurrent or treatment-resistant patients implicates a stepped-care strategy. An 8-month randomised controlled trial in 163

patients with an anxiety or depressive disorder in primary and secondary care⁵⁰ showed that stepped-care algorithms can be superior to treatment as usual. Moreover, stepped-care algorithms are most likely cost-effective, as was shown in a modelling study examining the cost-effectiveness of stepped-care algorithms for depressive disorders *versus* care as usual.⁵¹ Since a significant proportion of antidepressants are prescribed in general practice, continuing education of GPs and their patients in tandem, on the stepped-care approach, is needed.

Even when adhering to a stepped-care guideline, starting antidepressant treatment may be indicated or justified. Regular psycho-education in the first consultation includes information on the working mechanism of antidepressants, side effects, the expected recovery process, the expected treatment duration and the non-addictive nature of antidepressants.³¹ In addition, timely discussion of the pharmacological treatment following the acute phase also seems appropriate. Based on the review above, attention should be paid to the

recommended duration of continuing treatment following remission,²⁹ the relapse rates following discontinuation,^{13,15} and the possible occurrence of withdrawal symptoms when tapering the medication.³³ In addition, regular evaluations are required to monitor patients with long-term antidepressant use.²⁷ Patients and their physicians should agree on who initiates these evaluations.²⁴ The health-care system would benefit enormously from automatic warnings in the prescription system when an evaluation is due.²⁴

Prior to discontinuation

Information given in consultations appears to influence the decisions that patients make.³¹ When considering discontinuation, a thorough discussion between patients and their physicians, weighing probable risks and benefits of discontinuation *versus* continuation, is thus essential.

It appears that patients may have various and multiple fears influencing their willingness to discontinue.^{23,27–32} It is crucial that physicians actively ask whether such fears are present and, when possible, provide information. Patients should be told that although relapse risk is substantial, the majority of patients do not relapse when discontinuing antidepressants. In the same vein, information regarding withdrawal symptoms should be provided. This appears not to be standard procedure. For example, many patients indicate that they have never been informed about the possibility of withdrawal symptoms when lowering the dose.⁵²

Following a decision to discontinue the antidepressant, discontinuation should be prepared carefully.^{23,33} Because sufficient guidance of the discontinuation process and continuity of care is a concern frequently mentioned by patients, making appointments in advance may be helpful. Moreover, it appears that patients value an individualised dose-reduction programme and relapse prevention plan.²³ Therefore, patients should be encouraged to make a relapse prevention plan and discuss this with their physician.

During discontinuation

Once the process of tapering has started, the physician should opt for a rational tapering regime to limit the presence and severity of withdrawal symptoms.⁴⁰ Surprisingly, rational tapering has received little scientific attention as a result of which of the

recommendations following below reflect either practice-based advice or novel developments.

Tapering should be done in a stepwise manner, in time intervals of at least 4 weeks (for fluoxetine, 3 months). Where withdrawal symptoms have not disappeared by that time, the interval should be extended. Typically, five or more steps are needed to taper, thus resulting in a lengthy tapering period of multiple months. Antidepressants with a shorter half-life are associated with more severe withdrawal symptoms during dose reductions. Some authors therefore propose substituting such an antidepressant with an equivalent dose of an antidepressant with a long half-life first (such as fluoxetine), and subsequently tapering this antidepressant.⁴⁰ Some patients may not feel well when stopping the antidepressant altogether. In those cases, reducing the dose to a ‘minimal effective dose’ may still be worthwhile, for example, to reduce side effects and medication costs.

Currently, tapering is usually conducted using linear dose reductions (for example: 20–15–10–5–0 mg citalopram). However, linear dose reductions do not result in a gradual reduction of the occupancy of the serotonin transporter in the striatum.⁴⁰ By contrast, using a so-called ‘hyperbolic’ dose reduction (for example: 20–9.1–5.4–3.4–2.3–1.5–0.8–0.3 mg citalopram) would reduce the serotonin transporter occupancy gradually and is considered to substantially reduce withdrawal symptoms.⁴⁰ This interesting development in rational tapering increments deserves further investigation.

Where dose reduction induces withdrawal symptoms too severe to tolerate, the dose reduction may be reversed. This usually leads to withdrawal symptoms vanishing quickly. In a later attempt to taper the medication, smaller and slower dose reductions are advised. Another option in the case of severe withdrawal symptoms is to temporarily add clonazepam, gabapentin or lamotrigine.³⁶ Because the benefits of these ‘add-ons’ have not yet been examined, in our opinion, this strategy should be reserved for third-line patients. Some research suggests that adding cognitive behavioural therapy (CBT) facilitates the discontinuation process. In a case series on panic disorder, in patients who were not in remission, CBT was provided with the aim of facilitating discontinuation. It helped all 18 patients discontinue antidepressants, and even yielded clinical improvement.⁵³ In a qualitative study in depressed patients who had

received CBT and antidepressants in the acute phase of the disorder, CBT reduced patients' dependency on antidepressants and thereby fuelled the intention to discontinue in some, and aided reducing or stopping the antidepressant in others.⁵⁴

Whether psychological interventions, provided during the discontinuation phase, reduce the risk of relapse following discontinuation is inconclusive. To date, only a few attempts have been conducted in guiding discontinuation with psychological interventions like mindfulness-based cognitive therapy (MBCT) and CBT. Promising results were found in a randomised controlled trial in which discontinuation with CBT was compared with discontinuation alone in 40 patients who had recovered from depression.^{55,56} Recurrence rates were 15% in the discontinuation-with-CBT group *versus* 35% in the discontinuation-alone group after 2 years. Benefits of adding CBT persisted after 6 years, although recurrence was prevalent in both conditions (50% in the discontinuation-with-CBT group *versus* 75% in the discontinuation-alone group). In another study, discontinuation plus MBCT was compared with discontinuation plus clinical management in 56 patients recovered from depression.⁵⁷ Recurrence was significantly lower in the discontinuation plus MBCT group (38%) *versus* the discontinuation plus clinical management group (60%), but again, substantial in both conditions. However, a randomised controlled trial examining discontinuation in remitted anxiety disorder patients did not find a preventive effect of adding CBT during discontinuation (recurrence was 67% in the CBT group *versus* 65% in the care-as-usual group). Also, in this study, recurrence rates were high.³⁵

Following discontinuation

Once discontinuation is successful, there is risk of relapse or recurrence. Since more than one third of the patients will have a recurrence,^{13,15} the majority occurring in the first months, monitoring relapse is crucial. The physician who guides discontinuation could either actively monitor the patient through regular consultations or offer the patient easy access to consultation. Like in psycho-education on relapse, emphasising the positive side of monitoring, (e.g. 'to see whether things are still going well') seems important. Self-monitoring by the patients can be done by using a relapse prevention plan in which personal risk factors, early signs of relapse, and interventions in

the case of recurrence are noted. Identifying early signs is essential to enable timely interventions. In the case of actual recurrence, patients should have access to rapid and appropriate health care. Depending on the health-care system, practitioner assistants in the GP's practice, GPs or psychiatrists can play an important role in providing the necessary care, keeping in mind psychological treatment as an alternative option to medication.

Conclusion

As follows from the various barriers described in this review, discontinuing antidepressants is not always easy. Due to a paucity of data, treatment guidelines do not provide evidence-based recommendations on discontinuation of antidepressants. As a result, all decisions about discontinuation will be surrounded by uncertainty. It is obvious that clinical practice would benefit considerably from clear guidelines, indicating which patients can safely discontinue, at what moment discontinuation is possible, and how it should be done. In view of the high numbers of patients using antidepressants long-term and the perceived barriers to discontinuation, research addressing discontinuation should be prioritised. Future research should focus on identifying which patients can discontinue and which patients should not, on the best timing of discontinuation, and on how to stop safely. Meanwhile, the weighing of the pros and cons of starting discontinuation must be made in conjunction with the patient in a shared decision-making process. When a decision to discontinue the antidepressant has been taken, psycho-education, careful planning, slow tapering and systematic monitoring of withdrawal symptoms and relapse is advised. It is fundamental to realise that irrespective of the tapering regimen offered, recurrences frequently occur over time, reflecting the chronic nature of depressive and anxiety disorders.

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The authors declare that there is no conflict of interest.

Ethical statement

Approval by an ethical committee was not required as no patients or human subjects participated in the production of this manuscript.

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References

1. Organisation for Economic Co-operation and Development/European Union. *Health at a glance: Europe*. State of health in the EU cycle. Brussels: OECD Publishing, Paris/European Union, 2018.
2. Mojtabai R and Olfson M. National trends in long-term use of antidepressant medications: results from the U.S. National Health and Nutrition Examination Survey. *J Clin Psychiatry* 2014; 75: 169–177.
3. Brett J, Karanges EA, Daniels B, *et al*. Psychotropic medication use in Australia, 2007 to 2015: changes in annual incidence, prevalence and treatment exposure. *Aust N Z J Psychiatry* 2017; 51: 990–999.
4. Moore M, Yuen HM, Dunn N, *et al*. Explaining the rise in antidepressant prescribing: a descriptive study using the general practice research database. *BMJ* 2009; 339: b3999.
5. McCrea RL, Sammon CJ, Nazareth I, *et al*. Initiation and duration of selective serotonin reuptake inhibitor prescribing over time: UK cohort study. *Br J Psychiatry* 2016; 209: 421–426.
6. Sihvo S, Wahlbeck K, McCallum A, *et al*. Increase in the duration of antidepressant treatment from 1994 to 2003: a nationwide population-based study from Finland. *Pharmacoepidemiol Drug Saf* 2010; 19: 1186–1193.
7. Huijbregts KM, Hoogendoorn AW, Slotje P, *et al*. Long-term and short-term antidepressant use in general practice: data from a large cohort in The Netherlands. *Psychother Psychosom* 2017; 86: 362–369.
8. Johnson CF, Macdonald HJ, Atkinson P, *et al*. Reviewing long-term antidepressants can reduce drug burden: a prospective observational cohort study. *Br J Gen Pract* 2012; 62: e773–e779.
9. Petty DR, House A, Knapp P, *et al*. Prevalence, duration and indications for prescribing of antidepressants in primary care. *Age Ageing* 2006; 35: 523–526.
10. Verhaak PFM, de Beurs D and Spreeuwenberg P. What proportion of initially prescribed antidepressants is still being prescribed chronically after 5 years in general practice? A longitudinal cohort analysis. *BMJ Open* 2019; 9: e024051.
11. Scholten WD, Batelaan NM, Penninx BWJH, *et al*. Diagnostic instability of recurrence and the impact on recurrence rates in depressive and anxiety disorders. *J Affect Disord* 2016; 195: 185–190.
12. Scholten WD, Batelaan NM, Van Balkom AJ, *et al*. Recurrence of anxiety disorders and its predictors. *J Affect Disord* 2013; 147: 180–185.
13. Geddes JR, Carney SM, Davies C, *et al*. Relapse prevention with antidepressant drug treatment in depressive disorders: a systematic review. *Lancet* 2003; 361: 653–661.
14. Berwian IM, Walter H, Seifritz E, *et al*. Predicting relapse after antidepressant withdrawal—a systematic review. *Psychol Med*. Epub ahead of print 27 October 2016. DOI: 10.1017/S0033291716002580.
15. Batelaan NM, Bosman RC, Muntingh A, *et al*. Risk of relapse after antidepressant discontinuation in anxiety disorders, obsessive-compulsive disorder, and post-traumatic stress disorder: systematic review and meta-analysis of relapse prevention trials. *BMJ* 2017; 358: j3927.
16. Gardarsdottir H, Egberts TC, Stolker JJ, *et al*. Duration of antidepressant drug treatment and its influence on risk of relapse/recurrence: immortal and neglected time bias. *Am J Epidemiol* 2009; 170: 280–285.
17. Davies J and Read J. A systematic review into the incidence, severity and duration of antidepressant withdrawal effects: are guidelines evidence-based? *Addict Behav* 2019; 97: 111–121.
18. Piek E, Van der Meer K and Nolen WA. Guideline recommendations for long-term treatment of depression with antidepressants in primary care—a critical review. *Eur J Gen Pract* 2010; 16: 106–112.
19. Bandelow B, Zohar J, Hollander E, *et al*. World Federation of Societies of Biological Psychiatry (WFSBP) guidelines for the pharmacological treatment of anxiety, obsessive-compulsive and posttraumatic stress disorders. *World J Biol Psychiatry* 2002; 3: 171–199.
20. Reid I, Cameron I and MacGillivray S. Increased prescription of antidepressants shows correction of inadequate duration of treatment of depression. *BMJ* 2014; 348: g228.
21. Ambresin G, Palmer V, Densley K, *et al*. What factors influence long-term antidepressant use in primary care? Findings from the Australian Diamond Cohort Study. *J Affect Disord* 2015; 176: 125–132.
22. Piek E, Kollen BJ, van der Meer K, *et al*. Maintenance use of antidepressants in Dutch

- general practice: non-guideline concordant. *PLoS One* 2014; 9: e97463.
23. Maund E, Dewar-Haggart R, Williams S, *et al.* Barriers and facilitators to discontinuing antidepressant use: a systematic review and thematic synthesis. *J Affect Disord* 2019; 245: 38–62.
 24. Bosman RC, Huijbregts KM, Verhaak PF, *et al.* Long-term antidepressant use: a qualitative study on perspectives of patients and GPs in primary care. *Br J Gen Pract* 2016; 66: e708–e719.
 25. Sinclair JE, Aucott LS, Lawton K, *et al.* The monitoring of longer term prescriptions of antidepressants: observational study in a primary care setting. *Fam Pract* 2014; 31: 419–426.
 26. Middleton H and Moncrieff J. ‘They won’t do any harm and might do some good’: time to think again on the use of antidepressants? *Br J Gen Pract* 2011; 61: 47–49.
 27. Leydon GM, Rodgers L and Kendrick T. A qualitative study of patient views on discontinuing long-term selective serotonin reuptake inhibitors. *Fam Pract* 2007; 24: 570–575.
 28. Bowers HM, Williams SJ, Geraghty AWA, *et al.* Helping people discontinue long-term antidepressants: views of health professionals in UK primary care. *BMJ Open* 2019; 9: e027837.
 29. Eveleigh R, Speckens A, Van Weel C, *et al.* Patients’ attitudes to discontinuing not-indicated long-term antidepressant use: barriers and facilitators. *Ther Adv Psychopharmacol* 2019; 9: 2045125319872344.
 30. Verbeek-Heida PM and Mathot EF. Better safe than sorry—why patients prefer to stop using selective serotonin reuptake inhibitor (SSRI) antidepressants but are afraid to do so: results of a qualitative study. *Chronic Illn* 2006; 2: 133–142.
 31. Malpass A, Shaw A, Sharp D, *et al.* “Medication career” or “Moral career”? The two sides of managing antidepressants: a meta-ethnography of patients’ experience of antidepressants. *Soc Sci Med* 2009; 68: 154–168.
 32. Ridge D, Kokanovic R, Broom A, *et al.* “My dirty little habit”: patient constructions of antidepressant use and the ‘crisis’ of legitimacy. *Soc Sci Med* 2015; 146: 53–61.
 33. Wentink C, Huijbers MJ, Lucassen PL, *et al.* Enhancing shared decision making about discontinuation of antidepressant medication: a concept-mapping study in primary and secondary mental health care. *Br J Gen Pract* 2019; 69: e777–e785.
 34. Eveleigh R, Muskens E, Lucassen P, *et al.* Withdrawal of unnecessary antidepressant medication: a randomised controlled trial in primary care. *BJGP Open* 2018; 1: bjgpopen17X101265.
 35. Scholten WD, Batelaan NM, Van Oppen P, *et al.* The efficacy of a group CBT relapse prevention program for remitted anxiety disorder patients who discontinue antidepressant medication: a randomized controlled trial. *Psychother Psychosom* 2018; 87: 240–242.
 36. Chouinard G and Chouinard VA. New classification of selective serotonin reuptake inhibitor withdrawal. *Psychother Psychosom* 2015; 84: 63–71.
 37. Fava GA, Gatti A, Belaise C, *et al.* Withdrawal symptoms after selective serotonin reuptake inhibitor discontinuation: a systematic review. *Psychother Psychosom* 2015; 84: 72–81.
 38. Jha MK, Rush AJ and Trivedi MH. When discontinuing SSRI antidepressants is a challenge: management tips. *Am J Psychiatry* 2018; 175: 1176–1184.
 39. Hengartner MP, Davies J and Read J. How long does antidepressant withdrawal typically last? *Am J Psychiatry* 2019; 176: 487.
 40. Horowitz MA and Taylor D. Tapering of SSRI treatment to mitigate withdrawal symptoms. *Lancet Psychiatry* 2019; 6: 538–546.
 41. Jauhar S and Hayes J. The war on antidepressants: what we can, and can’t conclude, from the systematic review of antidepressant withdrawal effects by Davies and Read. *Addict Behav* 2019; 97: 122–125.
 42. Fava GA and Belaise C. Discontinuing antidepressant drugs: lesson from a failed trial and extensive clinical experience. *Psychother Psychosom* 2018; 87: 257–267.
 43. Borges S, Chen YF, Laughren TP, *et al.* Review of maintenance trials for major depressive disorder: a 25-year perspective from the US food and drug administration. *J Clin Psychiatry* 2014; 75: 205–214.
 44. Récalt AM and Cohen D. Withdrawal confounding in randomized controlled trials of antipsychotic, antidepressant, and stimulant drugs, 2000–2017. *Psychother Psychosom* 2019; 88: 105–113.
 45. Greenhouse JB, Stangl D, Kupfer DJ, *et al.* Methodologic issues in maintenance therapy clinical trials. *Arch Gen Psychiatry* 1991; 48: 313–318.

46. Allgulander C, Florea I and Huusom AKT. Prevention of relapse in generalized anxiety disorder by escitalopram treatment. *Int J Neuropsychopharmacol* 2006; 9: 495–505.
47. National Institute for Health and Care Excellence. First-choice antidepressant use in adults with depression or generalised anxiety disorder, <https://www.nice.org.uk/advice/ktt8> (2015, accessed November 2019).
48. Furukawa TA, Weitz ES, Tanaka S, *et al.* Initial severity of depression and efficacy of cognitive-behavioural therapy: individual-participant data meta-analysis of pill-placebo-controlled trials. *Br J Psychiatry* 2017; 210: 190–196.
49. Driessen E, Cuijpers P, Hollon SD, *et al.* Does pretreatment severity moderate the efficacy of psychological treatment of adult outpatient depression? A meta-analysis. *J Consult Clin Psychol* 2010; 78: 668–680.
50. Oosterbaan DB, Verbraak MJPM, Terluin B, *et al.* Collaborative stepped care v. care as usual for common mental disorders: 8-month, cluster randomised controlled trial. *Br J Psychiatry* 2013; 203: 132–139.
51. Meeuwissen JAC, Feenstra TL, Smit F, *et al.* The cost-utility of stepped-care algorithms according to depression guideline recommendations – results of a state-transition model analysis. *J Affect Disord* 2019; 242: 244–254.
52. Read J and Williams J. Adverse effects of antidepressants reported by a large international cohort: emotional blunting, suicidality, and withdrawal effects. *Curr Drug Saf* 2018; 13: 176–186.
53. Whittal ML, Otto MW and Hong JJ. Cognitive-behavior therapy for discontinuation of SSRI treatment of panic disorder: a case series. *Behav Res Ther* 2001; 39: 939–945.
54. Bayliss P and Holttum S. Experiences of antidepressant medication and cognitive-behavioural therapy for depression: a grounded theory study. *Psychol Psychother* 2015; 88: 317–334.
55. Fava GA, Grandi S, Zielesny M, *et al.* Cognitive behavioral treatment of residual symptoms in primary major depressive disorder. *Am J Psychiatry* 1994; 151: 1295–1299.
56. Fava GA, Rafanelli C, Grandi S, *et al.* Six-year outcome for cognitive behavioral treatment of residual symptoms in major depression. *Am J Psychiatry* 1998; 155: 1443–1445.
57. Segal ZV, Bieling P, Young T, *et al.* Antidepressant monotherapy vs sequential pharmacotherapy and mindfulness-based cognitive therapy, or placebo, for relapse prophylaxis in recurrent depression. *Arch Gen Psychiatry* 2010; 67: 1256–1264.