

## Review Article

# Discontinuation strategies and long-term outcome of antidepressant medications

Mohammad A. Bakhiader<sup>1\*</sup>, Ibrahim Alsultan<sup>2</sup>, Abdulrahman Alelowi<sup>3</sup>, Mohammed Aloufi<sup>4</sup>, Saleh Almatrafi<sup>4</sup>, Fahad Aljohani<sup>4</sup>, Tariq Almuzaini<sup>5</sup>, Hasan Shalaby<sup>6</sup>, Zobaidah Abuhawi<sup>7</sup>, Reyam Nassif<sup>8</sup>, Shadi Showaihi<sup>9</sup>

<sup>1</sup>Department of Psychiatry, Al Thager Hospital, Jeddah, Saudi Arabia

<sup>2</sup>College of Pharmacy, King Saud University, Riyadh, Saudi Arabia

<sup>3</sup>Department of Pharmaceutical Care, Ministry of Health, Medina, Saudi Arabia

<sup>4</sup>Assistant Ministry Office, First Health Cluster, Medina, Saudi Arabia

<sup>5</sup>Department of Pharmaceutical Care, Prince Sultan Armed Forces Hospital, Medina, Saudi Arabia

<sup>6</sup>College of Medicine, Umm Al-Qura University, Mecca, Saudi Arabia

<sup>7</sup>Department of Pharmacy, Aseer Central Hospital, Abha, Saudi Arabia

<sup>8</sup>College of Medicine, Ibn Sina National College, Jeddah, Saudi Arabia

<sup>9</sup>College of Medicine, King Khalid University, Aseer, Saudi Arabia

**Received:** 06 November 2023

**Accepted:** 10 November 2023

### \*Correspondence:

Dr. Mohammad A. Bakhiader,

E-mail: moh.bakhaidar@gmail.com

**Copyright:** © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

## ABSTRACT

In terms of the treatment of depression, it is proven by many research that antidepressant drug has a significant impact on the treatment of depression patients. They can make them feel better and cope with their challenges. However, discontinuing these medications can be challenging due to concerns such as relapse, withdrawal symptoms, recurrence, and patient preferences. In this paper, we conducted a review of research on strategies for stopping antidepressants. Explored their long-term effects. By analyzing randomized controlled trials, cohort studies, systematic reviews, and meta-analyses, we gained insights into discontinuation methods and the extended impact of antidepressant use. Findings from quality evidence suggest that abruptly stopping antidepressants increases the risk of relapse or recurrence compared to reducing dosage or continuing with medication. Similarly, reducing dosage gradually helps in decreasing the risk and severity of withdrawal symptoms when compared to discontinuation or continued use without tapering off. Furthermore, psychological interventions like therapy or mindfulness-based cognitive therapy are identified as a best protocol for preventing relapse or recurrence after discontinuing antidepressants. These interventions are found to be particularly effective for patients experiencing symptoms or having risk factors. Additionally, although there is evidence regarding the long-term outcomes of using antidepressants beyond two years, some studies suggest that additional interventions such as patient education, shared decision-making processes monitoring progress, and providing feedback can assist in supporting successful discontinuation by improving adherence and patient satisfaction. In summary, stopping antidepressant medication is a process that necessitates assessment.

**Keywords:** Antidepressants, Antidepressant medications, Discontinuation strategies, Long-term outcomes, Depression

## INTRODUCTION

Throughout the world, physiological conditions are currently creating a negative impact which is not much

focused. Among all the psychological illness depression is one of the common issues which is causing problems for millions of individuals worldwide. According to the World Health Organization, depression stands as the cause of

disability. Ranks fourth when it became one of the overall global burden conditions.<sup>1,2</sup> Depression is characterized by lasting feelings of sadness, loss of interest or enjoyment, low self-esteem, guilt, hopelessness, difficulty sleeping, fatigue, changes in appetite, restlessness or slowed movements, trouble concentrating or remembering things well as thoughts or behaviors related to self-harm. It can hinder interactions, occupational performance, and physical health. Increase susceptibility to various medical conditions. Some individuals may require medication to assist them with their health concerns, like depression or anxiety.<sup>3-5</sup> To control this depression, the drug used for treating this is known as antidepressants. They can alter brain function by influencing chemicals associated with our emotions, sleep patterns, appetite, cognition, and behavior. There are types of antidepressants that operate in manners. Antidepressants can enhance the quality of life for individuals with health problems by promoting feelings of happiness, calmness, restfulness, increased appetite, heightened energy levels, improved focus, and better overall functioning.<sup>6,7</sup> Though the names might sound complex, they describe how these medications impact brain chemicals. By improving happiness levels, promoting a sense of calmness and restfulness, increasing appetite and energy levels, enhancing motivation and focus capabilities, and facilitating functionality, antidepressants can significantly enhance the quality of life for individuals struggling with depression.<sup>8</sup> However, discontinuing these medications can pose challenges for patients due to factors. One such factor is the risk of relapse or recurrence; Relapse refers to the return of symptoms during or after treatment phases, while recurrence signifies the onset of a depressive episode following a period of recovery. The chances of experiencing a relapse or recurrence depend on factors, including the number and intensity of episodes, how they last, the presence of symptoms or other health conditions, and how long antidepressants have been taken. Research indicates that within a year after discontinuing antidepressants, relapse rates can vary between 20% and 80%, while recurrence rates, within two years, can range from 10% to 40%. Withdrawal symptoms refer to the emergence. Worsening of psychological symptoms when reducing or discontinuing antidepressant use. Research conducted on 1,431 people who have depression revealed a finding. It showed that individuals who used antidepressants for, than two years had a risk of experiencing a relapse compared to those who used them for a shorter duration.<sup>9</sup> Additionally, the study found a connection between long term use of antidepressants and an increased likelihood of developing diabetes as higher mortality rates after the two years follow up period. It is worth noting that withdrawal symptoms may vary depending on factors, like the type, dosage and duration of antidepressant usage.<sup>10</sup> It also depends on how the medication is discontinued, susceptibility, and patient tolerance. Withdrawal symptoms can vary in their nature, severity, and duration. Experienced symptoms include flu sensations, trouble sleeping, nausea, headaches, dizziness, anxiety, irritability, mood changes, tingling sensations ("pins and needles"), electric shock-like feelings, and

others. Typically, these symptoms start within a day after stopping antidepressant use. It may persist for a few weeks or even months in some cases. Patients frequently decide whether to continue or discontinue taking antidepressants based on their preferences and beliefs. Various factors are taken into account during this decision-making process, including perceived benefits of the medication and concerns regarding potential drawbacks. Some individuals may consider the positive effects of medication compared to any harm it could cause.<sup>11,12</sup> Moreover, personal perceptions regarding the necessity or reliance on antidepressant treatment can significantly influence this decision-making process. While some patients may feel that these medications are essential for their well-being, others may see them as a solution that can be gradually phased out when appropriate. The perception of stigma or shame associated with using antidepressants can also play a role in shaping patient's choices. The fear of societal judgment or self-stigmatization may lead some individuals to either persist with or discontinue their medication regimen. Furthermore, considerations of control and autonomy over one's mental health can factor into these decisions. Patients may assess whether continued antidepressant use aligns with their sense of self-determination and control, impacting their motivation to adhere to or discontinue treatment. The objective of this research is to examine the existing body of knowledge on the methods used for stopping antidepressant medications and the long-term effects they have.

## METHODS

For this review, we conducted a search for existing review on the topic of discontinuation strategies and long-term outcomes of antidepressant medications on 01 October 2023. For our study, we searched across databases, including Medline, PubMed, PsycINFO, and Cochrane Library. In each database, we utilized medical subject headings as relevant terms. Our search encompassed keywords such as antidepressants, discontinuation, withdrawal, relapse, recurrence, and more. Additionally, we manually searched Google Scholar for information. For this, we looked through the necessary references of the retrieved papers for additional sources. To ensure the quality of our review, we applied inclusion criteria, such as excluding papers published before 2008 or after 2023 and preferring English language publications. We did not apply any restrictions based on age or publication type.

## DISCUSSION

The discontinuation of antidepressant medications involves a nuanced approach, considering factors like abrupt versus gradual discontinuation, psychological interventions, other interventions, and combination interventions. Suddenly stopping antidepressants as opposed to reducing or continuing them seems to have a chance of relapse or recurrence. Gradual discontinuation, on the other hand, demonstrates potential benefits in reducing the risk and severity of withdrawal symptoms.

Psychological interventions are crucial in preventing a relapse or recurrence of symptoms after stopping antidepressant medication.<sup>13,14</sup> Both cognitive behavioral therapy and mindfulness-based cognitive therapy show promise for individuals who continue to experience symptoms or have significant risk factors. Other interventions, such as patient education and shared decision-making, have demonstrated the potential to facilitate discontinuation and improve adherence or satisfaction. However, the effectiveness of monitoring, feedback, motivational interviewing, self-help materials, or online programs remains inconclusive, warranting further investigation. Integrating other approaches, in combination with interventions, can offer added advantages in preventing relapse or recurrence for individuals who experience recurrent depression.

### ***Clinical manifestation***

Antidepressant medications are commonly prescribed for depressed conditions, and when it comes to stopping them, there are important factors to consider. When patients decide to discontinue antidepressants, they often experience symptoms.<sup>15,16</sup> One common set of symptoms is known as antidepressant discontinuation syndrome. It can range from flu discomfort to dizziness, nausea, fatigue, irritability, mood swings, anxiety, and disrupted sleep patterns. To understand the severity and the duration of these symptoms, several factors like the specific antidepressant used, its half-life, and the tapering schedule followed. For some individuals stopping antidepressants may result in the return of symptoms related to their underlying condition. This manifestation underscores the importance of meticulous monitoring, particularly for patients with a history of recurrent or chronic depression. Additionally, discontinuation may have ramifications for physical health. Some research indicates that using antidepressants for extended periods may be linked to a likelihood of developing health conditions like cardiovascular disease, diabetes, and weight gain.<sup>17,18</sup> On the other hand, stopping the use of these medications might bring about alterations in metabolic factors, blood pressure, and body weight that require attention. Cognitive function may also be influenced by both long-term antidepressants use and discontinuation. When patients stop taking these medications, they may encounter symptoms such as difficulties with memory, attention, and thinking skills. However, it's crucial to differentiate between these effects and potential cognitive impairment linked to the health condition itself. Considering the impact of discontinuing antidepressants on a person's quality of life is vital. During or after discontinuation, patients might experience a decline in their well-being, satisfaction with life, and social functioning. The effect of using antidepressants on quality of life is intricate.<sup>19</sup> It can depend on factors like how they have been used and whether there are any side effects. On the side, understanding the long-term outcomes associated with antidepressant use is equally complex. The main aim of using them for a period is often to prevent relapses in

individuals who experience recurring depression. Taking medication consistently has been shown to decrease the likelihood of experiencing a relapse. However, determining the duration of maintenance treatment remains a topic of research and clinical discussion. Moreover, prolonged use of antidepressants may have consequences for health as studies have suggested that it could potentially increase the risk factors for conditions like obesity, diabetes, and cardiovascular disease. Therefore, it's crucial to monitor and manage these effects to ensure overall well-being. The connection between long-term use of antidepressants and cognitive function, as well as emotional well-being, is complex. Through these drugs relieving from the symptoms of depression and enhance functioning become easier. Some patients have reported experiencing cognitive side effects such as difficulties with memory. It is crucial for practice and patient care to understand this interaction. The impact of long-term use of antidepressants on a patient's quality of life is an aspect of their treatment. While these medications can improve social involvement, the occurrence of side effects and individual variations can affect the quality of life experienced by the patient. Hence it holds value to foster an approach in decision-making and maintain ongoing communication between patients and healthcare providers. This ensures an equilibrium between the advantages of treatment and the need to uphold a quality of life. Additionally, after prolonged use, some patients may express an interest in discontinuing their medication. In some cases, it is necessary for clinical management to carefully assess the patient's readiness for this step while evaluating both risks and benefits. Shared decision-making plays a role in determining the suitable course of action.

### ***Management***

Managing the discontinuation of antidepressant medications is a nuanced process that necessitates a patient-centered and adaptable approach. The following comprehensive guidance outlines essential considerations and strategies to navigate this intricate challenge effectively. While starting the entire assessment of the patient's antidepressant history. Examine the specific antidepressant type, dosage, and duration of use. Evaluate the patient's individual risk of relapse or recurrence during the discontinuation process based on their unique clinical context.<sup>20,21</sup> These factors encompass a range of elements such as, having encountered instances of depression concurrently managing residual symptoms or other health issues and relying on antidepressants, for an extended duration. Patient education is a fundamental step in empowering individuals to navigate the discontinuation journey. Providing comprehensive patient education should encompass an overview of the discontinuation process, potential withdrawal symptoms, and the available management strategies. This education equips patients with knowledge, fostering a sense of control and alleviating anxiety. Patient education can cover subjects such as the reasons and advantages of stopping antidepressants, the anticipated

timeline and stages of discontinuation, managing withdrawal symptoms recognizing signs of relapse or recurrence and taking preventive measures, and accessing resources and support for discontinuation. Collaborative process like shared decision making involves the patient in determining the most suitable discontinuation strategy. The clinician and patient decide whether abrupt cessation or gradual tapering aligns best with the patient's specific circumstances. The sudden stop of antidepressant use, known as cessation, involves stopping the medication within a few days. On the other hand, gradual tapering refers to reducing the dose of antidepressants over weeks or months. It is important to discuss the advantages and disadvantages of each approach, with the patient considering factors such as the type, dosage, and duration of antidepressant use as the patient's expectations and concerns. In cases where patients have lingering symptoms or a higher risk of relapse, interventions can be beneficial. In order to prevent relapse and recurrence, it is proven that cognitive behavioral therapy and mindfulness-based cognitive therapy have been playing very significant roles. The key is to tailor these interventions according to each patient's needs. There is another form of psychotherapy called CBT that aims to modify thoughts and behaviors that contribute to depression. MBCT refers to a form of psychotherapy that merges therapy (CBT) with mindfulness techniques.<sup>22</sup> Its goal is to cultivate awareness and acceptance of thoughts and emotions in individuals. Both CBT and MBCT have proven effective in assisting patients in dealing with withdrawal symptoms recognizing and handling factors that may lead to relapse or recurrence, and building coping mechanisms and resilience to boost self-belief and overall well-being. Other Interventions should also be explored as complementary tools to support the discontinuation process. These may encompass monitoring, feedback mechanisms, motivational interviewing, self-help materials, or online programs. While ongoing research assesses their effectiveness, these resources offer promise in providing additional guidance and support during discontinuation. Monitoring refers to regular assessment of the patient's symptoms, functioning, and progress during discontinuation. Feedback mechanisms refer to providing feedback to the patient on their performance or outcomes during discontinuation. Motivational interviewing refers to a counseling technique that enhances the patient's motivation and readiness for change. Self-help materials refer to books, leaflets, videos, or audio that provide information or advice on discontinuation. Online programs refer to web-based or mobile applications that deliver interactive or personalized interventions for discontinuation. Combination Interventions hold particular relevance for patients with recurrent depression. These interventions integrate psychological strategies with other approaches, offering a holistic perspective on discontinuation. This comprehensive approach may enhance efficacy in preventing relapse or recurrence. For example, a combination intervention may involve MBCT plus tapering support, CBT plus tapering support, or CBT plus motivational interviewing. Recognize that long-term

outcomes associated with antidepressant use extending beyond two years can have both positive and negative consequences. Continuously monitor the patient's progress and assess the evolving clinical landscape. It should be considered what impact on health as well as cognitive function, and also overall quality of life, it is essential to balance the advantages of continued use of antidepressants with their potential drawbacks. Long-term management involves weighing the benefits, such as preventing relapse or recurrence, improving mood stability and social functioning, and reducing risk. However, it's important to be aware that there can also be effects associated with term antidepressant use. These may include an increased risk of conditions like diabetes and cardiovascular disease, higher mortality rates, weight gain, hypertension, dyslipidemia (lipid levels) impairment, a decline in quality of life, and potential adverse events.

## CONCLUSION

Discontinuing antidepressants is a personalized process that requires evaluation and monitoring. There is no agreement on the duration of antidepressant treatment for depression or the best approach for gradually stopping their usage. Existing evidence of low to quality suggests that discontinuing antidepressants may increase the risk of relapse, recurrence, and withdrawal symptoms compared to a gradual tapering or ongoing treatment. Although there are several therapies available for this, psychological therapy showed a significant result which includes therapy like cognitive behavioral therapy or mindfulness-based cognitive therapy. There are also studies that provide evidence that interventions such as education or shared decision-making can assist in discontinuing antidepressants while improving adherence and satisfaction. However, it's crucial to keep in mind that using antidepressants for a period might have implications in terms of avoiding relapse or recurrence; they could provide advantages.

*Funding: No funding sources*

*Conflict of interest: None declared*

*Ethical approval: Not required*

## REFERENCES

1. Blackburn TP. Depressive disorders: Treatment failures and poor prognosis over the last 50 years. *Pharmacol Res Perspect*. 2019;7(3):e00472.
2. Reddy MS. Depression: the disorder and the burden. *Indian J Psychol Med*. 2010;32(1):1-2.
3. Parish AL, Gillis B, Anthamatten A. Pharmacotherapy for Depression and Anxiety in the Primary Care Setting. *J Nurse Pract*. 2023;19(4):104556.
4. Brody DJ, Pratt LA, Hughes JP. Prevalence of Depression Among Adults Aged 20 and Over: United States, 2013-2016. *NCHS Data Brief*. 2018(303):1-8.
5. Ettman CK, Abdalla SM, Cohen GH, Sampson L, Vivier PM, Galea S. Prevalence of Depression

- Symptoms in US Adults Before and During the COVID-19 Pandemic. *JAMA Netw Open*. 2020;3(9):e2019686.
6. Dzevlan A, Redzepagic R, Hadzisalihovic M, et al. Quality of Life Assessment in Antidepressant Treatment of Patients with Depression and/or Anxiety Disorder. *Mater Sociomed*. 2019;31(1):14-8.
7. Kurian BT, Greer TL, Trivedi MH. Strategies to enhance the therapeutic efficacy of antidepressants: targeting residual symptoms. *Expert Rev Neurother*. 2009;9(7):975-84.
8. Unützer J, Park M. Strategies to improve the management of depression in primary care. *Prim Care*. 2012;39(2):415-31.
9. Gabriel M, Sharma V. Antidepressant discontinuation syndrome. *Cmaj*. 2017;189(21):E747.
10. Horowitz MA, Framer A, Hengartner MP, Sørensen A, Taylor D. Estimating Risk of Antidepressant Withdrawal from a Review of Published Data. *CNS Drugs*. 2023;37(2):143-57.
11. Jin J, Sklar GE, Min Sen Oh V, Chuen Li S. Factors affecting therapeutic compliance: A review from the patient's perspective. *Ther Clin Risk Manag*. 2008;4(1):269-86.
12. Jimmy B, Jose J. Patient medication adherence: measures in daily practice. *Oman Med J*. 2011;26(3):155-9.
13. Van Leeuwen E, van Driel ML, Horowitz MA. Approaches for discontinuation versus continuation of long-term antidepressant use for depressive and anxiety disorders in adults. *Cochrane Database Syst Rev*. 2021;4(4):Cd013495.
14. Huijbers MJ, Wentink C, Simons E, Spijker J, Speckens A. Discontinuing antidepressant medication after mindfulness-based cognitive therapy: a mixed-methods study exploring predictors and outcomes of different discontinuation trajectories, and its facilitators and barriers. *BMJ Open*. 2020;10(11):e039053.
15. Henssler J, Heinz A, Brandt L, Bschor T. Antidepressant Withdrawal and Rebound Phenomena. *Dtsch Arztebl Int*. 2019;116(20):355-61.
16. Liu X, Momen NC, Molenaar N, Rommel AS, Bergink V, Munk-Olsen T. Discontinuation of antidepressants: Is there a minimum time on treatment that will reduce relapse risk? *J Affect Disord*. 2021;290:254-60.
17. Barnard K, Peveler RC, Holt RI. Antidepressant medication as a risk factor for type 2 diabetes and impaired glucose regulation: systematic review. *Diabetes Care*. 2013;36(10):3337-45.
18. Stutzman DL. Long-term use of antidepressants, mood stabilizers, and antipsychotics in pediatric patients with a focus on appropriate deprescribing. *Ment Health Clin*. 2021;11(6):320-33.
19. Kendrick T, Geraghty AWA, Bowers H, Stuart B, Leydon G, May C, et al. REDUCE (Reviewing long-term antidepressant use by careful monitoring in everyday practice) internet and telephone support to people coming off long-term antidepressants: protocol for a randomised controlled trial. *Trials*. 2020;21(1):419.
20. Kato M, Hori H, Inoue T, Iga J, Iwata M, Inagaki T, et al. Discontinuation of antidepressants after remission with antidepressant medication in major depressive disorder: a systematic review and meta-analysis. *Mol Psychiatry*. 2021;26(1):118-33.
21. Marloes JH, Carolien W, Esther S, Jan S, Anne S. Discontinuing antidepressant medication after mindfulness-based cognitive therapy: a mixed-methods study exploring predictors and outcomes of different discontinuation trajectories, and its facilitators and barriers. *BMJ Open*. 2020;10(11):e039053.
22. Hofmann SG, Gómez AF. Mindfulness-Based Interventions for Anxiety and Depression. *Psychiatr Clin North Am*. 2017;40(4):739-49.

**Cite this article as:** Bakhiader MA, Alsultan I, Alelowi A, Aloufi M, Almatrafi S, Aljohani F, et al. Discontinuation strategies and long-term outcome of antidepressant medications. *Int J Community Med Public Health* 2023;10:5021-5.