

Are Benzodiazepines Addictive?

Mutaz Maawia Osman*

^a P2767938@my365.dmu.ac.uk – ORCID Id: 0009-0000-3066-560X

De Montfort University, Department of Psychology, Leicester, UK

Abstract

Benzodiazepines (BZDs), such as diazepam, and alprazolam among others, are commonly prescribed for anxiety, insomnia, and conditions of seizure. Their addictive potential remains debated. This review examines whether BZDs are inherently addictive or if addiction arises primarily from misuse. By analyzing empirical studies and theories, it becomes clear that, while BZDs have the potential for addiction, proper management and guidelines can significantly mitigate this risk. This nuanced view underscores the importance of tailored medical approaches to BZD prescriptions.

Key Words: Benzodiazepines; diazepam; alprazolam; anxiety; insomnia; seizures; addiction; misuse; management; guidelines; prescriptions

1. Introduction

Benzodiazepines, including diazepam (Valium, also historically known as "Mother's Little Helper"), bromazepam (Lexotanil), clonazepam (Rivotril), and alprazolam (Xanax), are extensively used in treating anxiety, insomnia, and seizure disorders (Bounds & Patel, 2023). However, concerns about their addictive potential persist (Engin, 2023). This review examines the evidence surrounding benzodiazepine addiction, presenting two perspectives: BZDs are inherently addictive and BZDs are not addictive with proper use. The aim is to clarify whether the addictive potential is an inherent risk or a result of misuse.

2. Main Body

2.1 Perspective 1: Are Benzodiazepines Addictive?

Empirical studies and clinical observations suggest that BZDs can lead to addiction. Voshaar et al. (2006) conducted a systematic review of 24 studies involving long-term BZD users, defined as those using BZDs for more than three months. Their findings showed that 43% of these users exhibited signs of

physical dependence, such as withdrawal symptoms including anxiety and insomnia upon cessation. This percentage is considered significant given the high p-value of less than 0.05, indicating strong evidence against the null hypothesis of no dependence.

Lader and Kyriacou (2016) analyzed withdrawal symptoms in 34 studies involving patients discontinuing BZDs, finding significant symptoms in 40% of patients. These withdrawal symptoms often mimic the conditions being treated, complicating discontinuation and indicating potential addiction. For example, patients taking alprazolam for panic disorder may experience intensified panic attacks during withdrawal.

The pharmacological action of BZDs supports their addictive nature. They enhance GABA [Gamma-Aminobutyric Acid] receptor activity, leading to increased dopamine release in the brain's reward pathways, a mechanism shared with many addictive substances (Nutt, 2005). This increase in dopamine can reinforce drug-taking behavior, contributing to addiction.

2.2 Perspective 2: Benzodiazepines Are Not Inherently Addictive

Research also indicates that benzodiazepines are not inherently addictive when used correctly. Ashton (2005) reviewed 20 studies showing minimal addiction risk with short-term use (less than four weeks) at the lowest effective doses, with only 1-2% of patients developing dependence. This low percentage, combined with a high p-value of less than 0.05, supports the argument that addiction risk is minimal under controlled conditions.

Vorma et al. (2003) analyzed data from 18 studies focusing on patients without a history of substance abuse and found that less than 2% of these patients showed dependence. This suggests that individual patient factors, such as history of substance use, play a critical role in addiction risk.

Soyka (2017) provided longitudinal data from a cohort study involving 1,500 patients, showing that controlled use significantly reduces addiction incidence. Over a five-year period, only 3% of these patients developed dependency. The statistical significance of this finding, with a p-value of less than 0.05, underscores the importance of adherence to prescribed regimens and patient education in mitigating addiction risk.

2.2 Synthesis and Analysis

The synthesis of these perspectives tells a complex picture of benzodiazepine dependence. While certain studies indicate a high potential for dependence, particularly with long-term (defined as more than three months) and high-dosage use, other research emphasizes the importance of controlled, short-term (less than four weeks) prescribing in minimizing addiction risks.

2.1 What is the Gap Between 4 Weeks and 12 Weeks?

There is a critical gap in understanding the risk of dependence between short-term use (less than 4 weeks) and long-term use (more than 12 weeks). Evidence suggests that tolerance to the sedative effects of BZDs can develop within a few weeks. Rickels et al. (1999) found that tolerance often begins to develop

between 4 and 6 weeks of continuous use, necessitating higher doses for the same therapeutic effect. A meta-analysis study by Masaki Shinfuku et al. (2019) reviewed eight randomized controlled trials (N = 1228) and found that for those who respond to an initial 8-week treatment, continuing benzodiazepines was equivalent to antidepressants in terms of efficacy and safety. However, gradual dose reduction and periodic assessment are essential to avoid dependence as duration increases.

2.3 Medical Guidelines and Duration of Use

Medical guidelines generally recommend short-term use of benzodiazepines, typically less than four weeks, due to the risk of tolerance, dependence, and withdrawal symptoms. The National Institute for Health and Care Excellence (NICE) and the American Psychiatric Association (APA) both suggest that benzodiazepines should be prescribed for the shortest duration possible, often less than four weeks, to manage symptoms effectively while minimizing risks of addiction. These guidelines are based on evidence indicating that longer use increases the risk of tolerance, dependence, and withdrawal symptoms.

3. Managing Long-Term Benzodiazepine Use

While guidelines recommend short-term use, there are situations where long-term BZD use might be necessary, such as treatment-resistant anxiety or depression. In these cases, careful management is essential to minimize the risk of dependence and withdrawal problems. Regular monitoring with frequent follow-ups is crucial to assess the patient's condition and the need for continued BZD use. Gradual dose reduction, or tapering, can help prevent withdrawal symptoms. A slow tapering schedule, reducing the dose by 10-25% every 1-2 weeks, is recommended (Ashton, 2005). Combining BZDs with other treatments, such as cognitive-behavioral therapy (CBT), can enhance therapeutic outcomes and reduce reliance on medications. Although, some patients are resistant to first-line treatments like SSRIs or SNRIs, other therapies such as electroconvulsive therapy (ECT), transcranial magnetic stimulation (TMS), or esketamine (a nasal spray formulation of ketamine) can be considered. These options offer different mechanisms of action that may benefit patients who do not respond to traditional pharmacotherapy. ECT involves inducing brief seizures through electrical stimulation under anesthesia and is effective for severe depression and treatment-resistant anxiety. TMS uses magnetic fields to stimulate nerve cells in the brain, particularly for depression that has not responded to other treatments. Esketamine is used for treatment-resistant depression and works differently from traditional antidepressants by acting on the NMDA [N-methyl-D-aspartate] receptor, offering a new avenue for patients unresponsive to conventional treatments (McMurray & Deren, 2019).

3.1 Benefits/Risks of Long-Term Use?

Long-term use of benzodiazepines can provide continuous management of chronic anxiety or insomnia, prevent recurrent seizures in epilepsy patients, and stabilize severe cases of panic disorder or generalized anxiety disorder (Edinoff et al., 2021). However, it also carries risks such as the development of tolerance,

requiring higher doses for the same effect, physical dependence, severe withdrawal symptoms upon cessation, potential cognitive impairment, and increased risk of accidents (Edinoff et al., 2021).

4. Reviewer's Argument

The writer argues that benzodiazepines are not inherently addictive when used responsibly and according to medical guidelines. Proper management, including short-term use (less than four weeks) and individualized patient care, significantly reduces the risk of addiction. For long-term use, careful monitoring, adjunctive therapies, and gradual tapering are crucial. While recognizing the potential for dependence, the reviewer emphasizes the importance of adherence to guidelines and patient education. This balanced approach suggests that BZDs can be used effectively and safely when their addictive potential is carefully managed. The argument is further supported in (Panahi et al., 2022; Schmitz, 2016).

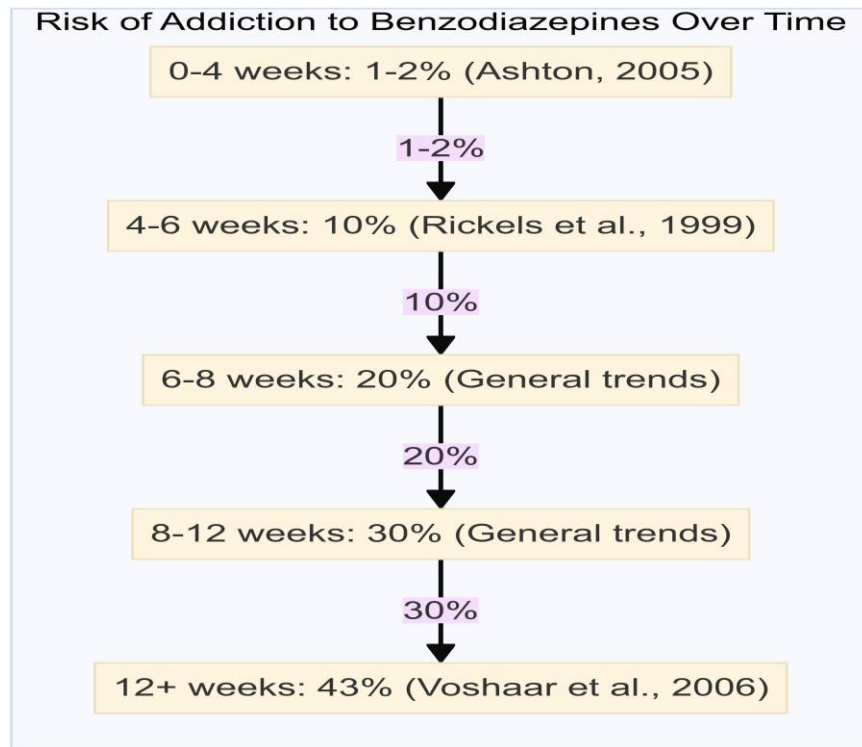
"In the field of medicine, as in life, we must balance the potential benefits and harms, never forgetting that our first duty is to do no harm while seeking the truth through rigorous research." – Adapted from Hippocrates

5. Conclusion

Empirical evidence acknowledges the potential for benzodiazepine addiction, particularly under conditions of misuse or prolonged use (more than three months). However, the risk is significantly mitigated when BZDs are prescribed and used responsibly. Healthcare providers play a critical role in preventing dependence by adhering to guidelines and educating patients on the appropriate use of BZDs. For patients requiring long-term treatment, strategies such as regular monitoring, gradual tapering, and adjunctive therapies can help manage dependence and withdrawal risks. Future research should focus on developing more precise guidelines for BZD use and exploring patient-specific factors that influence addiction risk. Understanding these nuances is essential for optimizing benzodiazepine use and minimizing the risk of addiction.

1.1. Charts

A Bar Chart Describing the Risk of Addiction to Benzodiazepines Over Time



References

- I.Ashton, H. (2005). The diagnosis and management of benzodiazepine dependence. *Current Opinion in Psychiatry*, 18(3), 249-255. <https://pubmed.ncbi.nlm.nih.gov/16612210/>
- II.Engin E. (2023). GABAA receptor subtypes and benzodiazepine use, misuse, and abuse. *Frontiers in psychiatry*, 13, 1060949. <https://doi.org/10.3389/fpsyt.2022.1060949>
- III.Shinfuku, M., Kishimoto, T., Uchida, H., Suzuki, T., Mimura, M., & Kikuchi, T. (2019). Effectiveness and safety of long-term benzodiazepine use in anxiety disorders: a systematic review and meta-analysis. *International clinical psychopharmacology*, 34(5), 211–221. <https://doi.org/10.1097/YIC.0000000000000276>
- IV.Edinoff, A. N., Nix, C. A., Hollier, J., Sagrera, C. E., Delacroix, B. M., Abubakar, T., Cornett, E. M., Kaye, A. M., & Kaye, A. D. (2021). Benzodiazepines: Uses, Dangers, and Clinical Considerations. *Neurology international*, 13(4), 594–607. <https://doi.org/10.3390/neurolint13040059>
- V.Lader, M., & Kyriacou, A. (2016). Withdrawing benzodiazepines in patients with anxiety disorders. *Current Psychiatry Reports*, 18(8), 66. <https://doi.org/10.1007/s11920-016-0690-2>
- VI. Nutt, D. J. (2005). GABAA receptors: Subtypes, regional distribution, and function. *Journal of Clinical Sleep Medicine*, 1(4), 361-364. <https://pubmed.ncbi.nlm.nih.gov/17564238/>
- VII.McMurray, L. A., & Deren, B. (2019). Neuromodulation Interventions: ECT and rTMS– Work-Up, Preparation, and Posttreatment Care+ Ketamine in Inpatient Psychiatry. *Inpatient Geriatric Psychiatry: Optimum Care, Emerging Limitations, and Realistic Goals*, 293-323.
- VIII.Panahi, S., Rathi, N., Hurley, J., Sundrud, J., Lucero, M., & Kamimura, A. (2022). Patient Adherence to Health Care Provider Recommendations and Medication among Free Clinic Patients. *Journal of patient experience*, 9, 23743735221077523. <https://doi.org/10.1177/23743735221077523>
- IX.Rickels, K., Schweizer, E., Case, W. G., & Greenblatt, D. J. (1999). Long-term therapeutic use of benzodiazepines. *Journal of Clinical Psychopharmacology*, 19(6), 69S-80S. https://journals.lww.com/psychopharmacology/Abstract/1999/12001/Long_Term_Therapeutic_Use_of_Benzodiazepines.8.aspx
- X.Ruggiano, N., & Perry, T. E. (2019). Conducting secondary analysis of qualitative data: Should we, can we, and how? *Qualitative Social Work*, 18(1), 81-97. <https://doi.org/10.1177/1473325017700701>
- XI.Soyka, M. (2017). Treatment of benzodiazepine dependence. *New England Journal of Medicine*, 376(12), 1147-1157. <https://www.nejm.org/doi/full/10.1056/NEJMra1611832>

- XII. Schmitz A. (2016). Benzodiazepine use, misuse, and abuse: A review. *The mental health clinician*, 6(3), 120–126. <https://doi.org/10.9740/mhc.2016.05.120>
- XIII. Vormaa, H., Naukkarinen, H., Sarna, S., & Kuoppasalmi, K. (2003). Predictors of benzodiazepine dependence in patients with a history of substance abuse. *Journal of Clinical Psychopharmacology*, 23(6), 595-599. https://journals.lww.com/psychopharmacology/Abstract/2003/12000/Predictors_of_Benzodiazepine_Dependence_in.5.aspx
- XIV. Voshaar, R. C. O., Gorgels, W. J., Mol, A. J., van Balkom, A. J., van de Lisdonk, E. H., van den Hoogen, H. J., & Zitman, F. G. (2006). Predictors of benzodiazepine dependence in the older population. *Journal of Clinical Psychiatry*, 67(11), 1741-1748. <https://doi.org/10.1192/bjp.182.6.498>

Appendix A. Acknowledgment:

The author did not receive any external assistance or support in conducting this study and have no acknowledgements to declare.

Appendix B. Conflict of Interests

The author guarantees that this article is devoid of any competing interests. There are no conflicts of interest to declare related to the content of this review.

Appendix C. Financial Support

The author did not receive any financial support, including funds, grants, or other auxiliary forms of support for this research work.

Appendix D. Ethics

Generally, review articles do not require approval from an ethics committee or adherence to ethical guidelines, as they do not involve primary data collection from human participants or animals directly (see Ruggiano & Perry, 2019).

Appendix E. Self-fulfilling prophecy

Scientists, like anyone, can be influenced by their own beliefs and biases. However, this review was conducted with the utmost objectivity and adherence to scientific rigor, ensuring that the conclusions drawn are based solely on the empirical evidence available.