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Benzodiazepines in the elderly: mechanisms, dependence risks, and clinical implications for geriatric practice

Abstract

Benzodiazepines (BZDs) remain among the most frequently prescribed psychotropic medications in geriatric populations, despite decades of evidence documenting their association with cognitive decline, falls, fractures, and dependence. This review synthesizes current understanding of BZD pharmacology, the mechanisms underlying tolerance and withdrawal, and the unique vulnerabilities of older adults to BZD-related adverse outcomes. We examine the epidemiological burden of BZD use in the elderly, the evidence linking prolonged exposure to dementia risk, and the clinical challenges of deprescribing in long-term users. Attention is given to the role of half-life in dependence severity, the phenomenon of paradoxical reactions in older patients, and the parallels between BZD and alcohol dependence that remain underexplored in geriatric research. We conclude with evidence-based recommendations for judicious prescribing, monitoring, and withdrawal management tailored to the geriatric population, emphasizing the need for non-pharmacological alternatives and systematic deprescribing protocols.

Keywords: Benzodiazepines, elderly, dependence, withdrawal, cognitive impairment, falls, deprescribing, GABA receptors, polypharmacy

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Introduction

Introduced in the 1960s as safer alternatives to barbiturates, benzodiazepines (BZDs) provide anxiolytic, hypnotic, muscle-relaxant, and anticonvulsant effects with a broader therapeutic index.[1] By enhancing gamma-aminobutyric acid (GABA)-mediated inhibition through specific receptor subtypes, they rapidly relieve anxiety, insomnia, and acute agitation.[2] Within a decade, BZDs had become among the most widely prescribed drugs worldwide, supported by marketing that presented them as safe, non-addictive substitutes for older sedatives.[3] This early confidence was later undermined by growing evidence of important drawbacks, including tolerance, psychological and physical dependence, and withdrawal syndromes that can sometimes require hospitalization.[4] In older adults, these risks are intensified by age-related physiological changes, polypharmacy, and frequent comorbidities. Although France introduced restrictions in 1991 limiting hypnotic prescriptions to 4 weeks and anxiolytics to 12 weeks, BZD use remains widespread in this population.[5] International studies report chronic BZD use in 10–30% of community-dwelling older adults and up to 40% of nursing home residents, often for years or even decades beyond recommended durations.[6]

This review examines the pharmacological basis of BZD effects and adverse outcomes in the elderly, the evidence for dependence and withdrawal in geriatric populations, and the clinical imperative for systematic deprescribing. We argue that BZD use in older adults represents a modifiable risk factor for cognitive decline, falls, fractures, and functional impairment, one that demands urgent attention from geriatricians, primary care physicians, and health systems.

Pharmacological properties and age-related vulnerabilities

Mechanisms of action

Benzodiazepines bind to an allosteric modulatory site on the GABAA receptor, increasing the frequency of GABA-induced chloride channel opening. As GABA is the brain's main inhibitory neurotransmitter, this effect promotes neuronal hyperpolarization and reduces excitability.[7] Compared with barbiturates, BZDs have a much wider therapeutic index; the ratio between lethal and therapeutic doses and fatal overdose from BZDs alone is uncommon. However, this perceived safety margin has often overshadowed clinically important non-fatal harms, particularly in older adults.[8]

Age-related pharmacokinetic and pharmacodynamic changes

The elderly exhibit multiple physiological changes that alter BZD disposition and response:[9]

Pharmacokinetic changes:

1. Reduced hepatic metabolism, particularly for BZDs undergoing oxidative metabolism (e.g., diazepam, chlordiazepoxide), leading to prolonged half-lives and accumulation[10]
2. Decreased renal clearance of active metabolites
3. -Increased volume of distribution for lipophilic drugs due to increased body fat ratio, prolonging elimination half-life
4. Reduced plasma albumin, increasing free drug concentration

Pharmacodynamic changes

Ageing is associated with reduced GABAA receptor density, changes in receptor subunit composition, and impaired homeostatic responses, all of which may increase sensitivity to BZD effects.[11] Increased blood-brain barrier permeability in some regions may further enhance central nervous system exposure.[12] Together, these changes lead to higher brain concentrations, prolonged drug effects, and greater sensitivity to BZDs in older adults, even at doses considered therapeutic in younger patients. Clinically, this narrows the effective window between benefit and adverse effects.[13]

Adverse effects in the geriatric population

Sedation and falls

Sedation is the most common dose-limiting adverse effect of BZDs in older adults. Although it may be therapeutic in younger patients with acute anxiety, sedation in the elderly reduces alertness, slows reaction time, and impairs postural stability, thereby markedly increasing the risk of falls.[14] A landmark meta-analysis showed that BZD use is associated with at least a 50% increase in hip fracture risk among older adults, with the greatest vulnerability occurring soon after treatment initiation.[15] This early risk reflects a period of neuroadaptation before tolerance to sedative effects develops. Short-acting BZDs, such as lorazepam and alprazolam, do not appear to offer better protection against falls than long-acting agents. Although some studies suggest that shorter-acting compounds may lessen daytime sedation, methodologically robust investigations in hospital and community settings have not shown a consistent safety advantage.[16] These findings challenge the common assumption that short-acting BZDs are preferable in older patients and support a cautious approach to all BZD prescribing in this population.

Cognitive Impairment and Dementia Risk

BZDs can cause anterograde amnesia by acting on hippocampal GABAA receptors, an effect that is more pronounced at higher doses and in older adults.[17] Although this property is useful in anesthesia and procedural sedation, it is problematic in outpatient geriatric care, where it may cause confusion, disorientation, and impaired memory consolidation. More concerning is the growing evidence linking long-term BZD exposure to cognitive decline and dementia. Cohort studies in adults aged 60–70 years suggest that prolonged use may increase dementia risk, with higher cumulative doses and longer treatment durations associated with greater risk.[18,19] Reported hazard ratios among long-term users are approximately 1.5–2.0 compared with non-users, even after adjustment for depression, anxiety, and concomitant medications. Causality remains debated, as reverse causation cannot be excluded; however, the consistency of findings across cohorts and the observed dose-response relationship support a possible neurotoxic effect.[20] Overall, the evidence suggests a limited but clinically relevant association between BZD use and dementia risk, while further research is needed to clarify causality. BZDs may also produce paradoxical reactions, including disinhibition, agitation, aggression, and behavioral activation, which can resemble alcohol intoxication.[21] These reactions are uncommon in younger patients but occur more often in older adults, especially those with cognitive impairment or dementia.[8] Clinical manifestations may include anxiety or panic, hostility, confusion, disorientation, wandering, purposeless behavior, or worsening behavioral and psychological symptoms of dementia. They are particularly problematic in nursing homes, where BZDs are often prescribed for behavioral disturbances. This may create an iatrogenic cycle in which BZD administration worsens agitation, leading to dose escalation.[21] High-potency, short-acting agents such as alprazolam and triazolam appear to carry the greatest risk.[22] Case series have also linked BZDs to suicide in older adults, particularly with flunitrazepam and nitrazepam, possibly through behavioral disinhibition and impaired judgment.[23,24] This risk is especially important given the high prevalence of depression and suicidal ideation in this population.

The phenomenon of dependence on the elderly

Defining Dependence

Dependence on BZDs encompasses three interrelated phenomena: *Tolerance*: Diminished therapeutic response over time, necessitating dose escalation to achieve the same effect. Tolerance to the sedative and hypnotic effects develops most rapidly (within days to weeks), while tolerance to anxiolytic effects develops more slowly and incompletely.[25]

Physical dependence

A state of neuroadaptation in which the central nervous system has adjusted to the presence of the drug, such that abrupt discontinuation precipitates a withdrawal syndrome. Physical dependence occurs even at therapeutic doses and is not equivalent to addiction, though it may contribute to it.[26]

Psychological dependence (addiction): Compulsive use despite harm, characterized by impaired control over drug use, craving, and continued use despite adverse consequences.[27] While psychological dependence is less common than physical dependence in elderly BZD users, it occurs and is frequently underrecognized in this population. The prevalence of BZD dependence on older adults is substantial. Among patients treated for six months or longer, up to 40% will experience withdrawal symptoms upon abrupt cessation.[28] In the elderly, the clinical presentation of withdrawal may differ from younger patients, with a higher prevalence of psychotic symptoms and delirium and a lower prevalence of severe physical symptoms such as seizures.[29] This atypical presentation often leads to misdiagnosis such as dementia, delirium, or primary psychiatric illness, delaying recognition of the underlying iatrogenic cause.

Factors influencing withdrawal severity

Several factors modulate the risk and severity of withdrawal in older adults:[30]

Half-Life

The pharmacokinetic profile of each BZD strongly influences the timing and severity of withdrawal.[31] With short- or intermediate-acting agents, such as alprazolam, lorazepam, and oxazepam, symptoms usually appear within 24–36 hours after discontinuation. The rapid fall in plasma concentrations produces an abrupt reversal of neuroadaptation, increasing the risk of severe and potentially dangerous withdrawal syndromes.[32] In contrast, long-acting BZDs, such as diazepam, chlordiazepoxide, and clorazepate, may delay withdrawal onset for 5–10 days, or even up to three weeks, because of the slow elimination of the parent drug and active metabolites.[33] This delayed onset may reduce the intensity of acute withdrawal, but prolonged exposure also increases the risk of accumulation, toxicity, and cognitive impairment. These distinctions are clinically important in older adults, in whom short-acting agents are often chosen to limit daytime sedation but may unintentionally increase dependence and withdrawal risk.

Dose and duration of use

Dependence risk increases with both dose and treatment duration. Higher doses produce faster and more marked neuroadaptation,

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but chronic use at therapeutic doses can also lead to dependence.[34] Duration is equally important: the risk rises after three months of continuous treatment, and after one year, 20–45% of patients may meet criteria for dependence. Among older adults who have taken BZDs for decades, dependence may approach 80–100%.[35] The speed of discontinuation is another key factor. Abrupt cessation carries substantially greater risk than gradual tapering, and the taper must be individualized according to the specific drug, duration of use, and patient characteristics. In older adults, slower dose reductions are usually needed because of reduced physiological reserve and greater vulnerability to withdrawal complications.[36]

Patient factors

Several patient characteristics influence withdrawal risk:[37] Premorbid personality: patients with passive-dependent or anxious traits may experience more severe psychological withdrawal symptoms.[38] History of alcohol or substance use: a prior history of alcohol dependence is associated with more severe BZD withdrawal, likely reflecting shared neurobiological vulnerability.[39] Cognitive status: elderly patients with pre-existing cognitive impairment are at higher risk for withdrawal delirium and psychotic symptoms.[40] Polypharmacy: Concurrent use of other central nervous system depressants (e.g., opioids, antipsychotics) increases the risk of withdrawal complications and complicates management.[41]

Evidence for dependence: from animal models to human studies

Animal models

Early animal studies faced challenges in demonstrating BZD dependence because, unlike opioids or barbiturates, BZDs did not reliably induce self-administration in simple oral consumption paradigms.[42] However, more sophisticated methodologies provided clear evidence of potential dependence: intravenous self-administration studies: rats trained to lever-press for drug infusions demonstrated that BZDs possess reinforcing properties, though less potent than barbiturates.[43] This finding confirmed that BZDs have abuse liability, even if lower than older sedatives. The development of flumazenil, a competitive BZD receptor antagonist, provided a powerful tool for demonstrating physical dependence. In baboons exposed to diazepam Flumazenil-precipitated withdrawal: The development of flumazenil, a competitive BZD receptor antagonist, provided a powerful tool for demonstrating physical dependence. In baboons exposed to diazepam (10 mg/kg/day for 14 weeks), administration of flumazenil precipitated an immediate withdrawal syndrome characterized by agitation, tremors, vomiting, and seizures.[44] This response, occurring within minutes of antagonist administration, definitively demonstrated that chronic BZD exposure produces profound neuroadaptation. Notably, the severity of precipitated withdrawal correlated with the duration and dose of diazepam exposure, confirming the dose-response relationship observed in human studies. Repeated episodes of withdrawal in animal models appear to "kindle" the nervous system, producing progressively more severe withdrawal syndromes with each cycle of drug exposure and discontinuation.[45] This phenomenon suggests that repeated attempts at discontinuation may, paradoxically, increase the difficulty of eventual cessation finding with direct relevance to geriatric patients who cycle between dose reduction and relapse.

Human studies

Human studies have confirmed and expanded these preclinical findings using several approaches.[46] In a landmark double-blind trial, patients receiving long-term diazepam therapy were assigned either to gradual tapering or abrupt discontinuation. Significant withdrawal symptoms occurred in 67% of those who stopped abruptly, compared with 13% of those who underwent tapering.[47] This study demonstrated both the high frequency of withdrawal and the critical importance of gradual dose reduction. Population-based studies estimate that 30–50% of long-term BZD users develop withdrawal symptoms after discontinuation, with 10–15% experiencing severe or prolonged symptoms.[48] In older adults, prevalence appears similar, although clinical manifestations may differ. Long-term follow-up studies show that withdrawal symptoms can persist for months or even years after discontinuation, a condition known as protracted withdrawal syndrome.[49] In elderly patients, this syndrome may present as persistent anxiety, insomnia, or cognitive complaints, often misattributed to aging or primary psychiatric illness. Benzodiazepine withdrawal therefore remains incompletely understood and requires further clinical attention.

The parallels between BZD and alcohol dependence

Despite their distinct pharmacological profiles, BZDs, and alcohol share remarkably similar dependence characteristics, a parallel that remains underexplored in geriatric research. Both BZDs and alcohol potentiate GABAergic neurotransmission, albeit through different mechanisms. Alcohol enhances GABA-mediated chloride flux through multiple receptor subtypes, while BZDs specifically modulate the benzodiazepine binding site on GABAA receptors.[50] The convergence of these pathways explains several clinical observations. Chronic alcohol exposure produces tolerance to BZD effects, and vice versa. This cross-tolerance reflects shared neuroadaptation in GABAergic signaling.[51]

Cross-dependence: BZDs are the treatment of choice for alcohol withdrawal precisely because they substitute for alcohol's GABAergic effects. This therapeutic use, however, highlights the fundamental similarity in their dependence mechanisms.[52] Shared withdrawal features: Both alcohol and BZD withdrawal syndromes include anxiety, insomnia, autonomic hyperactivity, tremor, and in severe cases , seizures, and delirium. The similarity reflects their common neurobiological basis.[53]

Differential risk in the elderly

Despite these parallels, important differences exist. Alcohol use is socially sanctioned and widely available, while BZD use requires medical prescription. This difference may paradoxically increase BZD dependence risk in the elderly, who may view prescription medications as inherently safe and underestimate their dependence potential.[54] BZD dependence is more easily concealed than alcohol dependence, as patients do not exhibit obvious intoxication and may maintain apparently normal functioning for years.[55] In the elderly, this may delay recognition until significant adverse outcomes (falls, cognitive decline) have occurred . The prolonged half-lives of many BZDs, particularly in the elderly, produce a "steady-state dependence" that differs from the intermittent intoxication-withdrawal cycles of alcohol use. This may affect the clinical presentation and management of withdrawal.[56]

Clinical implications

The parallels between alcohol and BZD dependence suggest that strategies used in alcohol dependence treatment may also inform the management of BZD dependence in older adults. As with alcohol dependence, BZD dependence often requires sustained management rather than a single acute intervention. Structured relapse-prevention

programs adapted from alcohol treatment may help older BZD users attempting discontinuation.[57] Psychosocial support is also essential. Counseling, peer support, and behavioral therapies used in alcohol treatment have clear relevance to BZD discontinuation. Studies in older patients show that adding cognitive-behavioral therapy or brief counseling to a supervised taper improves discontinuation rates compared with tapering alone.[58,59] Similarly, just as primary care routinely screens for alcohol misuse, geriatric assessments should include systematic screening for BZD use, dependence risk, and inappropriate prescribing.[60] For patients who are unable or unwilling to discontinue BZDs completely, harm-reduction strategies such as dose reduction, switching to a longer-acting agent, or limiting use to as-needed rather than scheduled dosing may lower overall risk even without full cessation.[61]

Clinical recommendations for geriatric practice

Prescribing principles

BZD prescribing in older adults should follow several core principles. BZDs should not be first-line treatment for anxiety, insomnia, or behavioral symptoms in this population. Evidence-based alternatives include cognitive-behavioral therapy for insomnia (CBT-I), which provides better long-term efficacy without drug-related adverse effects.[62] When medication is required, melatonin receptor agonists, low-dose doxepin, or trazodone may be considered, although each has limitations.[63] For anxiety disorders, selective serotonin reuptake inhibitors (SSRIs) or serotonin-norepinephrine reuptake inhibitors (SNRIs) are preferred because they target the underlying pathophysiology without causing dependence.[64] Because their full effect usually takes 2–6 weeks, short-term BZD bridging may occasionally be considered.[65] For behavioral symptoms of dementia, non-pharmacological approaches, including environmental modification, caregiver training, and structured activities, should remain first-line interventions. If pharmacotherapy is unavoidable, antidepressants, particularly citalopram, or antipsychotics may be used cautiously, recognizing that all carry significant risks in older adults.[66]

If a BZD is prescribed, indications should be specific, time-limited, and documented. Appropriate indications may include severe disabling anxiety that impairs function and fails to respond to non-BZD treatments, acute situational crisis (e.g., bereavement, medical diagnosis).[67] Pre-procedural anxiolysis as alcohol withdrawal management (short-term, under medical supervision). Treatment should not exceed 2-4 weeks of continuous use. For elderly patients, even shorter courses (7-10 days) are preferable.[68] If ongoing treatment is required, the need for continued BZD therapy should be reassessed at each visit.

When BZDs are necessary, clinicians should prescribe the lowest effective dose. Long-acting agents, such as diazepam or chlordiazepoxide, may be preferable in patients at high risk of dependence because they are generally associated with less severe withdrawal. In contrast, agents without active metabolites should be favored in hepatic impairment, and high-potency, short-acting BZDs such as alprazolam and triazolam should be avoided in older adults because of their greater association with falls and withdrawal severity.[69] Patients receiving BZDs should be regularly monitored for cognitive decline using validated tools such as the Montreal Cognitive Assessment,[70] as well as for gait instability, falls, sedation, daytime somnolence, tolerance, dose escalation, and concomitant use of alcohol or other central nervous system depressants.

Discontinuation strategies

For elderly patients who have been on long-term BZDs, discontinuation should be approached systematically:[71]

Step 1: Assessment and motivation: assess readiness to discontinue and identify barriers (fear of withdrawal, belief that BZD is necessary), provide education about the risks of long-term use and the benefits of discontinuation address underlying.[72]

Step 2: *Stabilization;* convert short-acting BZDs to an equivalent dose of a long-acting agent (e.g., ;diazepam) to smooth withdrawal symptoms. A conversion table should be used:

1. Alprazolam 0.5 mg ≈ diazepam 10 mg
2. Lorazepam 1 mg ≈ diazepam 10 mg
3. Clonazepam 0.5 mg ≈ diazepam 10 mg

Stabilize the patient on the equivalent dose for 1-2 weeks before beginning the taper

Step 3: Gradual taper: reduce the dose by approximately 10-25% every 1-2 weeks, depending on the patient's response. For elderly patients, slower tapers (over 8-16 weeks or longer) are generally recommended, as they are better tolerated and associated with higher long-term success rates .Monitor for withdrawal symptoms at each step; if symptoms emerge, hold the current dose until symptoms subside before resuming the taper .Consider a "symptom-triggered" approach in which the patient participates in dose adjustments within a prescribed range, which may improve adherence and reduce anxiety about withdrawal.[73]

Step 4: Symptom management during taper: *Psychological symptoms*. Anxiety, irritability, and mood lability are common during withdrawal. Supportive counseling, relaxation techniques, and cognitive-behavioral strategies can help patients cope without resorting to dose escalation.[74] Insomnia is frequently the most distressing withdrawal symptoms. Sleep hygiene measures, stimulus control, and CBT-I techniques should be emphasized. If pharmacotherapy is needed, melatonin or low-dose trazodone may be considered on a short-term basis.[75]

Physical symptoms. Muscle tension, headache, and gastrointestinal symptoms may occur. Symptomatic treatment (e.g., acetaminophen, antiemetics) can be used as needed.

Severe withdrawal. If severe symptoms (seizures, delirium, psychosis) develop, the taper should be paused, and the patient should receive immediate medical evaluation. In such cases, the dose may need to be increased temporarily, and the taper resumed more slowly.[76]

Step 5: post-discontinuation follow-up: .Continue monitoring for at least 6-12 months after complete discontinuation, as relapse rates are significant. Address the underlying condition (anxiety, insomnia) with ongoing non-pharmacological treatment. Be alert for "protracted withdrawal syndrome," which may present as persistent anxiety, insomnia, or cognitive complaints weeks to months after cessation.[77] If relapse occurs, consider whether non-BZD alternatives can be used instead of resuming BZDs.

The role of flumazenil

Flumazenil, a competitive BZD antagonist, has been studied as a potential aid for BZD discontinuation. Some protocols have used repeated low-dose infusions to facilitate withdrawal and reduce symptoms.[78] However, this strategy remains experimental and is not

recommended for routine geriatric practice because it may precipitate severe withdrawal seizures, has a short duration of action requiring repeated administration, lacks robust evidence of efficacy in older adults, and may cause cardiovascular complications in patients with underlying diseases.

Future directions and research needs

Despite decades of clinical experience with BZDs, major knowledge gaps remain regarding their use in older adults. Although their acute cognitive effects are well established, the long-term association between BZD exposure and dementia remains debated. Meta-analyses have reached conflicting conclusions, and reverse causation where early dementia symptoms are treated with BZDs continues to complicate interpretation. Long-term prospective studies with rigorous control of confounding factors are therefore needed. There is also no consensus on the optimal tapering rate, duration, or strategy for older patients, making comparative effectiveness trials essential for developing evidence-based guidance.[20] Better tools are needed to identify patients at greatest risk of dependence, withdrawal complications, and adverse outcomes, allowing more targeted interventions. In the future, genetic polymorphisms in GABAA receptor subunits may help personalize prescribing.[79] Finally, safer GABAergic alternatives, including partial agonists at the benzodiazepine site with lower dependence liability, could offer more appropriate treatment options for older adults.

Conclusion

Benzodiazepines remain among the most prescribed psychotropic medications in older adults, despite substantial evidence of risk and limited long-term efficacy. The close parallels between BZD and alcohol dependence including shared neurobiological mechanisms, similar withdrawal syndromes, and comparable therapeutic challenges underscore the clinical importance of BZD dependence and justify greater attention in geriatric practice. In older adults, BZD dependence is real, common, and often underrecognized, contributing substantially to morbidity among long-term users. Its neurobiological basis, involving GABAA receptor downregulation, altered subunit expression, and broader neuroadaptive changes, helps explain tolerance, withdrawal, and sustained dependence. Clinically, these similarities with alcohol dependence suggest that addiction-medicine principles, including chronic disease management, relapse prevention, and psychosocial support, should inform BZD discontinuation strategies. Prevention remains essential: whenever possible, BZD initiation in older adults should be avoided, non-pharmacological alternatives should be prioritized, and prescriptions should be limited to clearly justified short-term use. For established users, individualized and well-supported gradual tapering is feasible and beneficial, even in very old or frail patients, when combined with appropriate symptom management. Reducing inappropriate BZD use also requires system-level action, including prescriber education, clinical decision support, regulatory measures, and structured deprescribing programs. Ultimately, the challenge of BZD use in older adults extends beyond pharmacology and reflects broader issues in geriatric prescribing, including symptom-focused treatment, underuse of non-pharmacological care, and entrenched prescribing habits. Addressing these issues will require coordinated efforts from clinicians, patients, families, healthcare systems, and policymakers. The goal is not simply to reduce BZD prescribing, but to improve quality of life and functional outcomes in older adults. Judicious short-term BZD use may be appropriate for selected patients, whereas others will benefit more from careful discontinuation and alternative treatments. Effective geriatric prescribing requires making these distinctions thoughtfully, transparently, and in partnership with the patient.

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Conflicts of interest

The authors report no potential conflicts of interest relevant to this article.

References

1. Griffin CE 3rd, Kaye AM, Bueno FR, et al. Benzodiazepine pharmacology and central nervous system-mediated effects. *Ochsner J*. 2013;13(2):214–223.
2. Chen X, van Gerven J, Cohen A, et al. Human pharmacology of positive GABA-A subtype-selective receptor modulators for the treatment of anxiety. *Acta Pharmacol Sin*. 2019;40:571–582.
3. Navarrete F, Marín-Mayor M, Martínez-Hostyn L, et al. Benzodiazepine dependence: clinical and molecular aspects, preventive Strategies and therapeutic approaches. *Int J Mol Sci*. 2026;27(3):1430.
4. Edinoff AN, Nix CA, Hollier J, et al. Benzodiazepines: Uses, dangers, and clinical considerations. *Neurol Int*. 2021;13:594–607.
5. Gentile G, Lapeyre-MM, Micallef J. Combatting the misuse of benzodiazepines and related Z drugs in French general practice: a clinical review. *BJGP Open*. 2020;4(1):bjgpopen20X101014.
6. Lukačišinová A, Reissigová J, Ortner-Hadžiabdić M, et al. Prevalence, country-specific prescribing patterns and determinants of benzodiazepine use in community-residing older adults in 7 European countries. *BMC Geriatr*. 2024 ;24(1):240.
7. Goldschen-Ohm MP. Benzodiazepine modulation of GABAA receptors: a mechanistic perspective. *Biomolecules*. 2022;12(12):1784.
8. Edinoff AN, Nix CA, Hollier J, et al. Benzodiazepines: uses, dangers, and clinical considerations. *Neurol Int*. 2021;13:594–607.
9. Bourin M. Prescribed psychotropic drugs in the elderly. In: Gargiulo P.Á., Mesones Arroyo H.L. (eds) psychiatry and neuroscience update. Springer, Cham. 2021;647–660.
10. Weintraub SJ. Should chlordiazepoxide and diazepam be avoided when treating alcohol withdrawal syndrome in patients with hepatic insufficiency?. *Clin Toxicol (Phila)*. 2025 ;63:303–309.
11. Rissman RA, Mobley WC. Implications for treatment: GABAA receptors in aging, Down syndrome and Alzheimer's disease. *J Neurochem*. 2011 ;117:613–622.
12. Kim S, Jung UJ, Kim SR. The crucial role of the blood-brain barrier in neurodegenerative diseases: mechanisms of disruption and therapeutic implications. *J Clin Med*. 2025;14(2):386.
13. Bourin M. The problems with the use of benzodiazepines in elderly patients]. *Encephale*. 2010;36:340–347.
14. Na I, Seo J, Park E, Lee J. Risk of falls associated with long-acting benzodiazepines or tricyclic antidepressants use in community-dwelling older adults: a nationwide population-based case-crossover Study. *Int J Environ Res Public Health*. 2022;19(14):8564.
15. Poly TN, Islam MM, Yang HC, et al. Association between benzodiazepines use and risk of hip fracture in the elderly people: A meta-analysis of observational studies. *Joint Bone Spine*. 2020;87:241–249.
16. Díaz-GMJ, Martínez-CM, Sáez de E, et al. Relationship between the use of benzodiazepines and falls in older adults: A systematic review. *Maturitas*. 2017;101:17–22.

17. Kaplan K, Hunsberger HC. Benzodiazepine-induced anterograde amnesia: detrimental side effect to novel study tool. *Front Pharmacol*. 2023;14:1257030.

18. He Q, Chen X, Wu T, et al. Risk of dementia in long-term benzodiazepine users: evidence from a meta-analysis of observational studies. *J Clin Neurol*. 2019;15:9–19.

19. Ettcheto M, Olloquequi J, Sánchez-LE, et al. Benzodiazepines and related drugs as a risk factor in alzheimer's disease dementia. *Front Aging Neurosci*. 2020;11:344.

20. Wu CC, Liao MH, Su CH, et al. Benzodiazepine use and the risk of dementia in the elderly population: an umbrella review of meta-analyses. *J Pers Med*. 2023;13(10):1485.

21. Mancuso CE, Tanzi MG, Gabay M. Paradoxical reactions to benzodiazepines: literature review and treatment options. *Pharmacotherapy*. 2004;24:1177–1185.

22. Dailly E, Bourin M. The use of benzodiazepines in the aged patient: clinical and pharmacological considerations. *Pak J Pharm Sci*. 2008 ;21:144–150.

23. Carlsten A, Waern M, Holmgren P, et al. The role of benzodiazepines in elderly suicides. *Scand J Public Health*. 2003;31:224–248.

24. Smaoui N, Barkallah M, Charfi N, et al. Benzodiazepine addiction and suicidal risk in the elderly. *Eur Psychiatry*. 2026;69(Suppl 1):S757.

25. File SE. Tolerance to the behavioral actions of benzodiazepines. *Neurosci Biobehav Rev*. 1985;9:113–121.

26. Lerner A, Klein M. Dependence, withdrawal and rebound of CNS drugs: an update and regulatory considerations for new drugs development. *Brain Commun*. 2019;1(1):fcz025.

27. Volkow ND, Blanco C. Substance use disorders: a comprehensive update of classification, epidemiology, neurobiology, clinical aspects, treatment and prevention. *World Psychiatry*. 2023;22:203–229.

28. Juergens SM. Problems with benzodiazepines in elderly patients. *Mayo Clin Proc*. 1993;68:818–820.

29. Jobert A, Laforgue EJ, Grall-Bronnec M, et al. Benzodiazepine withdrawal in older people: what is the prevalence, what are the signs, and which patients?. *Eur J Clin Pharmacol*. 2021;77:171–177.

30. Bourin M, Thibaut F. Benzodiazepines: tackling the symptoms of withdrawal. *Neuropsychiatry*. 2013;3:263–265.

31. Chouinard G. Issues in the clinical use of benzodiazepines: potency, withdrawal, and rebound. *J Clin Psychiatry*. 2004;65 Suppl 5:7–12.

32. Lerner A, Klein M. Dependence, withdrawal and rebound of CNS drugs: an update and regulatory considerations for new drugs development. *Brain Commun*. 2019;1(1):fcz025.

33. Basińska SA. Use of a long-acting substitute in detoxification from benzodiazepines: safety (accumulation) problems and proposed mitigation procedure. *Eur J Clin Pharmacol*. 2022;78:1833–1841.

34. Reid FAJ, Macoubrie J, Huff C, et al. Experiences with benzodiazepine use, tapering, and discontinuation: an Internet survey. *Ther Adv Psychopharmacol*. 2022;12:20451253221082386.

35. Isomura K, Wang X, Chang Z, et al. Factors associated with long-term benzodiazepine and Z-drug use across the lifespan and 5-year temporal trajectories among incident users: a Swedish nationwide register-based study. *Eur J Clin Pharmacol*. 2023;79:1091–1105.

36. Brunner E, Chen CA, Klein T, et al. Clinical guideline committee (CGC) members; ASAM staff and contractors. joint clinical practice guideline on benzodiazepine tapering: considerations when risks outweigh benefits. *J Gen Intern Med*. 2025;40:2814-2859.

37. Tyrer P. Risks of dependence on benzodiazepine drugs: the importance of patient selection. *BMJ*. 1989;298(6666):104-105.

38. Schweizer E, Rickels K, De Martinis N, et al. The effect of personality on withdrawal severity and taper outcome in benzodiazepine dependent patients. *Psychol Med*. 1998;28:713–720.

39. Becker HC. Alcohol dependence, withdrawal, and relapse. *Alcohol Res Health*. 2008;31:348–361.

40. Bosshart H. Withdrawal-induced delirium associated with a benzodiazepine switch: a case report. *J Med Case Rep*. 2011;5:207.

41. Santana Ayala JR, Alberto Armas D, Hernández García V, et al. Benzodiazepine (BZD) Use and patient safety: opportunities for community pharmacy involvement in the management of drug interactions. *Pharmacy (Basel)*. 2025;13(6):181.

42. Bourin M. What Can we expect from the evaluation drug addiction in animals? in P. Á. Gargiulo, H. L. Mesones-Arroyo (eds.), Psychiatry and Neuroscience Update – Vol. V Springer 2024;181-186.

43. O'Connor EC, Chapman K, Butler P, et al. The predictive validity of the rat self-administration model for abuse liability. *Neurosci Biobehav Rev*. 2011;35:912–938.

44. Lukas SE, Griffiths RR. Precipitated withdrawal by a benzodiazepine receptor antagonist (Ro 15-1788) after 7 days of diazepam. *Science*. 1982;217(4565):1161–1163.

45. Chacur C, Raymond R, Hipólide DC, et al. Immediate increase in benzodiazepine binding in rat brain after a single brief experience in the plus maze: a paradoxical effect. *Neurosci Lett*. 1999;269:29–32.

46. Bourin M. Benzodiazepine addiction: a difficult story addiction in P. Á. Gargiulo, H. L. Mesones-Arroyo (eds.), Psychiatry and Neuroscience Update – Vol. V Springer 2024 pp195-203.

47. Tyrer P, Owen R, Dawling S. Gradual withdrawal of diazepam after long-term therapy. *Lancet*. 1983;1(8339):1402–1406.

48. Hertz Z, BarczakS. The use of benzodiazepines in the elderly population: epidemiology, risks and withdrawal management. *Euras J Fam Med*. 2025;14:87–93.

49. Shade KN, Ritvo AD, Silvernail B, et al. Long-term neurological consequences following benzodiazepine exposure: A scoping review. *PLoS One*. 2025;20(8):e0330277.

50. Cutler AJ, Mattingly GW, Maletic V. Understanding the mechanism of action and clinical effects of neuroactive steroids and GABAergic compounds in major depressive disorder. *Transl Psychiatry*. 2023;13(1):228.

51. Dharavath RN, Pina LC, Tang VM, et al. GABAergic signaling in alcohol use disorder and withdrawal: pathological involvement and therapeutic potential. *Front Neural Circuits*. 2023;17:1218737.

52. Navarrete F, Marín MM, Martínez HL, et al. Benzodiazepine dependence: clinical and molecular aspects, preventive strategies and therapeutic approaches. *Int J Mol Sci*. 2026;27(3):1430.

53. Day E, Daly C. Clinical management of the alcohol withdrawal syndrome. *Addiction*. 2022;117:804–814.

54. Ates Bulut E, Isik AT. Abuse/misuse of prescription medications in older adults. *Clin Geriatr Med*. 2022;38:85–97.

55. Hirschtritt ME, Palzes VA, Kline- AH, et al. Benzodiazepine and unhealthy alcohol use among adult outpatients. *Am J Manag Care*. 2019;25(12):e358-e365.

56. Maldonado JR, Nguyen LH, Schader EM, Brooks JO 3rd. Benzodiazepine loading versus symptom-triggered treatment of alcohol withdrawal: a prospective, randomized clinical trial. *Gen Hosp Psychiatry*. 2012;34:611–617.

57. Farhoudian A, Razaghi E, Hooshyari Z, et al. Barriers and facilitators to substance use disorder treatment: an overview of systematic reviews. *Subst Abuse*. 2022;16:11782218221118462.

Citation: Bourin M. Benzodiazepines in the elderly: mechanisms, dependence risks, and clinical implications for geriatric practice. *MOJ Gerontol Ger.* 2026;11(2):43–49. DOI: 10.15406/mojgg.2026.11.00358

58. Darker CD, Sweeney BP, Barry JM, et al. Psychosocial interventions for benzodiazepine harmful use, abuse or dependence. *Cochrane Database Syst Rev*. 2015;2015(5):CD009652.

59. Chapoutot M, Peter-Derex L, Bastuji H, et al. Cognitive behavioral therapy and acceptance and commitment therapy for the discontinuation of long-term benzodiazepine use in insomnia and anxiety disorders. *Int J Environ Res Public Health*. 2021;18(19):10222.

60. Fleming MF. Screening and brief intervention in primary care settings. *Alcohol Res Health*. 2004-2005;28(2):57–62.

61. Lader M. Benzodiazepine harm: how can it be reduced?. *Br J Clin Pharmacol*. 2014 ;77:295–301.

62. Morin CM, Khullar A, Robillard R, et al. Delphi consensus recommendations for the management of chronic insomnia in Canada. *Sleep Med*. 2024;124:598-605.

63. Del Rio Verduzco A, Salari A, Haghparast P. Efficacy and safety of pharmacotherapy in chronic insomnia: A review of clinical guidelines and case reports. *Ment Health Clin*. 2023;13:244–254.

64. . Bourin M. Mechanisms of action of anxiolytics. In: Gargiulo P.Á., Mesones Arroyo H.L. (eds) psychiatry and neuroscience update. Springer, Cham 2021;195–211.

65. Gosmann NP, Costa MA, Jaeger MB, et al. Selective serotonin reuptake inhibitors, and serotonin and norepinephrine reuptake inhibitors for anxiety, obsessive-compulsive, and stress disorders: A 3-level network meta-analysis. *PLoS Med*. 2021;18(6):e1003664.

66. Ijaopo EO. Dementia-related agitation: a review of non-pharmacological interventions and analysis of risks and benefits of pharmacotherapy. *Transl Psychiatry*. 2017;7(10):e1250.

67. Brandt J, Bressi J, Lê ML, et al. Prescribing and deprescribing guidance for benzodiazepine and benzodiazepine receptor agonist use in adults with depression, anxiety, and insomnia: an international scoping review. *EClinicalMedicine*. 2024;70:102507.

68. Sachdeva A, Choudhary M, Chandra M. Alcohol withdrawal syndrome: benzodiazepines and beyond. *J Clin Diagn Res*. 2015 ;9(9):VE01-VE07.

69. Sinclair JMA, Kalk NJ, Kaar SJ, et al. Evidence-based consensus guidelines for the pharmacological management of substance dependence: Recommendations from the British Association for Psychopharmacology. *J Psychopharmacol*. 2026;40:227–272.

70. Islam N, Hashem R, Gad M, et al. Accuracy of the Montreal Cognitive Assessment tool for detecting mild cognitive impairment: A systematic review and meta-analysis. *Alzheimers Dement*. 2023 ;19:3235–3243.

71. Bourin M. Do benzodiazepines still need to be used?. Open Access J Neurol Neurosurg. 2017;5(4):555669.

72. Bourin M. Benzodiazepines in older adults: between clinical benefit and misuse. *Int J Fam Commun Med.* 2026;10(2):83.

73. Brunner E, Chen CA, Klein T, et al. Clinical guideline committee (CGC) members; ASAM staff and contractors. joint clinical practice guideline on benzodiazepine tapering: considerations when risks outweigh benefits. *J Gen Intern Med*. 2025;40:2814-2859.

74. Wolitzky-Taylor K, Mooney LJ, et al. Augmenting the efficacy of benzodiazepine taper with telehealth-delivered cognitive behavioral therapy for anxiety disorders in patients using prescription opioids: A pilot randomized controlled trial. *Contemp Clin Trials*. 2023 ;133:107334.

75. Rossman J. Cognitive-behavioral therapy for insomnia: an effective and underutilized treatment for insomnia. *Am J Lifestyle Med*. 2019;13(6):544-547.

76. Schuckit MA. Recognition and management of withdrawal delirium (delirium tremens). *N Engl J Med*. 2014;371:2109–2113.

77. Reidenberg MM. Drug discontinuation effects are part of the pharmacology of a drug. *J Pharmacol Exp Ther*. 2011;339:324–328.

78. Hood SD, Norman A, Hince DA, et al. Benzodiazepine dependence and its treatment with low dose flumazenil. *Br J Clin Pharmacol*. 2014;77:285–294.

79. O'Mahony MS, Parbhoo A. Deprescribing in older people. *Br J Hosp Med (Lond)*. 2020;81:1–9.

Citation: Bourin M. Benzodiazepines in the elderly: mechanisms, dependence risks, and clinical implications for geriatric practice. *MOJ Gerontol Ger.* 2026;11(2):43–49. DOI: 10.15406/mojgg.2026.11.00358