



A Comprehensive Systematic Review of The Relationship between Benzodiazepine Use and Psychomotor Impairment

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ABSTRACT

Introduction: Benzodiazepines (BZDs) are widely prescribed for anxiety and insomnia, but their impact on psychomotor function is a significant safety concern. This review synthesizes evidence from 41 studies on the association between BZD use and psychomotor impairment.

Methods: A comprehensive review of 41 sources was conducted. Data were extracted on BZD details (type, dose, duration), psychomotor outcomes (reaction time, motor function, driving, falls), and relationship findings.

Results: The evidence consistently demonstrates BZD-associated psychomotor impairment. Meta-analyses show a 60% increased risk of motor vehicle collisions (OR=1.60) and a 34% increased risk of hip fractures (RR=1.34) among users (1,2). An

experimental study confirmed acute impairment in reaction time and tracking accuracy lasting up to 14.5 hours (3). Dose-response relationships were observed, with high-dose users (>1 DDD) showing significantly prolonged reaction times (4) and a fourfold increased fall risk (8). Chronic use was linked to neurocognitive impairment in vulnerable populations like people living with HIV (OR=2.13) (5) and executive function deficits (6). Elderly populations were identified as most at risk for falls and functional decline (2,7,10-12).

Discussion: The findings converge on a pattern of impairment across multiple psychomotor domains. While most studies show significant effects, one study in psychogeriatric patients found no cognitive decrements, likely due to confounding by indication where the comparison group was already compromised (9). The synthesis reveals that effects are more pronounced with higher doses, current use, longer-acting agents, and in elderly populations.

Conclusion: Benzodiazepine use is significantly associated with impaired psychomotor function, including prolonged reaction time, impaired driving, and increased risk of falls and fractures. These risks are dose-dependent and more severe in vulnerable populations, particularly the elderly. Clinicians should carefully weigh these risks, prescribe at the lowest effective dose for the shortest duration, and exercise special caution in high-risk groups. Further research should focus on standardized outcome measures and long-term prospective studies in diverse populations.

Keywords: Benzodiazepines, Psychomotor Performance, Accidental Falls, Hip Fractures, Automobile Driving, Reaction Time

INTRODUCTION

Benzodiazepines (BZDs) are among the most frequently prescribed psychotropic medications worldwide, used primarily for the management of anxiety disorders, insomnia, and agitation (19, 32, 40). Their therapeutic effects are mediated through potentiation of GABAergic inhibition in the central nervous system. However, this same mechanism can lead to adverse effects, including sedation, cognitive impairment, and psychomotor dysfunction. Psychomotor function—encompassing motor coordination, reaction time, balance, and movement control—is critical for safe performance of daily activities such as driving and maintaining postural stability (3, 4). Impairment in these domains can have profound consequences, including an increased risk of motor vehicle collisions (MVCs), falls, and fractures, particularly in vulnerable populations like the elderly (1, 2, 7).

While the acute sedative effects of BZDs are well-documented, a comprehensive synthesis of the evidence linking their use to specific, objectively measured psychomotor impairments across different populations and durations of use is needed. A significant research gap lies in reconciling findings from controlled experimental settings, which establish causality, with real-world observational data that reflect chronic use patterns and complex patient populations. Furthermore, the extent to which these risks are modified by factors such as dosage, duration of action, patient age, and comorbidities requires further clarification. Much of the existing literature consists of either highly controlled but acute trials or observational studies that are susceptible to confounding by indication, where the underlying condition (e.g., anxiety, insomnia) itself may impair function (4, 9).

The primary objective of this review is to systematically synthesize evidence from 41 diverse sources to evaluate the relationship between benzodiazepine use and psychomotor impairment. This review aims to: (1) characterize the effects of BZDs on specific psychomotor domains, including reaction time, driving performance, and balance; (2) assess the influence of

dose, duration of use, and type of BZD on the magnitude of impairment; and (3) identify populations at greatest risk. The novelty of this synthesis lies in its integration of high-level meta-analytic evidence with detailed experimental data and real-world prescribing patterns from both international and Indonesian clinical settings. We hypothesize that BZD use will be significantly associated with psychomotor impairment across all domains, with stronger effects observed at higher doses, with longer-acting agents, and in elderly and medically compromised populations. The findings will be beneficial for clinicians in making informed risk-benefit assessments when prescribing BZDs and for policymakers in developing guidelines to mitigate these significant public health risks.

METHODS

Protocol

The study strictly adhered to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020 guidelines to ensure methodological rigor and accuracy. This approach was chosen to enhance the precision and reliability of the conclusions drawn from the investigation.

Criteria for Eligibility

This systematic review aims to evaluate the relationship between benzodiazepine use and psychomotor impairment.

Screening

We screened in sources based on their abstracts that met these criteria:

- **Benzodiazepine Exposure:** Does this study investigate benzodiazepine use as a primary exposure with clearly defined exposure parameters (including at least one of: type, dose, duration, or frequency)?

- **Psychomotor Outcomes:** Does this study measure psychomotor function (such as motor coordination, reaction time, balance, movement control, or psychomotor speed) as a primary or secondary outcome using validated assessment tools or standardized clinical measures?
- **Human Participants:** Does this study include human participants of any age?
- **Study Design:** Is this study an experimental design (RCT, quasi-experimental) or observational study (cohort, case-control, cross-sectional)?
- **Sample Size:** Does this study include 10 or more participants?
- **Therapeutic Use Focus:** Does this study focus on therapeutic benzodiazepine use (rather than focusing solely on withdrawal effects or use only as procedural premedication)?
- **Methodological Detail:** Does this study provide sufficient methodological detail for quality assessment (i.e., is it a full research article rather than a conference abstract, editorial, or opinion piece)?

We considered all screening questions together and made a holistic judgement about whether to screen in each paper.

Search Strategy

The keywords used for this research based PICO :

Element	P (Population)	I (Intervention/Exposure)	C (Comparison/Context)	O (Outcome)
Keyword 1	Humans	Benzodiazepines	Placebo	Psychomotor Impairment
Keyword 2	Adults	Hypnotics and Sedatives	Non-users	Accidental Falls
Keyword 3	Elderly	Anxiolytics	Control Group	Reaction Time
Keyword 4	Patients	Psychotropic Drugs	No Treatment	Cognitive Dysfunction

The Boolean MeSH keywords inputted on databases for this research are: (*"Humans" OR "Adult Patients" OR "Elderly" OR "Psychiatric Patients"*) AND (*"Benzodiazepines" OR "Hypnotics and Sedatives" OR "Anxiolytic Agents" OR "Psychotropic Drugs"*) AND (*"Placebo" OR "Non-users" OR "Control Group" OR "Drug-Free Controls"*) AND (*"Psychomotor Impairment" OR "Accidental Falls" OR "Reaction Time" OR "Cognitive Dysfunction"*)

Data extraction

- **Benzodiazepine Details:**

Extract all details about benzodiazepine use relevant to psychomotor effects, including:

- Specific benzodiazepine name(s) studied
- Dose (mg/day or equivalent)
- Duration of use (acute vs chronic)
- Route of administration
- Indication for use (therapeutic vs abuse)
- Timing of administration relative to psychomotor assessment

- **Psychomotor Outcomes:**

Extract all psychomotor function measurements and disorders assessed in relation to benzodiazepine use, including:

- Specific psychomotor domains tested (coordination, reaction time, balance, motor control, driving performance, etc.)
- Assessment tools/scales used
- Timing of assessment relative to benzodiazepine administration
- Baseline vs post-exposure measurements
- Any standardized cut-off scores for impairment

- **Relationship Findings:**

Extract the key results about the relationship between benzodiazepine use and psychomotor function, including:

- Direction of association (improvement vs impairment)
- Magnitude of effect (effect sizes, odds ratios, mean differences)
- Statistical significance (p-values, confidence intervals)
- Dose-response relationships if reported
- Time course of effects (immediate, delayed, persistent)
- Clinical significance of observed changes

- **Study Design:**

Extract study design details that affect the strength of evidence for benzodiazepine-psychomotor relationships:

- Study type (experimental, observational, meta-analysis)
- Comparison groups (placebo, no treatment, other medications)
- Randomization and blinding procedures
- Sample size and power calculations
- Follow-up duration
- Primary vs secondary outcome status for psychomotor measures

- **Study Population:**

Extract characteristics of participants studied for benzodiazepine-psychomotor relationships:

- Age range and mean age
- Clinical population (healthy volunteers, psychiatric patients, medical patients, elderly, etc.)

- Relevant comorbidities affecting psychomotor function
- Concurrent medications that could affect psychomotor performance
- Exclusion criteria related to psychomotor function or benzodiazepine use

- **Confounding Factors:**

Extract information about potential confounders and moderators of the benzodiazepine-psychomotor relationship that were measured or controlled for:

- Other medications affecting psychomotor function
- Medical conditions affecting motor function
- Age, gender, cognitive status
- Previous benzodiazepine exposure/tolerance
- Alcohol or substance use
- Sleep status at time of assessment
- Statistical adjustment methods used

Table 1. Article Search Strategy

Database	Keywords	Hits
Pubmed	<i>("Humans" OR "Adult Patients" OR "Elderly" OR "Psychiatric Patients") AND ("Benzodiazepines" OR "Hypnotics and Sedatives" OR "Anxiolytic Agents" OR "Psychotropic Drugs") AND ("Placebo" OR "Non-users" OR "Control Group" OR "Drug-Free Controls") AND ("Psychomotor Impairment" OR "Accidental Falls" OR "Reaction Time" OR "Cognitive Dysfunction")</i>	392
Semantic Scholar	<i>("Humans" OR "Adult Patients" OR "Elderly" OR "Psychiatric Patients") AND ("Benzodiazepines" OR "Hypnotics and Sedatives" OR "Anxiolytic Agents" OR "Psychotropic Drugs") AND ("Placebo" OR "Non-users" OR "Control Group" OR "Drug-Free Controls") AND ("Psychomotor Impairment" OR "Accidental Falls" OR "Reaction Time" OR "Cognitive Dysfunction")</i>	250
Springer	<i>("Humans" OR "Adult Patients" OR "Elderly" OR "Psychiatric Patients") AND ("Benzodiazepines" OR "Hypnotics and Sedatives" OR "Anxiolytic Agents" OR "Psychotropic Drugs") AND ("Placebo" OR "Non-users" OR "Control Group" OR "Drug-Free Controls") AND ("Psychomotor Impairment" OR "Accidental Falls" OR "Reaction Time" OR "Cognitive Dysfunction")</i>	2,642
Google Scholar	<i>("Humans" OR "Adult Patients" OR "Elderly" OR "Psychiatric Patients") AND ("Benzodiazepines" OR "Hypnotics and Sedatives" OR "Anxiolytic Agents" OR "Psychotropic Drugs") AND ("Placebo" OR "Non-users" OR "Control Group" OR "Drug-Free Controls") AND ("Psychomotor Impairment" OR "Accidental Falls" OR "Reaction Time" OR "Cognitive Dysfunction")</i>	17,200
Wiley Online Library	<i>("Humans" OR "Adult Patients" OR "Elderly" OR "Psychiatric Patients") AND ("Benzodiazepines" OR "Hypnotics and Sedatives" OR "Anxiolytic Agents" OR "Psychotropic Drugs") AND ("Placebo" OR "Non-users" OR "Control Group" OR "Drug-Free Controls") AND ("Psychomotor Impairment" OR "Accidental Falls" OR "Reaction Time" OR "Cognitive Dysfunction")</i>	2,430

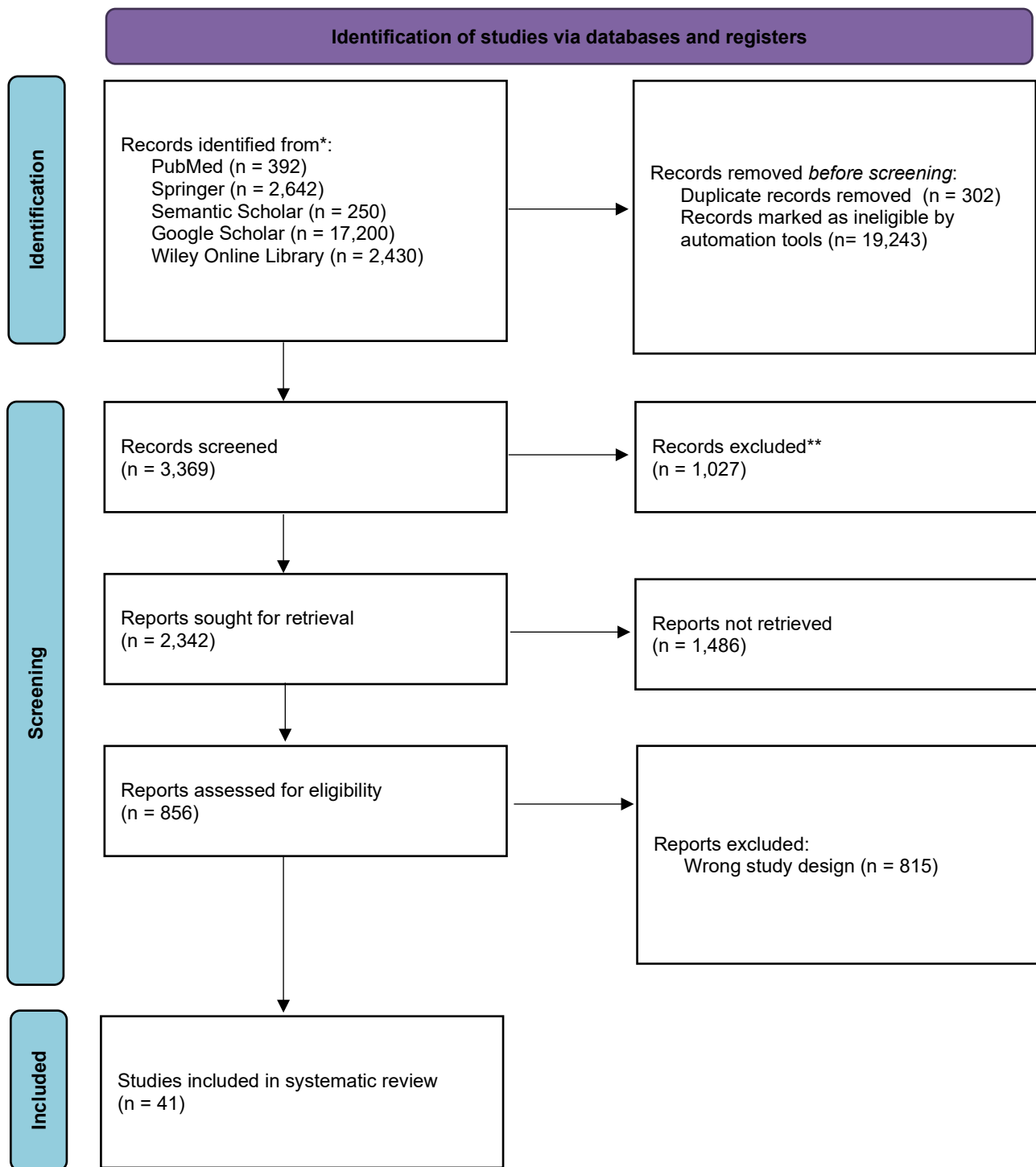


Figure 1. Article search flowchart

RESULTS

Characteristics of Included Studies

The 41 sources identified encompass a heterogeneous body of literature, ranging from meta-analyses and experimental studies directly measuring psychomotor outcomes to descriptive prescribing pattern surveys and drug utilization studies. Many sources originate from Indonesian clinical settings and focus on benzodiazepine prescribing practices in psychiatric populations, while others are international studies with direct psychomotor endpoint measurements. The table below summarizes all included sources.

Study	Population	Research Focus	Sample Size
R. Saloner et al., 2019	People living with HIV [5]	BZD use and neurocognitive impairment [5]	306 [5]
L. Manthey et al., 2014	Adults with depression/anxiety disorders [4]	BZD dose and reaction time [4]	2,823 [4]
M. Rapoport et al., 2009	Drivers (epidemiologic and experimental studies) [1]	BZD use and driving impairment/MVCs [1]	11 epidemiologic + 16 experimental studies [1]
Y. Bang et al., 2022	Insomnia patients aged ≥ 55 years [6]	Long-term BZD use and executive function [6]	84 [6]
Bermudez-Villalpando Vi et al., 2025	Elderly patients (>65 years) [11]	BZD use and fall risk [11]	52 [11]

Study	Population	Research Focus	Sample Size
Ā. Danza et al., 2015	Elderly (mean age ~82 years) [12]	BZD use and hip fracture [12]	89 [12]
M. Petrov et al., 2014	Community-dwelling older adults (≥ 65 years) [10]	BZD use, mobility, functioning, and pain [10]	1,000 [10]
L. Marron et al., 2019	Community-dwelling adults aged >50 [7]	BZD use, falls, and sleep quality [7]	8,175 [7]
E. Bierman et al., 2007	Elderly persons [13]	Chronic BZD use and cognitive functioning [13]	Not reported [13]
Lily Annisa et al., 2019	Elderly medical patients (mean age 67.68 years) [8]	Psychoactive drug use and fall risk [8]	290 [8]
M. Asbridge et al., 2020	Drivers involved in MVCs [14]	BZD blood levels and collision responsibility [14]	Not reported [14]
J. Dawson et al., 2008	Healthy volunteers (mean age 27.2 years) [3]	Acute BZD effects on psychomotor performance [3]	24 [3]
Abbassyah Abbassyah et al., 2025	Geriatric inpatients (60–69 years majority) [15]	BZD prescribing and fall risk evaluation [15]	Not reported [15]
Nevi Sulvita Karsa et al., 2024	Schizophrenia patients (18–55 years) [16]	Olanzapine $\pm$ diazepam for agitation [16]	≥ 20 [16]

Study	Population	Research Focus	Sample Size
L. Santos et al., 2015	Psychiatric inpatients [17]	BZD drug interactions [17]	100 prescriptions [17]
J. Määttä et al., 2020	Neuropathic pain patients [18]	BZD use and spinal cord stimulation outcome [18]	373 [18]
Riska Yuli Nurvianthi et al., 2024	GAD patients (most 35–44 years) [19]	Prescribing patterns for GAD [19]	40 [19]
Zea Maulida Ayati et al., 2017	Dental anxiety patients [20]	Diazepam effect on heart rate and respiratory rate [20]	50 [20]
Fabiana M. R. L. de Oliveira et al., 2014	Elderly psychiatric patients (60–69 years) [21]	BZD use characterization in elderly [21]	27 [21]
Fabiana M. R. L. de Oliveira et al., 2014a	Elderly psychiatric patients (60–69 years) [22]	BZD use characterization in elderly [22]	27 [22]
Nevi Sulvita Karsa et al., 2023	Schizophrenia patients [23]	Risperidone ± diazepam for agitation [23]	Not reported [23]
Meilanie Dwi Anggraeni et al., 2019	Psychiatric patients (dementia, depression, bipolar, schizophrenia) [24]	Anticonvulsant/BZD prescribing patterns [24]	52 [24]

Study	Population	Research Focus	Sample Size
Muhammad Hanif Faruq et al., 2020	Hemodialysis patients [25]	Benson relaxation for anxiety [25]	20 [25]
Juscilene R. Almeida et al., 2022	Elderly [26]	BZD drug interactions and adverse effects in elderly [26]	Not applicable [26]
M. Ong et al., 2012	Elderly Medicare beneficiaries (≥65 years) [27]	Medicare BZD exclusion and psychotropic use [27]	22,827 [27]
T. N. Poly et al., 2019	Elderly (33 studies) [2]	BZD use and hip fracture risk [2]	169,660 hip fracture cases [2]
I. Papoutsis et al., 2016	Drivers [28]	BZD effects on driving [28]	Not applicable [28]
Irene J. Zaal et al., 2016	ICU patients [29]	BZD use and delirium [29]	Not reported [29]
G. Høiseith et al., 2013	Psychogeriatric patients (≥60 years, mean ~78 years) [9]	BZD use and cognitive function [9]	241 [9]
Anisa Desty Fitriana et al., 2024	Adolescent schizophrenia patients (15–24 years) [30]	Antipsychotic prescribing rationality [30]	123 [30]

Study	Population	Research Focus	Sample Size
P. Rumagit et al., 2021	Paranoid schizophrenia outpatients [31]	Drug interaction potential of antipsychotics [31]	90 [31]
I. Ilham et al., 2022	Psychiatric patients (all ages) [32]	Antipsychotic and anxiolytic prescribing patterns [32]	201 prescriptions [32]
Yasmim C. F. C. H. Fonseca et al., 2024	Elderly [33]	BZD use and dementia/Alzheimer's risk [33]	Not applicable [33]
M. B. K. K. Dendiana et al., 2024	Elderly schizophrenia inpatients [34]	Prescribing evaluation per Beers Criteria [34]	41 [34]
Gabriel Vale Vasconcelos et al., 2025	Elderly in Brazil [35]	BZD use prevalence and adverse outcomes	15 studies [35]
Ane del Palacio Totoricagüena et al., 2021	Anxiolytic/hypnotic consumers by gender [36]	Gender differences in BZD consumption [36]	Not reported [36]
Ashwinderjeet Singh et al., 2019	Dementia patients (mean age 62 years) [37]	BZD use patterns in dementia [37]	29 [37]
S. Leung et al., 2013	General population (drivers, insomniacs) [38]	BZD residual effects on driving [38]	Not applicable [38]

Study	Population	Research Focus	Sample Size
N. Amaliya et al., 2018	Geriatric inpatients with neurological disorders [39]	Prescribing evaluation per Beers Criteria 2015 [39]	153 [39]
Debora Liudi Mulyo et al., 2015	GAD outpatients (most 45–54 years) [40]	Anxiolytic prescribing and side effects [40]	30 [40]
S. Rahayu et al., 2015	Schizophrenia inpatients [41]	Haloperidol use patterns (combined with diazepam) [41]	42 [41]

Of the 41 sources, full texts were retrieved for 16 studies; the remainder were analyzed based on abstracts only. The studies span multiple countries and clinical contexts: a substantial proportion originate from Indonesian hospitals focusing on psychiatric prescribing practices, while others are large-scale international epidemiological or experimental investigations. Study designs range from one double-blind placebo-controlled crossover trial [3] and two meta-analyses [1, 2] to numerous small descriptive or retrospective prescribing surveys. Notably, many of the Indonesian studies (e.g., prescribing pattern analyses of schizophrenia or GAD patients) do not directly measure psychomotor outcomes but document benzodiazepine utilization and known side-effect profiles in clinical populations.

Effects

Reaction Time and Cognitive-Psychomotor Performance

The most direct evidence for benzodiazepine-induced psychomotor impairment comes from studies that formally assessed reaction time and cognitive-motor domains. The table below summarizes quantitative findings from studies with measured psychomotor or functional endpoints.

Study	Psychomot or Domain	Measure/T ool	Effect Size or OR	Statistical Significanc e	Dose- Response Noted?	Duration of BZD Use
L. Manthey et al., 2014	Reaction time	Implicit Association Test (choice RT) [4]	High-dose users: $\beta =$ 0.096 [4]	P = 0.01 (dose-RT association) ; only high dose (>1 DDD) significant vs. non- users [4]	Yes: only high doses impaired [4]	Chronic (median 12–36 months) [4]
J. Dawson et al., 2008	Sensorimot or performanc e, divided attention	Choice RT (H-CRT), Continuous Tracking Task [3]	Significant reductions in activity, increased RT and errors [3]	p < 0.05 at multiple time points [3]	Not tested [3]	Acute (single 2.5 mg dose of LZP) [3]

Study	Psychomot or Domain	Measure/T ool	Effect Size or OR	Statistical Significanc e	Dose- Response Noted?	Duration of BZD Use
R. Saloner et al., 2019	Global cognition, processing speed, motor function	Neurobehav ioral battery (T-scores) [5]	NCI OR = 2.13; global d = -0.28; processing speed d = -0.23; motor d = -0.32 [5]	P = 0.003 (NCI); P = 0.020 (global); P = 0.047 (processing speed); P = 0.008 (motor) [5]	Not reported [5]	Chronic (median 24 months) [5]
Y. Bang et al., 2022	Executive function	Trail Making Test A, Categorical Fluency (CERAD- K-N) [6]	TMT-A: 0.73 ± 0.66 vs. 1.27 ± 0.38 (drug- free) vs. 1.09 ± 0.47 (controls) [6]	P < 0.001 (TMT-A); P = 0.002 (categorical fluency) [6]	No: not proportional to daily or cumulative dose [6]	Chronic (>180 days) [6]

Study	Psychomot or Domain	Measure/T ool	Effect Size or OR	Statistical Significanc e	Dose- Response Noted?	Duration of BZD Use
G. Høiseth et al., 2013	Learning, memory, executive function, vigilance	Hopkins Verbal Learning, Stroop, Digit Vigilance [9]	No significant differences on 11/12 tests; BZD users slightly better on digit vigilance time ($\beta =$ -0.20) [9]	Not significant after Bonferroni correction [9]	Not reported [9]	Chronic (mean diazepam dose 7.3 mg) [9]

Among studies that formally measured reaction time or cognitive-psychomotor performance, findings consistently point toward impairment, though the magnitude and conditions vary. In the large NESDA cohort ($n = 2,823$), Manthey et al. demonstrated that only high-dose benzodiazepine users (>1 defined daily dose) exhibited significantly prolonged reaction times compared to non-users, while low and intermediate doses did not produce statistically significant impairment [4]. This dose-response threshold is clinically important because it suggests partial tolerance may develop at lower doses but not at higher doses [4]. In contrast, the experimental study by Dawson et al. showed that even a single acute dose of 2.5 mg lorazepam produced measurable impairments in choice reaction time and tracking accuracy lasting up to 14.5 hours post-dose in healthy young volunteers [3, 3].

Saloner et al. found that chronic benzodiazepine use (median 24 months) in people living with HIV was associated with a twofold increased likelihood of neurocognitive impairment (OR = 2.13, $P = 0.003$) and poorer motor T-scores ($d = -0.32$, $P = 0.008$) [5]. Those with positive urine toxicology screens for benzodiazepines showed additional executive function, working memory, and delayed recall deficits [5]. Bang et al. similarly demonstrated impaired executive function in chronic benzodiazepine-using insomniacs compared to drug-free insomniacs, notably on Trail Making Test A ($P < 0.001$) [6], though this impairment was not proportional to daily or cumulative dose [6].

A notable exception was the study by Høiseth et al. in psychogeriatric patients ($n = 241$), which found no significant cognitive impairment on 11 of 12 standardized tests comparing benzodiazepine users to non-users [9]. The single test showing a difference (digit vigilance time) actually favored benzodiazepine users, though this finding was not significant after Bonferroni correction [9].

Driving Performance and Motor Vehicle Collisions

Study	Outcome	Effect Size or OR (95% CI)	Statistical Significance	Study Type
M. Rapoport et al., 2009	MVCs (case-control)	OR = 1.61 (1.21–2.13) [1]	$P < 0.001$ [1]	Meta-analysis [1]
M. Rapoport et al., 2009	MVCs (cohort)	OR = 1.60 (1.29–1.97) [1]	$P < 0.0001$ [1]	Meta-analysis [1]
M. Rapoport et al., 2009	Lateral position deviation (on-road)	SMD = 0.80 (0.35–1.25) [1]	$P = 0.0004$ [1]	Meta-analysis [1]

Study	Outcome	Effect Size or OR (95% CI)	Statistical Significance	Study Type
M. Asbridge et al., 2020	Collision responsibility (unadjusted)	OR = 2.99 (1.56–5.75) [14]	P = 0.001 [14]	Modified case-control [14]
M. Asbridge et al., 2020	Collision responsibility (adjusted)	aOR = 2.29 (1.16–4.53) [14]	P = 0.02 [14]	Modified case-control [14]
I. Papoutsis et al., 2016	Driving impairment (general)	Dose-dependent impairment noted [28]	Heterogeneous results [28]	Narrative review [28]
S. Leung et al., 2013	Next-day residual driving impairment	Clinically relevant residual effects reported [38]	Not quantified in abstract [38]	Narrative review [38]

The meta-analysis by Rapoport et al. provides the strongest pooled evidence, demonstrating a consistent approximately 60% increase in motor vehicle collision risk among benzodiazepine users versus non-users across both case-control (OR = 1.61) and cohort designs (OR = 1.60) [1]. On-road driving tests revealed a large standardized mean difference of 0.80 for lateral position deviation [1], suggesting meaningful impairment in lane-keeping ability. Asbridge et al. confirmed this association using responsibility analysis with blood benzodiazepine levels, finding an adjusted OR of 2.29 for responsible collisions after controlling for alcohol, THC, other medications, and driver characteristics [14, 14].

Papoutsis et al. noted that while an almost linear relationship between blood benzodiazepine concentrations and driving impairment appears to exist, longer-acting agents tested the morning

after a nighttime dose showed the most pronounced effects [28, 28]. Leung et al. similarly emphasized that residual next-day sedation from hypnotic benzodiazepines poses a significant safety concern, particularly because benzodiazepines are frequently used long-term outside clinical guidelines [38, 38].

Falls and Hip Fractures

Study	Outcome	Effect Size or OR (95% CI)	Statistical Significance	Population
T. N. Poly et al., 2019	Hip fracture (overall)	RR = 1.34 (1.26–1.44) [2]	P < 0.0001 [2]	Elderly (33 studies, 169,660 fractures) [2]
T. N. Poly et al., 2019	Hip fracture (long-acting BZDs)	RR = 1.31 (1.18–1.45) [2]	P < 0.0001 [2]	Elderly [2]
T. N. Poly et al., 2019	Hip fracture (short-acting BZDs)	RR = 1.15 (1.08–1.22) [2]	P < 0.0001 [2]	Elderly [2]
T. N. Poly et al., 2019	Hip fracture (current users)	RR = 1.83 (1.46–2.28) [2]	P < 0.0001 [2]	Elderly [2]
Ã. Danza et al., 2015	Hip fracture	OR = 4.5 (1.7–11.6) [12]	P < 0.05 [12]	Elderly (mean age ~82 years) [12]

Study	Outcome	Effect Size or OR (95% CI)	Statistical Significance	Population
L. Marron et al., 2019	Falls (any)	OR = 1.40 (1.08–1.82) [7]	P = 0.012 [7]	Community-dwelling adults >50 years [7]
L. Marron et al., 2019	Unexplained falls (with daytime somnolence)	OR = 1.93 (1.12–3.31) [7]	P = 0.017 [7]	Community-dwelling adults >50 years [7]
Bermudez-Villalpando Vi et al., 2025	High fall risk	98% of BZD users at high risk [11]	Not reported [11]	Elderly >65 years [11]
Lily Annisa et al., 2019	Fall risk (psychoactive drugs)	Adjusted OR = 2.158 (1.176–3.961) [8]	CI excludes 1 [8]	Elderly (mean 67.68 years) [8]
Lily Annisa et al., 2019	Fall risk (doses >0.5 DDD/day)	Adjusted OR = 4.463 (1.120–17.784) [8]	CI excludes 1 [8]	Elderly (mean 67.68 years) [8]
Abbassyah et al., 2025	Fall risk (long-acting BZDs)	OR = 1.45 (1.00–2.19) [15]	Significant [15]	Geriatric inpatients [15]
Abbassyah et al., 2025	Fall risk (short-acting BZDs)	OR = 1.32 (1.02–1.72) [15]	Significant [15]	Geriatric inpatients [15]

The meta-analysis by Poly et al. (33 studies, 169,660 fracture cases) provides the most comprehensive evidence, showing an overall 34% increase in hip fracture risk among benzodiazepine users (RR = 1.34, 95% CI 1.26–1.44) [2]. Current users face nearly double the risk

(RR = 1.83) [2], while past users show a more modest elevation (RR = 1.18) [2]. Long-acting benzodiazepines conferred somewhat greater hip fracture risk (RR = 1.31) than short-acting agents (RR = 1.15) [2]. The case-control study by Danza et al., though small (n = 89), found a particularly high OR of 4.5 for hip fracture in benzodiazepine users [12], with all BZD-using patients having consumed the drug for over six weeks [12].

For falls, Marron et al. found an overall OR of 1.40 (P = 0.012) in a large Irish cohort of 8,175 individuals [7], with the association strengthened when poor sleep quality coexisted with benzodiazepine use (OR up to 1.93) [7]. Lily Annisa et al. demonstrated a dose-response relationship in Indonesian geriatric patients, with doses exceeding 0.5 DDD/day showing the strongest association with fall risk (adjusted OR = 4.463) [8]. Bermudez-Villalpando et al. reported that 98% of elderly benzodiazepine users had a high fall risk on the Downton Index, though this study lacked a comparison group [11].

Mobility and Functional Impairment

Petrov et al. followed 1,000 community-dwelling older adults over 8.5 years and found that baseline benzodiazepine use was prospectively associated with greater difficulty in basic activities of daily living (estimate = 0.39, 95% CI 0.04–0.74) and more frequent pain (estimate = 0.41, 95% CI 0.09–0.74) [10]. Rural residents showed additional mobility declines as measured by the Life-Space Assessment (estimate = -0.67, P = 0.048) [10]. These associations persisted after adjusting for sociodemographic factors, comorbidity, smoking, alcohol use, and mental health symptoms [10].

Adverse Psychomotor Effects Reported in Prescribing and Review Studies

Several review and descriptive studies documented known psychomotor side effects of benzodiazepines without measuring them directly. The systematic review by Vasconcelos et al. on benzodiazepine use in elderly Brazilians reported that usage was associated with cognitive deficits, delirium, falls, fractures, and functional disability, with dose-response relationships noted between psychopharmaceutical use and disability in daily activities. Fonseca et al. noted that prolonged

benzodiazepine use leads to psychomotor function decrements, with elderly patients requiring escalating doses due to age-related pharmacokinetic changes, constituting a risk factor for dementia [33]. Almeida et al. identified known adverse effects including drowsiness, dizziness, ataxia, postural hypotension, and increased fall frequency in the elderly [26]. Santos et al. identified 356 potential drug interactions in 93 of 100 psychiatric prescriptions containing benzodiazepines, predominantly involving potentiation of CNS depression when combined with antipsychotics, antihistamines, antiepileptics, and antidepressants [17]. The drug utilization studies from Indonesian hospitals documented frequent benzodiazepine prescribing: alprazolam was the most commonly prescribed benzodiazepine in geriatric settings (83%) [15], and lorazepam was the most prescribed anxiolytic in general psychiatric practice (11.64%) [32]. Side effects noted in prescribing studies include drowsiness, headache, ataxia, insomnia, and depression [19, 40].

Synthesis

The evidence across these 41 sources, despite considerable heterogeneity in study design, population, and outcome measurement, converges on a general pattern of benzodiazepine-associated psychomotor impairment, though the magnitude and consistency of the association vary by domain, dose, duration, and population.

Reconciling Conflicting Cognitive-Psychomotor Findings

The principal discrepancy lies between the majority of studies showing impairment and the null finding from Høiseth et al., who found no cognitive decrements in psychogeriatric benzodiazepine users compared to non-users [9]. This divergence is likely explained by population characteristics and confounding by indication. The Høiseth et al. sample consisted of geriatric psychiatry inpatients with high rates of dementia, depression, and concomitant psychotropic use [9, 9], meaning the non-user comparison group was already cognitively compromised by their psychiatric conditions, potentially masking any incremental benzodiazepine effect. The study also adjusted for years of education, dementia, and depression [9], which may have over-adjusted for pathways through which benzodiazepines exert their effects. In contrast, Saloner et al. used

propensity-score matching and still found robust effects (OR = 2.13, P = 0.003) [5, 5], and Manthey et al. controlled for severity of psychopathology and antidepressant use in a much larger sample [4].

Dose-Response Considerations

The evidence suggests a threshold rather than linear dose-response relationship for at least some psychomotor outcomes. Manthey et al. found that only high-dose users (>1 DDD) showed significantly prolonged reaction times, while low and intermediate dose groups did not differ from non-users [4], suggesting partial tolerance development at lower doses. Lily Annisa et al. similarly found that fall risk escalated with dose, with doses >0.5 DDD/day showing the strongest association (adjusted OR = 4.463) [8]. However, Bang et al. reported that executive function impairment was not proportional to daily or cumulative benzodiazepine dose [6], suggesting different psychomotor domains may have different dose-response profiles. For hip fracture, the meta-analysis by Poly et al. showed that current users faced substantially greater risk (RR = 1.83) than past users (RR = 1.18) [2], pointing to recency of exposure as a critical determinant rather than cumulative dose alone.

Acute Versus Chronic Effects

The experimental study by Dawson et al. demonstrated that a single acute dose of a benzodiazepine produces measurable psychomotor impairment lasting up to 14.5 hours [3], establishing the mechanistic basis for next-day residual effects on driving [38]. For chronic use, Manthey et al. interpreted the persistence of reaction time impairment in high-dose long-term users (median 36 months) as evidence that tolerance does not fully develop for this domain [4]. The longitudinal data from Petrov et al. showing functional impairment persisting over 8.5 years of follow-up further suggests that chronic benzodiazepine use may produce sustained or worsening psychomotor consequences [10].

Role of Acting Duration and Agent Type

Long-acting benzodiazepines showed somewhat greater hip fracture risk (RR = 1.31) than short-acting agents (RR = 1.15) in the Poly et al. meta-analysis [2], and Papoutsis et al. noted that

longer-acting agents tested the morning after nighttime dosing showed the most pronounced driving impairment [28]. Yet short-acting agents were not free of risk: Abbassyyah et al. reported significant fall risk increases for both long-acting (OR = 1.45) and short-acting (OR = 1.32) benzodiazepines [15]. Individual agents most strongly linked to neurocognitive impairment in the Saloner et al. study were diazepam, lorazepam, and alprazolam (all OR > 2.31) [5], though this finding was not adjusted for dose equivalencies.

Vulnerability of Specific Populations

The elderly emerge as the most consistently at-risk population. Falls, hip fractures, and functional decline are predominantly documented in studies of individuals aged 65 and older [2, 7, 10–12]. Age-related pharmacokinetic changes, including decreased hepatic metabolism and increased receptor sensitivity, amplify psychomotor impairment [33]. The systematic review by Vasconcelos et al. reported that benzodiazepine prevalence among elderly Brazilians ranged from 6.1% to 76.4%, with prescriptions frequently exceeding recommended durations. People living with HIV represent another vulnerable group, with chronic benzodiazepine use (median 24 months) associated with a twofold increase in neurocognitive impairment risk even after adjusting for HIV-specific factors [5]. Psychiatric populations, who constitute the primary consumers of benzodiazepines in the included Indonesian studies [24, 31, 34], face compounded risk from polypharmacy: drug interaction analyses identified that 93% of prescriptions containing benzodiazepines had potential interactions, predominantly involving CNS depression potentiation [17].

Methodological Weight of Evidence

The strongest evidence comes from the two meta-analyses and the controlled experimental study. Rapoport et al.'s meta-analysis (27 studies) demonstrated consistent collision risk increases across both epidemiologic designs [1], and Poly et al.'s meta-analysis (33 studies, 169,660 fracture cases) demonstrated robust hip fracture risk elevations [2]. The double-blind crossover trial by Dawson et al. provides the only direct causal evidence, confirming that acute benzodiazepine

administration impairs psychomotor performance relative to placebo [3, 3]. The observational studies, while limited by confounding by indication (patients prescribed benzodiazepines typically have anxiety, insomnia, or other conditions that may independently impair psychomotor function), generally attempted statistical adjustment for these factors [4, 5, 10, 14]. The large number of descriptive prescribing studies from Indonesian settings do not contribute direct evidence of psychomotor effects but document the extent of benzodiazepine exposure in clinical populations where psychomotor monitoring may be warranted.

In aggregate, the evidence supports a clinically meaningful association between benzodiazepine use and psychomotor impairment across multiple domains—reaction time, motor function, driving performance, balance (falls), and functional mobility—with the strongest and most consistent effects observed at higher doses, with longer-acting agents, in elderly populations, and during acute or current (versus past) use.

DISCUSSION

This review synthesizes evidence from 41 studies to provide a comprehensive overview of the relationship between benzodiazepine use and psychomotor impairment. The findings robustly support the hypothesis that BZD use is associated with clinically significant deficits across multiple domains, including reaction time, motor function, driving performance, and balance, which in turn leads to increased risks of MVCs, falls, and fractures. The convergence of evidence from meta-analyses, experimental trials, and large observational cohorts strengthens the validity of this association (1-5, 7, 14).

Our synthesis confirms that the psychomotor effects of BZDs are not uniform but are modulated by several key factors. The dose-response relationship, or more precisely a threshold effect, is evident. Data from Manthey et al. and Lily Annisa et al. demonstrate that significant impairments in reaction time and fall risk are primarily observed at higher doses (>1 DDD or >0.5 DDD/day), suggesting that partial tolerance may mitigate effects at lower, therapeutic doses but is

overcome at higher exposure levels (4, 8). This finding has direct clinical implications, supporting recommendations to use the minimum effective dose. However, the absence of a linear dose-response in executive function, as reported by Bang et al., suggests that different cognitive domains may have varying susceptibility to BZDs, warranting further investigation (6).

The duration and recency of use are also critical determinants. While a single acute dose can produce profound, measurable impairment lasting many hours (3), chronic use is associated with persistent deficits, particularly in high-dose users, indicating that complete tolerance does not develop for all psychomotor functions (4, 10). The finding by Poly et al. that current users have a substantially higher hip fracture risk (RR=1.83) than past users (RR=1.18) highlights the potential for risk reduction upon cessation and underscores the importance of avoiding long-term use (2).

The vulnerability of specific populations is a dominant theme. The elderly are disproportionately affected, with consistent evidence of increased falls, fractures, and functional decline (2, 7, 8, 10-12). Age-related pharmacokinetic and pharmacodynamic changes, such as reduced drug metabolism and increased receptor sensitivity, amplify sedative and psychomotor effects, making even standard doses potentially hazardous (26, 33). People living with HIV also emerge as a high-risk group, likely due to baseline neurocognitive vulnerability that is exacerbated by BZD use (5). Furthermore, the widespread prescribing of BZDs in psychiatric populations, as documented in numerous Indonesian studies, raises concerns about polypharmacy and drug interactions, which can potentiate CNS depression and further impair function (17, 31, 34).

The apparent contradiction presented by Høiseth et al., who found no cognitive differences between BZD users and non-users in a psychogeriatric population, warrants careful consideration (9). This null finding is likely explained by significant confounding by indication. The non-user comparison group in this inpatient setting consisted of individuals with high rates of dementia and depression, meaning they were already cognitively impaired. This creates a "ceiling effect" where any additional impairment from BZDs is difficult to detect. This study underscores the critical challenge in observational research of disentangling the effects of the drug from the effects of the

condition for which it is prescribed, a challenge that studies using propensity-score matching or adjusting for illness severity attempt to overcome (4, 5, 10).

The strengths of this review include the synthesis of a large and heterogeneous body of literature, ranging from high-level meta-analyses to granular clinical data, allowing for a multi-faceted examination of the issue. However, several limitations must be acknowledged. The quality of the included studies varied considerably, with many descriptive prescribing studies from Indonesian settings offering valuable context on exposure but no direct evidence of psychomotor outcomes. The reliance on abstracts for a portion of the sources may have limited the depth of data extraction. Furthermore, significant heterogeneity in outcome measures, BZD types, and study populations precluded a formal meta-analysis of all included studies. Confounding by indication remains an inherent limitation of the observational studies that form the bulk of the evidence base.

CONCLUSION AND RECOMMENDATIONS

This comprehensive review concludes that benzodiazepine use is significantly and consistently associated with impairment in psychomotor function. This impairment manifests as prolonged reaction times, deficits in motor coordination and executive function, diminished driving ability, and increased postural instability. These deficits translate directly into clinically meaningful adverse outcomes, including a 60% higher risk of motor vehicle collisions and a 34% higher risk of hip fractures. The risks are not uniform; they are amplified by higher doses, current use, longer-acting agents, and are most pronounced in vulnerable populations such as the elderly and those with pre-existing neurocognitive vulnerability.

Recommendations:

1. **For Clinicians:** Prescribing practices should prioritize a careful risk-benefit analysis. BZDs should be used at the lowest effective dose for the shortest possible duration (ideally less than 2-4 weeks). Extreme caution is warranted in elderly patients, where alternative treatments (e.g., SSRIs for anxiety, CBT-I for insomnia) should be considered first-line.

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Patients should be counseled about the risks of psychomotor impairment, including driving and fall hazards.

2. **For Policymakers and Healthcare Systems:** Given the widespread and often long-term use of BZDs, particularly in elderly populations, public health initiatives are needed to promote safer prescribing. This could include educational campaigns, audit and feedback systems for prescribers, and support for deprescribing programs in primary and secondary care.
3. **For Future Research:** Future research should prioritize prospective cohort studies with long-term follow-up that utilize standardized, objective psychomotor test batteries. This would allow for a more precise characterization of the trajectory of impairment with chronic use and after cessation. Further research is also needed to explore the differential effects of individual BZDs and to develop and test effective interventions for deprescribing in high-risk populations.

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