Original article

Association between benzodiazepine use and substance use among older adults in a primary care setting in Nan province, Thailand

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Abstract

Objective: To investigate the prevalence of benzodiazepine use and its association with a history of substance use among older adults in a primary care setting.

Methods: A cross-sectional study was conducted among older adults aged 60 years and older at a community hospital in Northern Thailand. Data were collected using structured questionnaires, including the Alcohol, Smoking and Substance Involvement Screening Test (ASSIST), the Alcohol Use Disorders Identification Test (AUDIT), and the Fagerström Test for Nicotine Dependence (FTND). Multivariable logistic regression was performed to examine the association between benzodiazepine use and substance use, with sex-specific subgroup analyses.

Results: Among 218 participants, 21.1% reported benzodiazepine use and 45.9% reported any other substance use. Compared with non-users, benzodiazepine users were older, had lower educational attainment, and had a higher prevalence of type 2 diabetes mellitus and chronic kidney disease. After adjusting for covariates, benzodiazepine use was significantly associated with an increased likelihood of substance use (AOR = 11.25, 95% CI = 3.55 - 35.67). In subgroup analyses, a significant association was observed only among females (AOR = 15.05, 95% CI = 4.06 - 55.73), whereas the association among males did not reach statistical significance.

Conclusion: Concurrent benzodiazepine use and substance use are common among older adults and are significantly associated with each other, particularly among females. Routine screening for substance use should be considered for older adults prescribed benzodiazepines. Cautious prescribing practices are warranted to mitigate potential adverse outcomes in this population.

Keywords: benzodiazepine, older adult, primary care, substance use

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นิพนธ์ต้นฉบับ

ความสัมพันธ์ระหว่างการใช้ยากลุ่มเบนโซไดอะซีพีนและการใช้สารในผู้สูงอายุในสถานบริการปฐมภูมิ จังหวัดน่าน

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บทคัดย่อ

วัตถุประสงค์ : เพื่อศึกษาความชุกของการใช้เบนโซไดอะซีพีนและความสัมพันธ์กับการใช้สารในผู้สูงอายุที่มารับบริการในสถานบริการปฐมภูมิ

วิธีการ : การศึกษาภาคตัดขวางในผู้สูงอายุตั้งแต่ 60 ปีขึ้นไป ณ โรงพยาบาลอำเภอหนึ่งในจังหวัดน่าน เก็บรวบรวมข้อมูลด้วยแบบสอบถามโครงสร้างมาตรฐาน ได้แก่ Alcohol, Smoking and Substance Involvement Screening Test (ASSIST), Alcohol Use Disorders Identification Test (AUDIT) และ Fagerström Test for Nicotine Dependence (FTND) วิเคราะห์ความสัมพันธ์ระหว่างการใช้เบนโซไดอะซีพีนกับการใช้สารด้วยการวิเคราะห์ถดถอยโลจิสติกแบบหลายตัวแปรและวิเคราะห์แยกตามเพศ

ผล : กลุ่มตัวอย่าง 218 คน มีผู้ใช้เบนโซไดอะซีพีนร้อยละ 21.1 และมีประวัติใช้สารอื่น ๆ ร้อยละ 45.9 ผู้ที่ใช้เบนโซไดอะซีพีนมีอายุมากกว่า มีระดับการศึกษาต่ำกว่า และมีความชุกของโรคเบาหวานชนิดที่ 2 และโรคไตเรื้อรังสูงกว่าผู้ไม่ได้ใช้อย่างมีนัยสำคัญ พบความสัมพันธ์อย่างมีนัยสำคัญทางสถิติระหว่างการใช้เบนโซไดอะซีพีนกับประวัติการใช้สารหลังปรับตัวแปรกวน (AOR = 11.25, 95% CI = 3.55 - 35.67) การวิเคราะห์กลุ่มย่อยพบความสัมพันธ์ดังกล่าวอย่างมีนัยสำคัญเฉพาะในเพศหญิง (AOR = 15.05, 95% CI = 4.06 - 55.73) ขณะที่ในเพศชายไม่พบนัยสำคัญทางสถิติ

สรุป : ผู้สูงอายุมีการใช้เบนโซไดอะซีพีนและสารอื่น ๆ ร่วมกันได้บ่อย และมีความสัมพันธ์กันอย่างมีนัยสำคัญโดยเฉพาะในเพศหญิง ควรมีการคัดกรองการใช้สารในผู้สูงอายุที่ได้รับเบนโซไดอะซีพีนอย่างสม่ำเสมอ รวมถึงควรใช้ความระมัดระวังในการสั่งใช้ยาดังกล่าวเพื่อลดความเสี่ยงด้านสุขภาพที่ไม่พึงประสงค์ในประชากรกลุ่มนี้

คำสำคัญ : การใช้สาร, บริการปฐมภูมิ, ผู้สูงอายุ, เบนโซไดอะซีพีน

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Previous knowledge: Benzodiazepines are frequently prescribed to older patients for various medical conditions. However, their use in this population is associated with an increased risk of misuse and adverse outcomes.

New knowledge: One-fifth of older adults in primary care settings reported benzodiazepine use. Those who used benzodiazepines had a higher prevalence of certain medical conditions, including type 2 diabetes mellitus and chronic kidney disease. Benzodiazepine use was significantly associated with an increased likelihood of substance use, with a stronger association observed among women.

Application: Routine screening for substance use should be implemented for older adults prescribed benzodiazepines, with particular attention to sex-specific risks. The appropriateness of prescribing practices should be carefully reviewed to reduce concurrent substance use and related adverse events.

Introduction

Benzodiazepines are commonly prescribed to older adults for conditions such as anxiety disorders, sleep disorders, seizure disorders, and alcohol withdrawal.[1,2] However, the appropriateness of benzodiazepine use remains an area of ongoing investigation, particularly with regard to balancing potential benefits against known adverse effects. According to the 2023 Beers Criteria,[2] benzodiazepines should generally be avoided in older adults because of the increased risks of misuse, dependence, and serious adverse outcomes, including falls, fractures, cognitive impairment, and delirium. These complications may substantially worsen health outcomes in this population.[2,3]

Studies in clinical settings have demonstrated the frequent co-occurrence of benzodiazepine and other substance use among patients with diverse physical and psychiatric conditions.[4-6] These associations may be attributed to neuroadaptive changes following prolonged exposure, which increase the risk of both dependence and concurrent substance use.[7] Additionally, patients with psychiatric comorbidities who use benzodiazepines to alleviate their symptoms may also use other substances as a form of self-medication or maladaptive coping.[6] Social isolation, which is commonly experienced among older adults, may further increase the likelihood of both substance and non-medical drug use.[8] Notably, among older adults, concurrent use of benzodiazepines and other substances is associated with an increased risk of exacerbation of underlying health conditions, accidents, disabilities, and mortality.[9,10]

Despite these concerns, screening and risk assessment for substance use disorders remain insufficiently prioritized and are frequently overlooked in primary care settings, resulting in missed opportunities for early identification and appropriate management. Consequently, untreated substance use disorders can lead to poorer health outcomes and adversely affect patients, families, and communities.[11,12]

Nonetheless, evidence regarding the association between benzodiazepine use and other substance use among older patients in primary care settings remains limited in Southeast Asia, including Thailand.[13] Moreover, although sex differences in patterns and risks of substance use have been suggested, sex-specific associations between benzodiazepine use and other substance use remain poorly understood, particularly among older adults.[14,15]

This study aims to determine the prevalence of benzodiazepine and other substance use among older adults and to examine their relationships, including sex-specific patterns. The findings are expected to inform the appropriate prescribing and monitoring of benzodiazepines and contribute to the development of effective strategies to reduce substance-related adverse health outcomes in Thailand's rapidly growing older population.

Methods

Study design

This was an observational cross-sectional study, reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement.[16] The study was approved by the Faculty of Medicine Chiang Mai University Ethics Committee (FAM-2567-0179, Research ID: 0179).

Setting

The Outpatient Clinic for Non-Communicable Diseases at a community hospital in Nan province, Thailand, primarily provides services to older adults with chronic non-communicable diseases (NCDs), who account for more than 90% of the total patient population. This setting was selected because older adults with NCDs often have multiple psychiatric comorbidities, such as insomnia, anxiety, and depression, which place them at higher likelihood of benzodiazepine use and substance use.[17] The clinic operates on all official working days and serves approximately 40 - 60 patients per day.

Population and sample

The participants in this study were patients aged 60 years and older, in accordance with Thailand's definition of older adults. The inclusion criteria were the ability to communicate effectively and make independent decisions. Participants were excluded if they had dementia or mild cognitive impairment, as defined by a prior diagnosis. Functional dependency was assessed using the Barthel Index of Activities of Daily Living (Barthel ADL Index).[18,19] In this study, complete dependency was defined as an ADL score of less than 5. Participants who met this criterion were excluded, as they typically require caregiver assistance with medication, have limited autonomy in substance use, and may introduce health-related confounding factors.

The sample size for this study was calculated using the infinite population proportion formula, based on the previous study that investigated the prevalence of benzodiazepine use (13.5%) among elderly patients.[20] A sample size of 218 was determined to provide a statistical power greater than 90%.

Data collection

Data were collected between August and September 2024 by trained nurses who were not involved in the patients' care. Convenience sampling was used to recruit older adults attending the primary care clinic. Potential participants were approached consecutively on clinic days and screened for eligibility based on the inclusion and exclusion criteria. Recruitment continued until the target sample size was reached. Relatives/caregivers were not present during the interview unless requested by the participant. Written informed consent was obtained from all participants, and no identifiable personal data were collected. Data were collected using structured questionnaires administered via face-to-face interviews, conducted in a private room at the clinic to ensure privacy. Each interview took approximately 20 - 30 minutes. Questionnaire data were confirmed with electronic medical records (EMR).

Measures

Prior to recruitment, participants were screened for eligibility using the Barthel ADL Index,[18,19] which evaluates independence in basic daily activities (i.e., feeding, bathing, grooming, dressing, bowel and bladder control, toileting, transfers, mobility, and stair climbing). The total score ranges from 0 to 20, where lower scores indicate greater dependency. The Thai version has acceptable reliability and internal consistency, with intraclass correlation coefficients (ICCs) between 0.714 and 0.968, and Cronbach's alpha coefficient of 0.694.[19] The questionnaires used for data collection consisted of four sections:

Section 1: General Information, including age, sex, marital status, education level, monthly income, healthcare coverage, medical conditions, and medication. The type and dosing of benzodiazepines were obtained through self-report and subsequently clarified and verified by medication inspection and/or EMR, when necessary.

Section 2: The Alcohol, Smoking and Substance Involvement Screening Test (ASSIST),[21] an eight-item screening tool for tobacco, alcohol, and other substances (e.g., cannabis, cocaine, amphetamines, sedatives, hallucinogens, inhalants, opioids). The Thai version has acceptable internal consistency, with Cronbach's alpha coefficients of 0.82 for tobacco and 0.73 for alcohol.[22] Participants with a history of using at least one substance were classified as having substance use. Scores were categorized as follows: For each substance except alcohol, 0 - 3 = low risk, 4 - 26 = moderate risk, and ≥ 27 = high risk; for alcohol, 0 - 10 = low risk, 11 - 26 = moderate risk, and ≥ 27 = high risk.

Section 3: The Alcohol Use Disorders Identification Test (AUDIT),[23] administered to participants with a history of alcohol use. The Thai version has acceptable internal consistency, with a Cronbach's alpha coefficient of 0.70.[24] The interpretation of scores was as follows: 0 - 7 = low risk, 8 - 15 = moderate risk, 16 - 19 = high risk, and 20 - 40 = probable alcohol dependence.

Section 4: The Fagerström Test for Nicotine Dependence (FTND),[25] administered to participants with a history of smoking. The Thai version demonstrated fair internal consistency, with Cronbach's alpha coefficient of 0.52, and good test–retest reliability (ICC (3,1) = 0.83).[26] Scores were interpreted as follows: 1 - 2 = low-level dependence, 3 - 4 = low to moderate dependence, 5 - 7 = moderate dependence, and ≥ 8 = high dependence.

Participants who used at least one substance, excluding benzodiazepines, within the past three months were defined as having a history of substance use. Benzodiazepine use within the past three months was assessed using the ASSIST.[21] Because the ASSIST assesses sedatives as a class, participants who reported sedative use were further asked to identify the specific type (generic/brand name) and dosing information. When possible, participants were asked to show the medication package/blister strip to support identification. Self-reported information was cross-checked against the patients' EMR, which provided the prescribed sedative agent(s) and dose. Self-report was accepted when medication identification was considered reliable (e.g., correct drug name and dose or medication shown). When self-report and EMR were discordant, EMR data were used as the primary source. Therefore, non-benzodiazepine sedative-hypnotics identified in the EMR were not classified as benzodiazepine use. Regular use was defined

as self-reported benzodiazepine use on a weekly or more frequent basis during the past three months, corresponding to a score of ≥ 4 on ASSIST Question 2, consistent with the moderate-risk scoring criteria.[21]

Data analysis

Participant characteristics were summarized using frequencies and percentages for categorical variables and means with standard deviation (SD) for continuous variables. Chi-square tests or Fisher's exact tests, as appropriate, were used to compare the distribution of categorical variables between participants with and without benzodiazepine use, while independent t-tests were used for continuous variables. Multivariable logistic regression was performed to examine the association between substance use and benzodiazepine use, sex, and the interaction term between benzodiazepine use and sex, adjusting for relevant covariates. Subgroup analyses were conducted to assess sex-specific effects. Strength of association was presented as adjusted odds ratios (AORs) with 95% confidence intervals (CIs). Statistical significance was set at $p < .05$.

Results

A total of 218 participants were included in the study. The majority were female (n = 137, 62.8%), with a mean age of 68.7 ± 7.0 years. Most participants had completed primary education (53.7%), were married (42.7%), and were not living alone (81.2%). Universal health coverage was the most common healthcare coverage (65.1%), and most participants reported a monthly income of less than 5,000 baht (63.8%). All participants had at least one underlying disease, with the most prevalent conditions being hypertension (73.4%), dyslipidemia (67.0%), and type 2 diabetes mellitus (32.1%). Among psychiatric comorbidities, only depression (0.9%) was identified (Table 1).

Among all the participants, 46 (21.1%) reported benzodiazepine use (BZD group), whereas 172 (78.9%) reported no current benzodiazepine use (non-BZD group). In the BZD group, lorazepam 0.5 mg was the only benzodiazepine used. Significant differences between participants with and without benzodiazepine use were observed in age, educational level, and certain medical conditions, including type 2 diabetes mellitus, chronic kidney disease (CKD), a history of falls, and depression (Table 1).

As shown in Table 2, 45.9% of participants had a history of using at least one type of substance. The most commonly reported substances were alcoholic beverages (36.7%) and tobacco products (19.7%). The BZD group had a significantly higher proportion of participants with any substance use compared with the non-BZD group (73.9% vs. 38.4%). However, no significant differences were observed in the use of specific substances or in severity between the BZD and non-BZD groups.

Table 3 presents the multiple logistic regression analysis adjusted for age, education, and marital status. Substance use was significantly associated with benzodiazepine use (AOR = 11.25, 95% CI = 3.55 - 35.67), and being male (AOR = 12.94, 95% CI = 5.57 - 30.04). No interaction between benzodiazepine use and sex was observed. Subgroup analysis by sex showed no significant association between a history of benzodiazepine use and substance use among males. However, among females, history of substance use remained significantly associated with benzodiazepine use (AOR = 15.05, 95% CI = 4.06 - 55.73).

Table 1 Demographic characteristics of participants and benzodiazepine use

	All (n = 218) n (%)	BZD (n = 46) n (%)	non-BZD (n = 172) n (%)	*p-value*
Age (mean ± SD)[a]	68.7 ± 7.0	73.0 ± 8.9	67.6 ± 6.0	< .001
Sex				.090
Male	81 (37.2)	22 (47.8)	59 (34.3)	
Female	137 (62.8)	24 (52.2)	113 (65.7)	
Educational level				< .001[b]
No education	96 (44.0)	32 (69.6)	64 (37.2)	
Primary education	117 (53.7)	14 (30.4)	103 (59.9)	
Secondary education or higher	5 (2.3)	0 (0.0)	5 (2.9)	
Marital status				.100
Single	54 (24.8)	9 (19.6)	45 (26.2)	
Married	93 (42.7)	15 (32.6)	78 (45.4)	
Widowed	50 (22.9)	16 (34.8)	34 (19.8)	
Divorced	21 (9.6)	6 (13.0)	15 (8.7)	
Living status				.120
Not living alone	177 (81.2)	41 (89.1)	136 (79.1)	
Living alone	41 (18.8)	5 (10.9)	36 (20.9)	
Health benefits scheme				.482[b]
Universal health coverage	142 (65.1)	28 (60.8)	114 (66.3)	
Civil Servant Medical Benefits Scheme	73 (33.5)	17 (37.0)	56 (32.6)	
Social security scheme	1 (0.5)	0 (0.0)	1 (0.6)	
State enterprise	2 (0.9)	1 (2.2)	1 (0.6)	
Monthly income (Thai Baht)				.139[b]
< 5,000	139 (63.8)	36 (78.3)	103 (59.9)	
5,000 - 10,000	77 (35.3)	10 (21.7)	67 (39.0)	
10,000 - 20,000	1 (0.5)	0 (0.0)	1 (0.6)	
> 20,000	1 (0.5)	0 (0.0)	1 (0.6)	
Medical conditions				
Hypertension	160 (73.4)	38 (82.6)	122 (70.9)	.110
Type 2 diabetes mellitus	70 (32.1)	21 (45.7)	49 (28.5)	.030
Dyslipidemia	146 (67.0)	32 (69.6)	114 (66.3)	.670
Chronic kidney disease	35 (16.1)	15 (32.6)	20 (11.6)	.010
Chronic respiratory disease	26 (11.9)	8 (17.4)	18 (10.5)	.200
Stroke	7 (3.2)	3 (6.5)	4 (2.3)	.164[b]
Gout	4 (1.8)	2 (4.4)	2 (1.2)	.197[b]
Falling in the past year	8 (3.7)	5 (10.9)	3 (1.7)	.012[b]
Osteoporosis	8 (3.7)	2 (4.4)	6 (3.5)	.677[b]
Depression	2 (0.9)	2 (4.4)	0 (0.0)	.044[b]

Note: Participants may have multiple medical conditions; therefore, percentages may exceed 100%.

BZD = benzodiazepine; SD = standard deviation. [a] p-value calculated using independent t-test. [b] p-value calculated using Fisher exact test.

Discussion

Among older adult patients attending the outpatient department for chronic NCDs at a primary care setting in Thailand, 21.1% reported benzodiazepine use. The prevalence is higher than that reported among older adults in other Thai contexts, including a large population-based cohort (11.1%),[27] inpatients in a tertiary setting (14%),[28] and outpatients in a tertiary setting (16%).[29] Compared with international research, a study among older patients in academic medical centers in the USA reported a prevalence of 13.5%,[20]

Table 2 History of substance use and severity (n = 218)

	All (n = 218) n (%)	BZD (n = 46) n (%)	non-BZD (n = 172) n (%)	*p-value*
Any substance use[a]	100 (45.9)	34 (73.9)	66 (38.4)	< .001
Alcohol	80 (36.7)	20 (43.5)	60 (34.9)	.283
ASSIST				.661
Low risk	69 (86.6)	17 (85.0)	52 (86.7)	
Moderate risk	5 (6.3)	2 (10.0)	3 (5.0)	
High risk	6 (7.5)	1 (5.0)	5 (8.3)	
AUDIT				.642
Low risk	65 (81.3)	15 (75.0)	50 (83.3)	
Moderate risk	11 (13.8)	4 (20.0)	7 (11.7)	
High risk	0 (0.0)	0 (0.0)	0 (0.0)	
Dependence	4 (5.0)	1 (5.0)	3 (5.0)	
Smoking	43 (19.7)	12 (26.1)	31 (18.0)	.222
ASSIST				.739
Low risk	37 (86.6)	11 (91.7)	26 (83.9)	
Moderate risk	5 (11.6)	1 (8.3)	4 (12.9)	
High risk	1 (2.3)	0 (0.0)	1 (3.2)	
FTND				.315
Low level	11 (25.6)	3 (25.0)	8 (25.8)	
Low-moderate level	20 (46.5)	6 (50.0)	14 (45.2)	
Moderate level	9 (20.9)	1 (8.3)	8 (25.8)	
High level	3 (7.0)	2 (16.7)	1 (3.2)	
Cannabis	4 (1.8)	2 (4.3)	2 (1.2)	.153
ASSIST				
Low risk	0 (0.0)	0 (0.0)	0 (0.0)	
Moderate risk	3 (75.0)	2 (100.0)	1 (50.0)	
High risk	1 (25.0)	0 (0.0)	1 (50.0)	
Kratom	1 (0.5)	0 (0.0)	1 (0.6)	.604
ASSIST				< .001
Low risk	0 (0.0)	0 (0.0)	0 (0.0)	
Moderate risk	0 (0.0)	0 (0.0)	0 (0.0)	
High risk	1 (100.0)	0 (0.0)	1 (100.0)	

Note: BZD = benzodiazepine; ASSIST = Alcohol, Smoking and Substance Involvement Screening Test; AUDIT = Alcohol Use Disorders Identification Test; FTND = Fagerström Test for Nicotine Dependence.

[a] Defined as self-reported use of alcohol, tobacco, cannabis, or kratom, as assessed by the ASSIST.

whereas a study among community-dwelling older adults in Brazil found a prevalence of 18.3%.[30] This discrepancy may reflect differences in operational criteria as well as clinical characteristics of the sample, as our OPD sample consisted of older patients with multiple comorbidities and frequent healthcare contact, which may increase the likelihood of benzodiazepine prescribing.

We found that the BZD group was older, which is consistent with previous evidence.[31] Prescription benzodiazepine use in older adults continues to be an important and persistent clinical

Table 3 Multiple logistic regression analysis of factors associated with history of substance use, overall and stratified by sex (n = 218)

	All (n = 218)		Male (n = 81)		Female (n = 137)	
	AOR (95% CI)[a]	*p-value*	AOR (95% CI)[a]	*p-value*	AOR (95% CI)[a]	*p-value*
BZD use	11.25 (3.55 - 35.67)	< .001	2.27 (0.50 - 10.34)	.290	15.05 (4.06 - 55.73)	< .001
Male	12.94 (5.57 - 30.04)	< .001				
BZD use × sex[b]	0.27 (0.05 - 1.59)	.148				

Note: AOR = adjusted odds ratio; CI = confidence interval; BZD = benzodiazepine.

[a] Adjusted for age, education, and marital status. [b] Reference group: female.

concern. We also found lower educational attainment in the BZD group, which may reflect that non-pharmacological management requires health literacy.[32] In addition, the BZD group had higher proportions of CKD, depression, and a history of falls. These findings support previous evidence that patients with multiple comorbidities may be harmed by inappropriate prescribing.[29] In primary care settings within community hospitals, time constraints and the limited availability of behavioral interventions or specialized mental health services may further contribute to benzodiazepine prescribing. Therefore, benzodiazepines should be prescribed cautiously, particularly in vulnerable older adults and those with comorbidities, with regular medication review and monitoring for adverse outcomes.

Approximately 45.9% of participants reported using at least one type of substance, with alcohol and tobacco being the most commonly used substances. This finding aligns with global evidence indicating that alcohol and tobacco are the most widely consumed substances worldwide.[33,34] Due to its sedative effects, the concurrent use of alcohol and benzodiazepines may increase the risk of falls, fractures, and accidents, particularly among older adults.[35] Cannabis ranked third in frequency of use, which may partially reflect Thailand's 2022 cannabis liberalization under the Narcotics Act. However, we could not distinguish whether cannabis use among participants was for medical or recreational purposes. This distinction should be taken into account when interpreting its association with benzodiazepine use.[36]

A significant association was observed between benzodiazepine use and a history of substance use after adjusting for potential confounders. This finding may be explained by several mechanisms, primarily related to the pharmacological properties of benzodiazepines. These agents act on gamma-aminobutyric acid-A (GABA-A) receptors, producing sedative and anxiolytic effects. Prolonged use can induce neuroadaptive changes, such as decreased endogenous GABA activity, leading to increased dependence on external substances to maintain psychological stability.[7] Consequently, individuals may turn to other substances, including alcohol, opioids, or stimulants, to mitigate withdrawal symptoms.[6] Moreover, the shared pharmacodynamic effects of benzodiazepines and alcohol may further increase the risk of cross-substance use and polysubstance dependence.[37] Conversely, individuals with prior substance use disorder may be particularly vulnerable to benzodiazepine misuse, using it as a coping mechanism for withdrawal symptoms or psychological distress related to coexisting mental health conditions.[37] In older adults, additional risk

factors such as late-life depression, social isolation, and sleep disturbances may also contribute to substance use behaviors.[38]

In stratified analyses, the association between benzodiazepine use and other substance use appeared stronger among females than males. This pattern is consistent with previous studies suggesting that women are more likely to use benzodiazepines to cope with negative emotions and may be more vulnerable to co-occurring mental health conditions.[39] Women have also been reported to exhibit greater sensitivity to certain substances and stronger cravings, which could increase susceptibility to polysubstance use.[39] In contrast, although men generally have a higher risk of developing substance use disorders, this elevated risk is not necessarily specific to benzodiazepine use.[40] Biological, social, and cultural factors, including differences in drug availability, peer influences, and gender norms, have been proposed to explain the higher prevalence of substance use disorders among men.[41] However, the interaction between benzodiazepine use and sex was not statistically significant in our model, indicating insufficient evidence to conclude that the strength of the association differs by sex. Moreover, the wide confidence intervals observed in both overall and sex-stratified analyses suggest imprecision, likely due to the relatively small number of benzodiazepine users, particularly among males. These findings should therefore be interpreted with caution.

In Thailand, benzodiazepines are strictly regulated and can only be prescribed by hospital-based physicians, with over-the-counter access prohibited.[42] Nonetheless, despite this controlled environment and awareness of the potential adverse consequences of these medications, general practitioners continue to face challenges in appropriately regulating their prescribing practices.[43] These findings underscore the need to raise awareness among healthcare professionals regarding the risks of addiction,[44] as well as to implement targeted interventions for older adults who use benzodiazepines.

In addition, differences in screening results were observed across assessment tools. While the ASSIST frequently classified most participants as low risk for alcohol and tobacco use, the AUDIT and FTND identified greater proportions of individuals at higher risk levels. This discrepancy highlights the added value of administering substance-specific tools alongside the broader tools such as the ASSIST to improve early detection and risk stratification, which could enhance and facilitate more effective clinical intervention strategies in primary care.[45]

A key strength of this study is its focus on older adults receiving care in primary settings, with data collected by trained professional nurses to ensure reliability. However, several limitations should be considered. First, as a cross-sectional study relying on self-reported measures, we cannot determine the temporal sequence between substance use and benzodiazepine use. Our findings hence reflect co-occurrence and associations rather than causal relationships. Second, we did not collect detailed information on the clinical indications or patients' reasons for benzodiazepine use. Differences in indications may be associated with different baseline risks of other substance use and may introduce clinical heterogeneity and unmeasured confounding. Consequently, the pooled adjusted odds ratio may be underestimated or overestimated. Third, detailed patterns of substance use as well as the reasons for use were not assessed and may represent unmeasured confounding factors influencing

the observed associations. Future research should investigate specific substance use patterns to provide a more detailed understanding of these associations.

Conclusion

Among older adults, benzodiazepine use was significantly associated with a higher prevalence of substance use, with women tending to demonstrate a stronger association than men. These findings highlight the importance of cautious prescribing practices and may inform the development of targeted strategies to reduce substance use in this population. Brief screening for addictive behaviors among patients who use benzodiazepines may support early identification and timely intervention in primary care settings.

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Author contributions

Peerawit Ngamsittiroek: conceptualization, data collection, data analysis, writing of the manuscript; Nida Buawangpong: conceptualization, data analysis, writing of the manuscript; Wichuda Jiraporncharoen: conceptualization, revision of the manuscript; Kanokporn Pinyopornpanish: conceptualization, funding acquisition; Somthanon Pongsananurak: data collection; Thanachat Yotruangsri: conceptualization, data collection, data analysis, revision of the manuscript, corresponding author.

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