

Supplemental Material

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eTable 1. *International Classification of Diseases, Ninth Revision, Clinical Modification ICD-9-CM* codes for dementia and Alzheimer’s disease

Condition	ICD-9-CM Code
Alzheimer’s disease	290.0, 290.1x, 290.2x, 290.3, 294.10, 294.11, 331.0
Vascular dementia	290.4x
Alcoholic dementia	291.2
Frontotemporal dementia	331.1x
Lewy body dementia	331.82
Dementia, unspecified	294.20, 294.21

eTable 2. Association of incident dementia during follow-up years with 8-year benzodiazepine exposure with 3-year lag time.

Benzodiazepine Exposure ^a	Follow Up Time ^b , Person Years	Incident Dementia (N=41630), N(%)	Hazard Ratio (95% Confidence Interval)		
			Model 1: Unadjusted	Model 2: Demographics + Clinical Characteristics ^c	Model 3: Model 2 + Anticholinergic Exposure
None	1,570,537	29,012 (69.7)	1 (Reference)	1 (Reference)	1 (Reference)
Low	118,553	2,573 (6.2)	1.17 (1.13, 1.22)	1.05 (1.01, 1.10)	1.02 (0.98, 1.06)
Medium	168,488	3,993 (9.6)	1.29 (1.24, 1.33)	1.06 (1.02, 1.09)	1.02 (0.99, 1.06)
High	237,570	6,052 (14.5)	1.38 (1.34, 1.42)	1.10 (1.06, 1.13)	1.03 (1.00, 1.07)

^a Benzodiazepine exposure: total standardized daily dose summed over the 10-year exposure window, categorized as none (0), low (1-30), medium (31-365), and high (366+).

^b Follow-up time starts from October 1, 2010 until September 30, 2015, incident dementia, gap in VA care more than 365 days or death, whichever is earliest.

^c Model 2: Adjusted for patient sociodemographic (age, income, education) and clinical conditions (stroke, diabetes, hypertension, myocardial infarction, congestive heart failure, angina, arrhythmia, hyperlipidemia, peripheral artery disease, depression, anxiety, post-traumatic stress disorder, insomnia, traumatic brain injury, tobacco and alcohol use).

eTable 3. Association of incident Alzheimer’s disease during follow-up years with 10-year benzodiazepine exposure

Benzodiazepine Exposure ^a	Follow Up Time ^b , Person Years	Incident Dementia (N=41630), N (%)	Hazard Ratio (95% Confidence Interval)		
			Model 1: Unadjusted	Model 2: Demographics + Clinical Characteristics ^c	Model 3: Model 2 + Anticholinergic Exposure
None	1,540,061	7,478 (68.8)	1 (Reference)	1 (Reference)	1 (Reference)
Low	137,023	724 (6.7)	1.09 (1.01, 1.17)	1.06 (0.98, 1.15)	1.03 (0.96, 1.12)
Medium	186,176	1,059 (9.7)	1.17 (1.10, 1.25)	1.03 (0.97, 1.11)	1.00 (0.93, 1.07)
High	280,525	1,611 (14.8)	1.18 (1.12, 1.25)	1.01 (0.95, 1.08)	0.96 (0.90, 1.03)

^a Benzodiazepine exposure: total standardized daily dose summed over the 10-year exposure window, categorized as none (0), low (1-30), medium (31-365), and high (366+).

^b Follow-up time starts from October 1, 2010 until September 30, 2015, incident dementia, gap in VA care more than 365 days or death, whichever is earliest.

^c Model 2: Adjusted for patient sociodemographic (age, income, education) and clinical conditions (stroke, diabetes, hypertension, myocardial infarction, congestive heart failure, angina, arrhythmia, hyperlipidemia, peripheral artery disease, depression, anxiety, post-traumatic stress disorder, insomnia, traumatic brain injury, tobacco and alcohol use).

eTable 4: Risk of incident dementia during follow-up years dividing benzodiazepine use into past, recent, and continuous use among Veterans with high benzodiazepine exposure^a

Type of User ^b	Follow Up Time, Person Years	Incident Dementia (N=6864), N (%)	Adjusted Hazard Ratio ^c (95% CI)
BZD across FY00-09 (continuous)	207465	5328 (77.6)	1 (Reference)
BZD all in FY00-04 (past)	22375	531 (7.7)	0.96 (0.87, 1.05)
BZD all in FY05-09 (recent)	41647	1005 (14.6)	1.03 (0.96, 1.10)

^a High benzodiazepine exposure was defined as a total standardized daily dose (TSDD) of 366+ over the 10-year exposure period.

^b The 10-year exposure period was divided into 2 periods: the proximal 5 years of the period (recent period) and the prior 5 years of the period (past period). Veterans were considered to be recent users if they had high benzodiazepine cumulative exposure only during the recent period. Veterans were considered to be past users if they had high benzodiazepine exposure only during the past period. The remaining participants were defined as continuous users.

^c Adjusted for age, income, education, stroke, diabetes, hypertension, myocardial infarction, congestive heart failure, angina, arrhythmia, hyperlipidemia, peripheral artery disease, depression, anxiety, post-traumatic stress disorder, insomnia, traumatic brain injury, tobacco use, alcohol use, and 10-year cumulative anticholinergic exposure.

eTable 5. Association of incident dementia during follow-up years with 10-year benzodiazepine exposure with death treated as a competing risk^a

Benzodiazepine Exposure^a	Hazard Ratio (95% Confidence Interval)		
	Model 1: Unadjusted	Model 2: Demographics + Clinical Characteristics^c	Model 3: Model 2 + Anticholinergic Exposure
None	1 (Reference)	1 (Reference)	1 (Reference)
Low	1.20 (1.15, 1.24)	1.09 (1.05, 1.14)	1.06 (1.02, 1.10)
Medium	1.28 (1.24, 1.32)	1.06 (1.03, 1.10)	1.03 (0.99, 1.06)
High	1.36 (1.32, 1.39)	1.07 (1.04, 1.11)	1.01 (0.98, 1.05)

^a Benzodiazepine exposure: total standardized daily dose summed over the 10-year exposure window, categorized as none (0), low (1-30), medium (31-365), and high (366+). We fit Fine and Gray models to differentially account for death as a competing risk.

^b Follow-up time starts from October 1, 2010 until September 30, 2015, incident dementia, gap in VA care more than 365 days or death, whichever is earliest.

^c Model 2: Adjusted for patient sociodemographic (age, income, education) and clinical conditions (stroke, diabetes, hypertension, myocardial infarction, congestive heart failure, angina, arrhythmia, hyperlipidemia, peripheral artery disease, depression, anxiety, post-traumatic stress disorder, insomnia, traumatic brain injury, tobacco and alcohol use).