

Supplement to: Kim Y, Choo E, Shin S, Choi YJ. Comparative risk of psychiatric comorbidities associated with codeine and tramadol in patients with hip osteoarthritis: a nationwide population-based cohort study. J Glob Health. 2026;16:04121.

Table S1. Incidence rates and hazard ratios of psychiatric disorders and all-cause mortality in codeine versus tramadol users: inverse probability of treatment weighting (IPTW) analysis

Event counts are IPTW-weighted and may appear as fractional values

Outcome	Incidence Rate						aHR	
	Codeine			Tramadol			IPTW-weighted Cox models	
	Events	Total PY	IR/ 1000PY	Events	Total PY	IR/ 1000PY	aHR* (95% CI)	P-value
Composite Psychiatric Outcome All *	385	10,602	36.3	15,187	432,289	35.1	0.87 (0.78-0.96)	0.005
Composite Psychiatric Outcome 1	372	10,622	35	14,728	433,869	33.9	0.87 (0.78-0.96)	0.007
Anxiety	165	11,087	14.9	7,202	459,440	15.7	0.83 (0.71-0.97)	0.021
Depression	170	11,098	15.3	6,588	461,296	14.3	0.89 (0.76-1.04)	0.137
Sleep Disorder	90.2	11,271	8.01	4,305	469,189	9.18	0.76 (0.62-0.94)	0.012
Composite Psychiatric Outcome 2	16.4	11,434	1.43	918	479,869	1.91	0.63 (0.38-1.02)	0.060
Bipolar disorder	14.2	11,440	1.24	752	480,447	1.57	0.67 (0.40-1.14)	0.137
Schizophrenia	2.93	11,459	0.26	207	482,052	0.43	0.49 (0.15-1.54)	0.219

* Adjusted for age, sex, index year, insurance type, Charlson Comorbidity Index, comorbidities (hypertension, dyslipidemia, arrhythmia, heart failure, myocardial infarction, cardiovascular disease, diabetes mellitus, stroke, chronic kidney disease, chronic obstructive pulmonary disease, asthma, dyspnea, other respiratory diseases, pulmonary edema, musculoskeletal diseases, rheumatic diseases, osteoporosis, Parkinson's disease, Alzheimer's disease, epilepsy, other neurological disorders, peripheral vascular disease, sleep disorders, hyperthyroidism, hypothyroidism, liver disease, peptic ulcer disease, gastroesophageal reflux disease, inflammatory bowel disease, and other gastrointestinal diseases), history of medication abuse and fracture, and concomitant medications (benzodiazepines, anticonvulsants, antidepressants, antipsychotics, hypnotics, psychotropic drugs, non-opioid analgesics, non-steroidal anti-inflammatory drugs [NSAIDs], AAP, and corticosteroids).

Table S2. Incidence rates and hazard ratios of psychiatric disorders and all-cause mortality in codeine versus tramadol users: 1:1 propensity score-matched sensitivity analysis

Outcome	Incidence Rate						HR					
	Codeine			Tramadol			Crude		Adjusted*		Adjusted [†]	
	Events	Total PY	IR/ 1000PY	Events	Total PY	IR/ 1000PY	HR (95% CI)	P-value	HR (95%CI)	P-value	HR (95% CI)	P-value
Composite Psychiatric Outcome All Composite Psychiatric Outcome1	428	10,720	39.9	701	18,090	38.8	0.84 (0.74–0.95)	0.005	0.87 (0.77-0.98)	0.025	0.83 (0.73-0.94)	0.004
Anxiety	177	11,265	15.7	331	19,380	17.1	0.78 (0.65–0.94)	0.009	0.82 (0.68-0.99)	0.041	0.82 (0.68-1.00)	0.049
Depression	202	11,237	18.0	331	19,344	17.1	0.85 (0.71–1.01)	0.070	0.90 (0.76-1.08)	0.269	0.81 (0.68-0.98)	0.029
Sleep Disorder	99	11,451	8.65	188	19,858	9.47	0.77 (0.60–0.98)	0.035	0.79 (0.62-1.01)	0.065	0.80 (0.62-1.03)	0.082
Composite Psychiatric Outcome 2	23	11,617	1.98	39	20,334	1.92	0.84 (0.50–1.42)	0.520	0.80 (0.46-1.38)	0.415	0.67 (0.37-1.22)	0.186
Bipolar disorder	19	11,626	1.63	32	20,361	1.57	0.87 (0.49–1.55)	0.637	0.83 (0.46-1.52)	0.554	0.67 (0.34-1.30)	0.233
Schizophrenia	5	11,650	0.43	11	20,402	0.539	0.62 (0.21–1.80)	0.378	0.44 (0.14-1.43)	0.173	0.41 (0.09-1.98)	0.269

* Adjusted for age, sex, Charlson Comorbidity Index, index year, insurance type, history of sleep disorder, and concomitant medication use (benzodiazepines,

anticonvulsants, antidepressants, antipsychotics, hypnotics, AAP, NSAIDs, and corticosteroids).

† Adjusted for age, sex, index year, insurance type, Charlson Comorbidity Index, comorbidities (hypertension, dyslipidemia, arrhythmia, heart failure, myocardial infarction, cardiovascular disease, diabetes mellitus, stroke, chronic kidney disease, chronic obstructive pulmonary disease, asthma, dyspnea, other respiratory diseases, pulmonary edema, musculoskeletal diseases, rheumatic diseases, osteoporosis, Parkinson's disease, Alzheimer's disease, epilepsy, neurological disorders, peripheral vascular disease, hyperthyroidism, hypothyroidism, liver disease, peptic ulcer disease, gastroesophageal reflux disease, inflammatory bowel disease, and gastrointestinal diseases), history of medication abuse and fracture, history of sleep disorder, and concomitant medication use (benzodiazepines, anticonvulsants, antidepressants, antipsychotics, hypnotics, psychotropic drugs, non-opioid analgesics, NSAIDs, AAP, and corticosteroids).

Table S3. Duration-restricted sensitivity analysis

Outcome	HR							
	≥7 Days		≥14 Days		≥30 Days		≥60 Days	
	HR (95% CI)	<i>P</i> -value	HR (95%CI)	<i>P</i> -value	HR (95% CI)	<i>P</i> -value	HR (95% CI)	<i>P</i> -value
Composite								
Psychiatric	0.92 (0.80–1.05)	0.202	0.84 (0.70–1.02)	0.078	0.93 (0.65–1.32)	0.679	0.75 (0.40–1.40)	0.363
Outcome								
Anxiety	0.80 (0.64–0.99)	0.039	0.77 (0.56–1.04)	0.085	0.68 (0.38–1.24)	0.211	0.66 (0.23–1.85)	0.430
Bipolar	0.96 (0.55–1.70)	0.896	1.29 (0.65–2.56)	0.470	2.51 (0.87–7.29)	0.090	0.00 (0.00–Inf)	0.999
Depression	1.01 (0.84–1.22)	0.893	0.87 (0.66–1.15)	0.338	0.93 (0.55–1.59)	0.802	0.71 (0.25–2.02)	0.526
Schizophrenia	0.66 (0.20–2.20)	0.495	1.11 (0.32–3.86)	0.871	2.18 (0.21–22.25)	0.510	0.00 (0.00–Inf)	0.999
Sleep disorder	0.80 (0.61–1.05)	0.101	0.75 (0.51–1.10)	0.139	0.88 (0.44–1.78)	0.726	1.31 (0.54–3.17)	0.555