Supplementary Material

Article Title: Association Between Receipt of Antidepressants and Retention in Buprenorphine Treatment for Opioid Use Disorder: A Population-Based Retrospective Cohort Study

Authors: Kun Zhang, PhD; Christopher M. Jones, PharmD, DrPH; Wilson M. Compton, MD, MPE; Gery P. Guy, PhD, MPH; Mary E. Evans, MD; and Nora D. Volkow, MD

DOI Number: 10.4088/JCP.21m14001

List of Supplementary Material for the article

Disclaimer

This Supplementary Material has been provided by the author(s) as an enhancement to the published article. It has been approved by peer review; however, it has undergone neither editing nor formatting by in-house editorial staff. The material is presented in the manner supplied by the author.

Supplementary Material

Supplementary Table 1: Buprenorphine products included in the analysis as MOUD

Non-injection Buprenorphine products	Included in analysis as MOUD	Suboxone dosage conversion factor
Buprenorphine Hydrochloride	Yes	1
Buprenorphine-Naloxone	Yes	1
BUNAVAIL	Yes	1.905
SUBLOCADE	Yes	N/A*
SUBOXONE	Yes	1
SUBUTEX	Yes	N/A*
ZUBSOLV	Yes	1.4
BELBUCA	No	N/A
BUTRANS	No	N/A

* No prescription was identified in our data

Abbreviations: MOUD (medication for opioid use disorder)

Supplementary Table 2: Generic drug names of antidepressants included in the analysis

Antidepressant categories	Generic drug names
Selective serotonin reuptake inhibitors (SSRIs)	citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline
Serotonin–norepinephrine reuptake inhibitors (SNRIs)	desvenlafaxine, duloxetine, levomilnacipran, venlafaxine
Tricyclic antidepressants (TCAs)	amitriptyline, amoxapine, clomipramine, desipramine, doxepin, Imipramine, maprotiline, nortriptyline, protriptyline, trimipramine
Other	bupropion, chlorprothixene, mirtazapine, nefazodone, nortriptyline, trazodone, vilazodone, vortioxetine

Supplementary Table 3: Comorbid conditions and associated ICD-10 CM codes

Comorbid conditions	ICD-10 CM Codes
Substance use disorder	
Alcohol use disorder	F10.1X, F10.2X, F10.9X
Cannabis use disorder	F12.1X, F12.2X, F12.9X
Cocaine use disorder	F14.1X, F14.2X, F14.9X
Sedative and hypnotic related disorder	F13.1X, F13.2X, F13.9X
Stimulant use disorder	F15.1X, F15.2X, F15.9X
Other psychoactive substance use disorder	F16.1X, F16.2X, F16.9X, F18.1X, F18.2X, F18.9X, F19.1X, F19.2X, F19.9X
Psychiatric conditions	
Anxiety	F40.0X, F40.1X, F40.2X, F40.8X, F40.9X, F41.0, F41.1, F41.3, F41.8, F41.9, F42.2, F42.3, F42.4, F42.8, F42.9

Bipolar disorder	F30.1X, F30.2, F30.3, F30.4, F30.8, F30.9
Major depression	F32.0, F32.1, F32.2, F32.3, F32.4, F32.5, F32.81, F32.89, F32.9
Other mood disorder	F34.0, F34.1, F34.81, F34.89, F34.9, F39
Attention deficit hyperactivity Disorder (ADHD)	F90.0, F90.1, F90.2, F90.8, F90.9
Post-traumatic stress disorder (PTSD)	F43.10, F43.11, F43.12
Schizophrenia	F20.0, F20.1, F20.2, F20.3, F20.5, F20.8X, F20.9, F25.0, F25.1, F25.8, F25.9, F29
Pain conditions	
Back pain	M2578, M4000, M4003, M4004, M4005, M40202, M40203, M40204, M40205, M40209, M40292, M40293, M40294, M40295, M40299, M4030, M4035, M4036, M4037, M4100, M4102, M4103, M4104, M4105, M4106, M4107, M4108, M41112, M41113, M41114, M41115, M41116, M41117, M41119, M41122, M41123, M41124, M41125, M41126, M41127, M41129, M4120, M4122, M4123, M4124, M4125, M4126, M4127, M4130, M4134, M4135, M4180, M4182, M4183, M4184, M4185, M4186, M4187, M419, M4300, M4301, M4302, M4303, M4304, M4305, M4306, M4307, M4308, M4309, M4310, M4311, M4312, M4313, M4314, M4315, M4316, M4317, M4318, M4319, M4320, M4321, M4322, M4323, M4324, M4325, M4326, M4327, M4328, M438X9, M4640, M4644, M4645,M4646, M4647, M4648, M4649, M4710, M4714, M4715, M4716, M4720, M4724, M4725, M4726, M4727, M4728, M47814, M47815, M47816, M47817, M47818, M47819, M47894, M47895, M47896, M47897, M47898, M47899, M479, M4800, M4804, M4805, M4806, M48061, M48062, M4807, M4808, M4810, M4811, M4812, M4813, M4814, M4815, M4816, M4817, M4818, M4819, M4820, M4821, M4822, M4823, M4824, M4825, M4826, M4827, M4830, M4831, M4832, M4833, M4834, M4835, M4836, M4837, M4838, M489, M5104, M5105, M5106, M5114, M5115, M5116, M5117,M5124, M5125, M5126, M5127, M5134, M5135, M5136, M5137, M5146, M5147, M5184, M5185, M5186, M5187, M519, M532X7, M532X8, M533, M5380, M5384, M5385, M5386, M5387, M5388, M539, M5403, M5404, M5405, M5406, M5407, M5408, M5409, M5414, M5415, M5416, M5417, M5418, M5430, M5431, M5432, M5440, M5441, M5442, M545, M546, M5489, M549, M62830, M961, M962, M963, M965, M9922, M9923, M9924, M9925, M9926, M9927, M9928, M9929, M9932, M9933, M9934, M9935, M9936, M9937, M9938, M9939, M9942, M9943, M9944, M9945, M9946, M9947, M9948, M9949, M9952, M9953, M9954, M9955, M9956, M9957, M9958, M9959, M9962, M9963, M9964, M9965, M9966, M9967, M9968, M9969, M9972, M9973, M9974, M9975, M9976, M9977, M9978, M9979, M9983, M9984, M9902, M9904, Q762
Neck pain (e.g., cervical spinal stenosis)	M47811, M47891, M4723, M4722, M4721, M47813, M47893, M47892, M47812, M47012, M4711, M47014, M47011, M4712, M47022, M47029, M47019, M47016, M47013, M47021, M4713, M47015, M50220, M5022, M5023, M5020, M50221, M50222, M50223, M5021, M5002, M5000, M5001, M50022, M50023, M50021, M50020, M5003, M5082, M5091, M5012, M50922, M50821, M5080, M5011, M50123, M50822, M50820, M50921, M5010, M4643, M5093, M50120, M50823, M5083, M50121, M5090, M4641, M50920, M50122, M4642, M5092, M50923, M5013, M5081, M9930, M9971, M9921, M9970, M4803, M9931, M9940, M9960, M9950, M4802, M9951, M4801, M9961, M9941, M9920, M542, M530, M531, M5413, M5411, M5412, M436, M5400, M5402, M5401, M5382, M5481, M5381, M5383
Migraine	G43001, G43009, G43011, G43019, G43101, G43109, G43111, G43119, G43C0, G43B0, G43D0, G43A0, G43A1, G43C1, G43B1, G43D1, G43401, G43409, G43411, G43419, G43501, G43509, G43511, G43519, G43609, G43619, G43601, G43611, G43701, G43711, G43709, G43719, G43801, G43811, G43809, G43819, G43901, G43911, G43909, G43919, G43821, G43829, G43831, G43839
Fibromyalgia	M797
Osteoarthritis/joint cartilage	M129, M131X, M138X, M15X, M16X, M17X, M18X, M19X, M2210, M2211, M2212, M222X, M223X, M224X, M228X, M2290, M2291, M2292, M23X, M241X
Inflammatory joint disorder (e.g., rheumatoid arthritis, ankylosing spondylitis)	M05X, M06X, M08X, M120X, M255X, M353, M45X, M460X, M461, M465X, M468X, M469X, M488X, M498X, M790

	M2570, M25711, M25712, M25719, M25721, M25722, M25729, M25731, M25732, M25739, M25741, M25742, M25749, M25751, M25752, M25759, M25761, M25762, M25769, M2577X, M701X, M702X, M704X, M705X, M706X, M707X, M7500, M7501, M7502, M751X, M7520, M7521, M7522, M7530, M7531, M7532, M7540, M7541, M7542, M7550, M7551, M7552, M7580, M7581, M7582, M7590, M7591, M7592, M76X, M77X, M2161X, M2162X, M65X, M66X, M67X, M700X, M7030, M7031, M7032, M71X
Periarticular/soft tissue Disorders (e.g., peripheral enthesopathies, synovitis, bursitis)	

Note: a code ending with X means that the code includes all digits at X's position.

Supplementary Table 4: Generic drug names of other psychotropic medications included in the analysis

Therapeutic classes of other psychotropic medications	Generic drug names
Benzodiazepines	alprazolam, chlordiazeproxide, clobazam, clonazepam, clorazepate, diazepam, estazolam, flurazepam, lorazepam, oxazepam, prazepam, quazepam, temazepam, triazolam
Stimulants	amphetamine, dexmethylphenidate, dextroamphetamine, lisdexamfetamine, methylphenidate
Opioid analgesics	buprenorphine (only Butrans and Belbuca), butorphanol, codeine, dihydrocodeine, fentanyl, hydrocodone, hydromorphone, levorphanol, meperidine, methadone, morphine, oxycodone, oxymorphone, pentazocine, tapentadol, tramadol
Other psychotropics	aripiprazole, buspirone, carbamazepine, chlorpromazine, clozapine, divalproex, droperidol, felbamate, fluphenazine, gabapentin, haloperidol, lamotrigine, levetiracetam, lithium, loxapine, lurasidone, olanzapine, oxcarbazepine, paliperidone, perphenazine, pregabalin, prochlorperazine, promazine, quetiapine, risperidone, thioridazine, thiothixene, trifluoperazine, valproic, ziprasidone

Supplementary Table 5: Results of Cox proportional hazard model for sensitivity analysis 1 - 3

Parameter	Level	Analysis 1 (only patients with baseline OUD diagnosis), N=7,799			Analysis 2 (using 30-day gap to define discontinuation), N=11,619			Analysis 3 (patients with no antidepressants and those received antidepressants < 15 days), N=6,933		
		Hazard Ratio	[95% Conf. Interval]		Hazard Ratio	[95% Conf. Interval]		Hazard Ratio	[95% Conf. Interval]	
Antidepressant status (ref=no antidepressants at all)	Antidepressants only in 6 months prior to buprenorphine treatment	1.318	1.170	1.485	1.405	1.284	1.537	1.345	1.229	1.472
	Antidepressants during treatment:									
	Antidepressants only during treatment	0.702	0.637	0.774	0.734	0.683	0.789	3.014	2.100	4.327
	Antidepressants in 6 months prior to and during treatment	0.540	0.489	0.610	0.509	0.464	0.557	2.864	2.410	3.404
Age group (ref=18-34)	35-44	0.649	0.592	0.710	0.669	0.627	0.714	0.735	0.677	0.797
	45-54	0.786	0.709	0.872	0.805	0.748	0.867	0.880	0.799	0.969
	55-64	0.736	0.649	0.835	0.853	0.782	0.930	0.974	0.870	1.091
Daily dose of buprenorphine (ref=2-8mg)	9-12mg	0.806	0.729	0.892	0.781	0.724	0.844	0.761	0.688	0.841
	13-16mg	0.845	0.778	0.918	0.803	0.755	0.854	0.806	0.747	0.871
	17-24mg	0.713	0.644	0.790	0.666	0.619	0.717	0.674	0.614	0.739
	>24mg	1.012	0.804	1.273	0.912	0.776	1.071	0.966	0.792	1.177
Gender (ref = Female)	Male	0.952	0.888	1.021	0.911	0.865	0.959	0.907	0.847	0.970
Use of benzodiazepine (ref=no benzodiazepines at all)	Benzodiazepines only in 6 months prior to treatment	1.197	1.069	1.341	1.312	1.204	1.430	1.271	1.131	1.427
	Benzodiazepines only during treatment	0.983	0.868	1.112	0.942	0.859	1.033	0.932	0.820	1.060
	Benzodiazepines in 6 months prior to and during treatment	1.176	1.066	1.298	1.168	1.087	1.255	1.224	1.103	1.357
Use of opioid analgesics (ref=no opioid analgesics at all)	Opioid analgesics only in 6 months prior to treatment	1.016	0.932	1.107	1.000	0.938	1.067	1.065	0.982	1.155
	Opioid analgesics only during treatment	0.522	0.439	0.622	0.511	0.447	0.583	0.430	0.355	0.522
	Opioid analgesics in 6 months prior to and during treatment	0.859	0.761	0.970	0.951	0.874	1.034	1.042	0.930	1.168
Use of stimulant (ref=no stimulants at all)	Stimulants only in 6 months prior to treatment	1.208	0.991	1.473	1.357	1.166	1.581	1.312	1.076	1.600

	Stimulants only during treatment	0.518	0.428	0.627	0.530	0.459	0.612	0.454	0.360	0.574
	Stimulants in 6 months prior to and during treatment	0.878	0.747	1.031	0.887	0.792	0.994	0.826	0.700	0.974
Use of other psychotropic prescriptions (OPP) (ref=no OPP at all)	OPP only in 6 months prior to treatment	1.257	1.115	1.417	1.298	1.184	1.423	1.248	1.118	1.393
	OPP only during treatment	0.938	0.847	1.040	0.949	0.879	1.025	0.957	0.857	1.069
	OPP in 6 months prior to and during treatment	0.951	0.864	1.047	1.005	0.935	1.081	1.035	0.932	1.150
Alcohol use disorder	Diagnosis present at baseline	1.042	0.931	1.167	1.026	0.926	1.137	1.043	0.901	1.207
Cannabis use disorder	Diagnosis present at baseline	1.273	1.133	1.431	1.266	1.134	1.412	1.161	0.991	1.361
Sedative and hypnotic related disorder	Diagnosis present at baseline	1.009	0.891	1.142	0.997	0.888	1.119	1.029	0.878	1.206
Cocaine use disorder	Diagnosis present at baseline	1.270	1.100	1.468	1.230	1.069	1.416	1.015	0.830	1.241
Stimulant use disorder	Diagnosis present at baseline	1.373	1.194	1.579	1.311	1.148	1.497	1.292	1.060	1.575
Other psychoactive substance use disorder	Diagnosis present at baseline	1.090	0.991	1.200	1.048	0.965	1.139	1.030	0.922	1.151
Anxiety	Diagnosis present at baseline	0.971	0.896	1.053	0.939	0.880	1.002	0.932	0.851	1.019
Bipolar disorder	Diagnosis present at baseline	1.177	1.027	1.349	1.112	0.991	1.248	1.105	0.923	1.324
Major depression	Diagnosis present at baseline	1.128	1.036	1.227	1.077	1.005	1.153	1.177	1.061	1.306
ADHD	Diagnosis present at baseline	1.045	0.898	1.216	1.064	0.943	1.200	1.019	0.853	1.218
Other mood disorder	Diagnosis present at baseline	0.944	0.793	1.125	0.939	0.812	1.085	1.085	0.832	1.416
PTSD	Diagnosis present at baseline	1.074	0.887	1.301	1.065	0.913	1.243	1.054	0.821	1.352
Schizophrenia	Diagnosis present at baseline	0.925	0.692	1.237	1.038	0.805	1.339	1.190	0.807	1.757
Back pain	Diagnosis present at baseline	1.020	0.936	1.112	1.034	0.968	1.104	0.990	0.907	1.082
Neck pain	Diagnosis present at baseline	1.049	0.935	1.176	1.079	0.991	1.174	1.090	0.964	1.232
Migraine	Diagnosis present at baseline	0.984	0.821	1.179	1.069	0.944	1.210	1.078	0.916	1.270
Fibromyalgia	Diagnosis present at baseline	1.071	0.851	1.348	1.151	0.978	1.355	1.211	0.939	1.562
Osteoarthritis/joint cartilage	Diagnosis present at baseline	0.932	0.806	1.079	0.987	0.887	1.097	0.971	0.830	1.135
Inflammatory joint disorder	Diagnosis present at baseline	0.977	0.876	1.090	1.002	0.925	1.085	1.052	0.944	1.172
Periarticular/soft tissue disorders	Diagnosis present at baseline	1.321	1.120	1.559	1.294	1.145	1.461	1.214	1.036	1.422

Abbreviations: ADHD (Attention deficit hyperactivity disorder), PTSD (Post-traumatic stress disorder)