

Supplementary Material

Article Title: Association Between Receipt of Antidepressants and Retention in Buprenorphine Treatment

for Opioid Use Disorder: A Population-Based Retrospective Cohort Study

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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	F90.0, F90.1, F90.2, F90.8, F90.9
Disorder (ADHD)	
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	
Full Conditions	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, M4126, M4127, M4129, 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, M328, M43889, 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, M4836, M4877, M4830, M4831, M4832, M4833, M4834, M4835, M4836, M4837, M4838, M489, M5104, M5105, M5106, M5114, M5115, M5116, M5117, M5124, M5125, M5126, M5127, M5134, M5135, M536, 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, M6431, M6432, M5440, M5441, M5442, M545, M5926, M9927, M9928, M9929, M9932, M9933, M9934, M9934, M9934, M9934, M9934, M9934, M9949, M9955, M9966, M9967, M9968, M9969, M9972, M9937, M9938, M9939, M9942, M9943, M9944, M9945, M9946, M9947, M9948, M9949, M9956, M9966, M9967, M9968, M9969, M9972, M9973, M9974, M9975, M9976, M9977,
Back pain	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, M47012, M47022, M47029, M47019, M47016, M47013, M47021, M4713, M47015, M50220, M5022, M5023, M5020, M50221, M50222, M50223, M50221, M50222, M50223, M50221, M50020, M50020, 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,
Periarticular/soft tissue	M25739, M25741, M25742, M25749, M25751, M25752, M25759, M25761, M25762,
Disorders (e.g., peripheral	M25769, M2577X, M701X, M702X, M704X, M705X, M706X, M707X, M7500, M7501,
enthesopathies, synovitis, bursitis)	M7502, M751X, M7520, M7521, M7522, M7530, M7531, M7532, M7540, M7541,
enthesopathies, synovitis, bursitis)	M7542, M7550, M7551, M7552, M7580, M7581, M7582, M7590, M7591, M7592,
	M76X, M77X, M2161X, M2162X, M65X, M66X, M67X, M700X, M7030, M7031, M7032,
	M71X

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

	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		
Parameter		Hazard Ratio	[95% Conf. Interval]		Hazard Ratio	[95% Conf. Interval]		Hazard Ratio	[95% Conf. Interval]	
	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
Antidepressant status (ref=no antidepressants at all)	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
	35-44	0.649	0.592	0.710	0.669	0.627	0.714	0.735	0.677	0.797
Age group (ref=18-34)	45-54	0.786	0.709	0.872	0.805	0.748	0.867	0.880	0.799	0.969
(161-10-54)	55-64	0.736	0.649	0.835	0.853	0.782	0.930	0.974	0.870	1.091
	9-12mg	0.806	0.729	0.892	0.781	0.724	0.844	0.761	0.688	0.841
Daily dose of	13-16mg	0.845	0.778	0.918	0.803	0.755	0.854	0.806	0.747	0.871
buprenorphine (ref=2-8mg)	17-24mg	0.713	0.644	0.790	0.666	0.619	0.717	0.674	0.614	0.739
(101 2 01116)	>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
	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
Use of benzodiazepine (ref=no benzodiazepines at all)	Benzodiazepines only during treatment	0.983	0.868	1.112	0.942	0.859	1.033	0.932	0.820	1.060
at any	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	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
(ref=no opioid analgesics at all)	Opioid analgesics only during treatment	0.522	0.439	0.622	0.511	0.447	0.583	0.430	0.355	0.522
ac a,	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

	0.540	0.420	0.627	0.520	0.450	0.642	0.454	0.260	0.574
,									0.574
·	0.878	0.747	1.031	0.887	0.792	0.994	0.826	0.700	0.974
	1 257	1 115	1 /117	1 200	1 10/	1 // 22	1 2/10	1 110	1.393
	1.237	1.113	1.41/	1.230	1.104	1.423	1.240	1.110	1.555
	0.938	0.847	1.040	0.949	0.879	1.025	0.957	0.857	1.069
OPP only during treatment									
OPP in 6 months prior to and during	0.951	0.864	1.047	1.005	0.935	1.081	1.035	0.932	1.150
treatment									
Diagnosis present at baseline		0.931		1.026	0.926		1.043		1.207
Diagnosis present at baseline	1.273	1.133	1.431	1.266	1.134	1.412	1.161	0.991	1.361
Diagnosis present at baseline	1.009	0.891	1.142	0.997	0.888	1.119	1.029	0.878	1.206
Diagnosis present at baseline	1 270	1 100	1 460	1 220	1.060	1 /16	1.015	0.020	1 2/1
									1.241
Diagnosis present at baseline	1.373	1.194	1.579	1.311	1.148	1.497	1.292	1.060	1.575
Diagnosis present at baseline	1.090	0.991	1.200	1.048	0.965	1.139	1.030	0.922	1.151
Diagnosis present at baseline	0.971	0.896	1.053	0.939	0.880	1.002	0.932	0.851	1.019
Diagnosis present at baseline	1.177	1.027	1.349	1.112	0.991	1.248	1.105	0.923	1.324
Diagnosis present at baseline	1.128	1.036	1.227	1.077	1.005	1.153	1.177	1.061	1.306
Diagnosis present at baseline	1.045	0.898	1.216	1.064	0.943	1.200	1.019	0.853	1.218
Diagnosis present at baseline	0.944	0.793	1.125	0.939	0.812	1.085	1.085	0.832	1.416
Diagnosis present at baseline	1.074	0.887	1.301	1.065	0.913	1.243	1.054	0.821	1.352
Diagnosis present at baseline	0.925	0.692	1.237	1.038	0.805	1.339	1.190	0.807	1.757
Diagnosis present at baseline	1.020	0.936	1.112	1.034	0.968	1.104	0.990	0.907	1.082
Diagnosis present at baseline	1.049	0.935	1.176	1.079	0.991	1.174	1.090	0.964	1.232
Diagnosis present at baseline	0.984	0.821	1.179	1.069	0.944	1.210	1.078	0.916	1.270
Diagnosis present at baseline	1.071	0.851	1.348	1.151	0.978	1.355	1.211	0.939	1.562
Diagnosis present at baseline	0.932	0.806	1.079	0.987	0.887	1.097	0.971	0.830	1.135
Diagnosis present at baseline	0.977	0.876	1.090	1.002	0.925	1.085	1.052	0.944	1.172
	treatment Diagnosis present at baseline	Stimulants in 6 months prior to and during treatment OPP only in 6 months prior to treatment OPP only during treatment OPP in 6 months prior to and during treatment Diagnosis present at baseline Diagnosis present at baseline	Stimulants in 6 months prior to and during treatment OPP only in 6 months prior to treatment OPP only during treatment OPP only during treatment OPP in 6 months prior to and during treatment Diagnosis present at baseline Diagnosis present at baseline	Stimulants in 6 months prior to and during treatment 0.878 0.747 1.031 OPP only in 6 months prior to treatment 1.257 1.115 1.417 OPP only during treatment 0.938 0.847 1.040 OPP in 6 months prior to and during treatment 0.951 0.864 1.047 Diagnosis present at baseline 1.042 0.931 1.167 Diagnosis present at baseline 1.273 1.133 1.431 Diagnosis present at baseline 1.009 0.891 1.142 Diagnosis present at baseline 1.270 1.100 1.468 Diagnosis present at baseline 1.090 0.991 1.200 Diagnosis present at baseline 1.090 0.991 1.200 Diagnosis present at baseline 0.971 0.896 1.053 Diagnosis present at baseline 1.128 1.036 1.227 Diagnosis present at baseline 1.045 0.898 1.216 Diagnosis present at baseline 0.944 0.793 1.125 Diagnosis present at baseline 1.074 0.887	Stimulants in 6 months prior to and during treatment 0.878 0.747 1.031 0.887 OPP only in 6 months prior to treatment 1.257 1.115 1.417 1.298 OPP only during treatment 0.938 0.847 1.040 0.949 OPP in 6 months prior to and during treatment 0.951 0.864 1.047 1.005 Diagnosis present at baseline 1.042 0.931 1.167 1.026 Diagnosis present at baseline 1.273 1.133 1.431 1.266 Diagnosis present at baseline 1.009 0.891 1.142 0.997 Diagnosis present at baseline 1.270 1.100 1.468 1.230 Diagnosis present at baseline 1.090 0.991 1.200 1.048 Diagnosis present at baseline 1.090 0.991 1.200 1.048 Diagnosis present at baseline 1.177 1.027 1.349 1.112 Diagnosis present at baseline 1.045 0.898 1.216 1.064 Diagnosis present at baseline 1.045 0.898	Stimulants in 6 months prior to and during treatment 0.878 0.747 1.031 0.887 0.792 during treatment OPP only in 6 months prior to treatment 1.257 1.115 1.417 1.298 1.184 treatment OPP only during treatment 0.938 0.847 1.040 0.949 0.879 OPP in 6 months prior to and during treatment 0.951 0.864 1.047 1.005 0.935 treatment Diagnosis present at baseline 1.042 0.931 1.167 1.026 0.926 Diagnosis present at baseline 1.273 1.133 1.431 1.266 1.134 Diagnosis present at baseline 1.009 0.891 1.142 0.997 0.888 Diagnosis present at baseline 1.270 1.100 1.468 1.230 1.069 Diagnosis present at baseline 1.090 0.991 1.200 1.048 0.965 Diagnosis present at baseline 1.090 0.991 1.200 1.048 0.965 Diagnosis present at baseline 1.177 1.027 1.349 1.112	Stimulants in 6 months prior to and during treatment 0.878 0.747 1.031 0.887 0.792 0.994 OPP only in 6 months prior to treatment 1.257 1.115 1.417 1.298 1.184 1.423 OPP only during treatment 0.938 0.847 1.040 0.949 0.879 1.025 OPP in 6 months prior to and during treatment 0.951 0.864 1.047 1.005 0.935 1.081 Diagnosis present at baseline 1.042 0.931 1.167 1.026 0.926 1.137 Diagnosis present at baseline 1.273 1.133 1.431 1.266 1.134 1.412 Diagnosis present at baseline 1.009 0.891 1.142 0.997 0.888 1.119 Diagnosis present at baseline 1.270 1.100 1.468 1.230 1.069 1.416 Diagnosis present at baseline 1.090 0.991 1.200 1.048 0.965 1.139 Diagnosis present at baseline 1.077 0.896 1.053 0.939 0.8	Stimulants in 6 months prior to and during treatment 0.878 0.747 1.031 0.887 0.792 0.994 0.826 OPP only in 6 months prior to treatment 1.257 1.115 1.417 1.298 1.184 1.423 1.248 OPP only during treatment 0.938 0.847 1.040 0.949 0.879 1.025 0.957 OPP in 6 months prior to and during treatment 0.951 0.864 1.047 1.005 0.935 1.081 1.035 Diagnosis present at baseline 1.042 0.931 1.167 1.026 0.926 1.137 1.043 Diagnosis present at baseline 1.273 1.133 1.431 1.266 1.134 1.412 1.161 Diagnosis present at baseline 1.270 1.100 1.468 1.230 1.069 1.416 1.015 Diagnosis present at baseline 1.270 1.100 1.468 1.230 1.069 1.416 1.015 Diagnosis present at baseline 1.090 0.991 1.200 1.048 0.965	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 OPP only in 6 months prior to treatment 0.938 0.847 1.040 0.949 0.879 1.025 0.957 0.857 OPP only during treatment 0.938 0.847 1.040 0.949 0.879 1.025 0.957 0.857 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 Diagnosis present at baseline 1.042 0.931 1.167 1.026 0.926 1.137 1.043 0.901 Diagnosis present at baseline 1.273 1.133 1.431 1.266 1.134 1.412 1.161 0.991 Diagnosis present at baseline 1.200 1.100 1.468 1.230 1.069 1.416 1.015 0.830 Diagnosis present at baseline 1.270 1.100 1.468 1.230 1.069 1.416 1.015 0.830

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