

Supplementary materials

Table S1. ICD-9 codes for antidepressant treatment indications

Treatment Indication	ICD-9 code	Code description
Depressive disorders	296.2	Major depressive disorder, single episode
	296.3	Major depressive disorder, recurrent episode
	296.9	Other and unspecified episodic mood disorder
	300.4	Dysthymic disorder
	301.1	Affective personality disorder (includes chronic depressive personality disorder)
	309.0	Adjustment disorder with depressed mood
	309.1	Prolonged depressive reaction
	311.x	Depressive disorder, not elsewhere classified
Anxiety/stress disorders	300.0	Anxiety states
	300.2	Phobic disorders
	308.x	Acute reaction to stress
	309.2	Adjustment reaction with predominant disturbance of other emotions
	309.8	Other specified adjustment reactions (includes posttraumatic stress disorder)
Sleeping disorders	307.4	Specific disorders of sleep of nonorganic origin
	780.5	Sleep disturbances
Pain	053.1	Herpes zoster with other nervous system complications
	250.6	Diabetes with neurological manifestations
	307.8	Pain disorders related to psychological factors
	337.2	Reflex sympathetic dystrophy
	338.x	Pain, not elsewhere classified
	350.1	Trigeminal neuralgia
	350.2	Atypical face pain
	352.1	Glossopharyngeal neuralgia
	353.X	Nerve root and plexus disorders
	354.x	Mononeuritis of upper limb and mononeuritis multiplex
	355.x	Mononeuritis of lower limb
	357.2	Polyneuropathy in diabetes
	714.x	Rheumatoid arthritis and other inflammatory polyarthropathies
	715.x	Osteoarthritis and allied disorders
	719.4	Pain in joint
	721.x	Spondylosis and allied disorders
	722.x	Intervertebral disc disorders
	723.x	Other disorders of cervical region
	724.x	Other and unspecified disorders of back
	729.2	Neuralgia, neuritis, and radiculitis, unspecified
	729.5	Pain in limb
737.x	Curvature of spine	
786.5	Chest pain	
789.0	Abdominal pain	
Migraine	346.x	Migraine
	784.0	Headache
Fibromyalgia	729.1	Myalgia and myositis, unspecified
Obsessive-compulsive disorder	300.3	Obsessive-compulsive disorder
Vasomotor symptoms of menopause	627.2	Symptomatic menopausal or female climacteric states

Nicotine dependence	305.1	Tobacco use disorder
Treatment Indication	ICD-9 code	Code description
Attention deficit/hyperactivity disorder	314.x	Hyperkinetic syndrome of childhood
Sexual dysfunction	302.7	Psychosexual dysfunction
	607.8	Other specified disorders of penis
Pre-menstrual dysphoric disorder	625.4	Premenstrual tension syndromes
Eating disorders	307.1	Anorexia nervosa
	307.5	Other and unspecified disorders of eating
	783.0	Anorexia
	783.3	Feeding difficulties and mismanagement

Table S2 Top 15 four-digit ICD-9 codes recorded for patients in physician billings or hospital discharge summary data over the past year for MOXXI patients who were prescribed antidepressants^a

Four-digit ICD-9 code	Description	Diagnostic code in the past 365 days	
		No. prescriptions	%
V999	No diagnosis or unspecified	25509	34.67
V700	General medical examination	13476	18.32
401.9	Hypertension, unspecified	11309	15.37
401.1	Hypertension, benign	5489	7.46
465.9	Upper respiratory infection, acute, NOSS	4651	6.32
786.0	Dyspnea and respiratory abnormalities	4403	5.98
V723	Special investigations and examinations	3875	5.27
733.0	Osteoporosis	3793	5.16
309.9	Unspecified adjustment reaction	3572	4.85
414.9	Ischemic heart disease	3539	4.81
780.7	Malaise and fatigue	3470	4.72
473.9	Sinusitis, chronic, NOS	3304	4.49
726.9	Unspecified enthesopathy	3223	4.38
692.9	Contact dermatitis, NOS	2915	3.96
300.9	Neurosis, NOS	2680	3.64

^aAfter excluding diagnostic codes for plausible antidepressant treatment indications and diagnostic codes for conditions in the Charlson comorbidity index

Table S3 Top 15 billing code categories from medical billings in the past year for MOXXI patients who were prescribed antidepressants

Description of medical service ^a	Category no.	Billing code for the medical service in the past year	
		No. prescriptions	%
Examen complet cabinet - omnipraticien	114	58 323	79.27
Forfaits de responsabilité clientèle vulnérables	170	46 726	63.51
Examen sommaire cabinet - omnipraticien	112	40 449	54.98
Traitements psychiatriques - cabinet	373	34 912	47.45
Examen complet majeur - cabinet	116	24 838	33.76
Actes diagnostiques	211	24 542	33.36
Consultations – spécialistes - établissement	167	23 586	32.06
Examen complet cabinet - spécialiste	115	19 961	27.13
Examen complet – établissement malade externe	141	19 636	26.69
Radiologie	350	19 092	25.95
Consultations – spécialistes – cabinet	165	16 830	22.87
Examen complet – établissement malade externe	135	16 625	22.60
Forfait de prise en charge et de suivi (GMF)	183	16 318	22.18
Examen ordinaire – établissement malade externe	139	15 801	21.48
Examen ordinaire – établissement malade externe	133	15 653	21.27

^aThese are the exact (French) definitions of the billing code categories that were provided by RAMQ. The descriptions provided by RAMQ were not unique for each billing code group. The category numbers for each billing code category (column 2) were also provided by RAMQ.

Table S4. Top 15 in-hospital procedures (CCP codes) performed in the past year for MOXXI patients who were prescribed antidepressants

Three-digit CCP code	Description	CCP code in the past year	
		No. prescriptions	%
27.7	Insertion of prosthetic lens	1176	1.60
27.6	Other extraction of lens	1175	1.60
13.0	Transfusion of blood and blood components	632	0.86
13.5	Other injection or infusion of other therapeutic or prophylactic substance	572	0.78
53.0	Bone marrow transplant	536	0.73
48.9	Other operations on vessels of heart	459	0.62
13.6	Respiratory therapy	427	0.58
92.0	Arthrotomy for removal of prosthesis	362	0.49
17.3	Freeing of adhesions and decompression of cranial and peripheral nerves	325	0.44
13.4	Injection or infusion of other therapeutic or prophylactic substance	309	0.42
66.6	Other repair of abdominal wall and peritoneum	266	0.36
90.5	Internal fixation of bone (without fracture reduction)	263	0.36
11.6	Nonoperative removal of therapeutic device from urinary system	258	0.35
93.4	Arthroplasty of knee and ankle	246	0.33
63.1	Cholecystectomy	245	0.33

Abbreviations: CCP = Canadian Classification of Diagnostic, Therapeutic, and Surgical Procedures (CCP)

Table S5 Top 15 drugs prescribed in the past year to MOXXI patients who were prescribed antidepressants

Molecule name	Drug prescribed in the past year	
	No. prescriptions	%
Venlafaxine	12674	17.23
Citalopram	10450	14.20
Levothyroxine	7415	10.08
Trazodone	7175	9.75
Atorvastatin	6597	8.97
Lorazepam	6595	8.96
Clonazepam	6382	8.67
Acetaminophen	6186	8.41
Bupropion	6112	8.31
Pantoprazole	5733	7.79
Esomeprazole	5249	7.13
Paroxetine	5205	7.07
Salbutamol	4995	6.79
Amitriptyline	4910	6.67
Metformin	4842	6.58

Table S6 Distribution of the outcome and selected variables among antidepressant prescriptions the training and test sets

Variable	No. prescriptions (%) or median (IQR)		
	Overall (N = 73 576)	Training set (N = 52 019)	Test set (N = 21 557)
Outcome			
Treatment indication			
Depression	41 171 (56.0)	28 887 (55.5)	12 284 (57.0)
Anxiety/stress disorders	16 374 (22.3)	11 490 (22.1)	4884 (22.7)
Sleeping disorders	7295 (9.9)	5192 (10.0)	2103 (9.8)
Pain	4137 (5.6)	3046 (5.9)	1091 (5.1)
Other indications	4599 (6.3)	3404 (6.5)	1195 (5.5)
Prescription characteristics			
Top five molecules			
Venlafaxine	15 398 (20.9)	11 385 (21.9)	4013 (18.6)
Citalopram	13 623 (18.5)	9146 (17.6)	4477 (20.8)
Trazodone	6891 (9.4)	5152 (9.9)	1739 (8.1)
Paroxetine	6751 (9.2)	4923 (9.5)	1828 (8.5)
Amitriptyline	6196 (8.4)	4336 (8.3)	1860 (8.6)
Drug prescribed on a 'take-as-needed' basis	2117 (2.9)	1951 (3.8)	166 (0.8)
Patient characteristics			
Female	50 689 (68.9)	35 134 (67.5)	15 555 (72.2)
Age	55 (45 – 65)	54 (45 – 64)	55 (45 – 65)
Type of drug insurance			
Public plan	40 912 (55.6)	29 171 (56.1)	11 741 (54.5)
Private plan	32 664 (44.4)	22 848 (43.9)	9816 (45.5)
No diagnostic code for a plausible antidepressant treatment indication			
±3 days around the index prescription date	42 248 (57.4)	29 394 (56.5)	12 864 (59.7)
+3 to -365 days around the index prescription date	16 538 (22.5)	12 081 (23.2)	4457 (20.7)
Chronic condition in the Charlson comorbidity index	23 297 (31.7)	16 145 (31.0)	7152 (33.2)
Previous hospitalization in the past 365 days	6769 (9.2)	4701 (9.0)	2068 (9.6)
Previous ER visit in the past 365 days	23 923 (32.5)	17 280 (33.2)	6643 (30.8)
Physician characteristics			
Place of medical training			
Canada/US	66 223 (90.0)	48 868 (93.9)	17 355 (80.5)
Other country	7353 (10.0)	3151 (6.1)	4202 (19.5)
Years in practice			
15+ years	69 168 (94.0)	49 082 (94.4)	20 086 (93.2)
<15 years	4408 (6.0)	2937 (5.7)	1471 (6.8)
Average number of patients per working day	18 (13 – 23)	18 (12 – 23)	19 (16 – 22)
Factors affecting physician response to new information on evidence-based clinical practice			
Evidence score	20 (19 – 22)	21 (19 – 22)	20 (19 – 21)
Nonconformity score	17 (15 – 19)	16 (15 – 18)	19 (15 – 20)
Practicality score	15 (14 – 17)	15 (14 – 18)	15 (14 – 15)

Table S7 Coefficients for the final prediction model used to estimate the probability of indications besides depression among prescriptions in the test set

Variable	Regression coefficient	Standard deviation^a
Intercept	-2.14	0.617
Prescription-related factors		
Molecule name		
Venlafaxine	0.00 [Reference]	-
Amitriptyline	2.997	0.440
Trazodone	2.693	0.491
Nortriptyline	2.714	2.442
Doxepin	1.801	1.430
Imipramine	1.676	4.257
Desipramine	1.995	4.415
Duloxetine	0.939	0.531
Paroxetine	0.553	0.372
Clomipramine	-0.515	1.407
Citalopram	-0.047	0.269
Escitalopram	-0.339	0.319
Sertraline	-0.612	0.318
Fluvoxamine	-0.421	0.686
Trimipramine	-0.299	1.791
Fluoxetine	-0.713	0.518
Mirtazapine	-1.068	0.506
Bupropion	-1.989	0.470
Desvenlafaxine	-1.858	5.150
Prescribed dose (mg/day), per 10 mg increase by molecule		
Mirtazapine	-0.342	0.176
Nortriptyline	-0.331	0.581
Paroxetine	-0.220	0.100
Desvenlafaxine	-0.125	1.012
Doxepin	-0.084	0.176
Citalopram	-0.172	0.072
Imipramine	-0.109	0.431
Fluoxetine	-0.050	0.169
Desipramine	-0.236	0.504
Amitriptyline	-0.041	0.093
Escitalopram	-0.044	0.192
Duloxetine	-0.085	0.090
Venlafaxine	-0.049	0.013
Trimipramine	-0.104	0.680
Sertraline	-0.009	0.025
Trazodone	-0.004	0.030
Fluvoxamine	-0.012	0.047
Clomipramine	0.098	0.152
Bupropion	0.029	0.018
Drug prescribed on a 'take-as-needed' basis	1.188	0.452

^aAcross 1000 bootstrap re-samples of the training set, where prescriptions were resampled using a two-stage cluster bootstrap to account for non-independence of prescriptions from the same physician and for the same patient.

APPENDIX D. (continued) Coefficients for the final prediction model used to estimate the probability of indications besides depression among prescriptions in the test set

Variable	Regression coefficient		Standard deviation ^a	
Patient-related factors				
Age (years ⁻²)	234.900		90.596	
Any diagnostic procedure in the past year	0.176		0.076	
Less than university education (%), per 1% increase	0.067		0.021	
Number of outpatient visits in the past year (visits ^{-0.5}) ^b	0.546		0.229	
Diagnostic codes in the past year				
Unspecified nonpsychotic mental disorder following organic brain damage (310.9)	-0.828		0.412	
Dementia	-0.484		0.269	
Diabetes without chronic complication	-0.336		0.122	
<u>Plausible antidepressant treatment indications</u>				
	± 3 days	-4 to -365 days	± 3 days	-4 to -365 days
Depression	-1.087	-0.876	0.130	0.106
Anxiety/stress disorders	0.655	0.453	0.161	0.115
Sleeping disorders	0.568	-0.007	0.244	0.143
Pain	0.197	0.011	0.123	0.060
Migraine	0.163	-0.006	0.278	0.120
Fibromyalgia	0.836	0.176	0.281	0.155
Obsessive-compulsive disorder	2.559	1.260	2.022	0.475
Vasomotor symptoms of menopause	0.201	-0.008	0.288	0.135
Nicotine dependence	0.878	-0.097	0.699	0.318
Attention deficit/hyperactivity disorder	0.791	0.299	0.525	0.340
Sexual dysfunction	-2.939	0.342	5.930	1.020
Pre-menstrual dysphoric disorder	0.703	-0.135	3.936	1.027
Eating disorders	1.141	0.869	3.453	0.664
Drugs prescribed in the past year				
Furosemide	-0.670		0.344	
Trazodone	-0.349		0.165	
Quetiapine	-0.332		0.175	
Physician-related factors				
Average number of patients per working day (patients ^{-0.5})	2.022		0.904	

^aAcross 1000 bootstrap re-samples of the training set, where prescriptions were resampled using a two-stage cluster bootstrap to account for non-independence of prescriptions from the same physician and for the same patient.

^bBecause the domain of this variable included 0, the original values were shifted up by 1 before applying the power