The Impact of Antidepressant Treatment Adherence on the Use of Diagnostic Radiology and Laboratory Tests in Patients with Depressive/Anxiety Disorders: A Population-Based Study

Table 1: ICD9-CM codes used to identify different diagnostic tests/specialist visits.

Diagnostic test	ICD-9 CM	Labelling
Computed tomography	87.03	Computerized axial tomography of head
	88.01	Computerized axial tomography of abdomen
	87.41	Computerized axial tomography of thorax
	87.42	Other tomography of thorax
	87.71	Computerized axial tomography of kidney
	87.72	Other nephrotomogram
	88.38	Other computerized axial tomography
	88.90	Diagnostic imaging, not elsewhere classified
Magnetic resonance imaging	88.91	Magnetic resonance imaging of brain and brain stem
	88.92	Magnetic resonance imaging of chest and myocardium
	88.93	Magnetic resonance imaging of spinal canal
	88.94	Magnetic resonance imaging of musculoskeletal
	88.95	Magnetic resonance imaging of pelvis, prostate, and bladder
X- ray	87.09	Other soft tissue x-ray of face, head, and neck
	87.11	Full-mouth x-ray of teeth
	87.18	Other x-ray of skull
	87.22	Other x-ray of cervical spine
	87.23	Other x-ray of thoracic spine
	87.24	Other x-ray of lumbosacral spine
	87.29	Other x-ray of spine
	87.43	X-ray of ribs, sternum, and clavicle
	87.44	Routine chest x-ray
	87.61	Barium swallow
	87.62	Upper GI series
	87.64	Lower GI series
	88.21	Skeletal x-ray of shoulder and upper arm

	88.22	Skeletal x-ray of elbow and forearm
	88.23	Skeletal x-ray of upper limb, not otherwise specified
	88.26	Other skeletal x-ray of pelvis and hip
	88.27	Skeletal x-ray of thigh, knee, and lower leg
	88.28	Skeletal x-ray of ankle and foot
	88.29	Skeletal x-ray of lower limb, not otherwise specified
	87.37	Other mammography
	87.49	Other chest x-ray
	87.79	Other x-ray of the urinary system
	88.19	Other x-ray of abdomen
	88.31	Skeletal series
Ultrasound	88.71	Diagnostic ultrasound of head and neck
	88.72	Diagnostic ultrasound of heart
	88.73	Diagnostic ultrasound of other sites of thorax
	88.74	Diagnostic ultrasound of digestive system
	88.75	Diagnostic ultrasound of urinary system
	88.76	Diagnostic ultrasound of abdomen and retro peritoneum
	88.79	Other diagnostic ultrasound
Other tests	92.01	Thyroid scan and radioisotope function studies
	92.02	Liver scan and radioisotope function study
	92.03	Renal scan and radioisotope function study
	92.04	GI scan and radioisotope function study
	92.05	Cardiovascular and hematopoietic scan and radioisotope function study
	92.13	Radioisotope; Parathyroid scan
	92.14	Radioisotope; Bone scan
	92.15	Radioisotope; Pulmonary scan
	92.16	Radioisotope; Scan of lymphatic system
	92.18	Radioisotope; Total body scan
	92.19	Radioisotope; Scan of other sites

Specialist Visits

Cardiologist	93.36	Physical therapy; Cardiac re-training
	89.7	General physical examination
Oculist	95.0*	General And Subjective Eye Examination

	95.02	Comprehensive eye examination
	95.05	Visual field study
	95.07	Dark adaptation study
	95.15	Ocular motility study
Gynaecologist	89.26, (V72.3)	Gynaecological examination
Neurologist	89.13	Neurologic examination
	94.0*, 94.1*	Psychiatric Interviews, Consultations, And Evaluations
	94.12	Routine psychiatric visit, not otherwise specified
Dentist	23.01	Forceps; Extraction of deciduous tooth
	23.09	Forceps; Extraction of other tooth
	23.19	Other surgical extraction of tooth
	23.2	Restoration of tooth by filling
	23.5	Implantation of tooth
	23.6	Prosthetic dental implant
	23.49	Other dental restoration
	23.71	Root canal therapy with irrigation
	24.4	Excision of dental lesion of jaw
	97.35	Removal of dental prosthesis
	99.97	Fitting of denture

Legend:* All visits.**Abbreviations:** GI: gastrointestinal.Blood test were classified according to Campania region medical procedure price-list codes.

Table 2: Criteria for definition of inappropriate request for diagnostic tests.

Diagnostic Test	Indication(s)	ICD-9-CM code(s)	Drugs as proxy of the indication	ATC code	Time windows
Cardiac ultrasound	Acute myocardial infarction (AMI), stroke, cardiomyopathies, heart failure, diabetes mellitus and pericarditis	390-429, 440-449, 250	Cardiovascular drugs, low dose aspirin, antidiabetic	C*, B01AC06, A10*	No codes registered any-time prior and within 90 days after the date of the test/visit request
ECG	AMI, angina pectoris, arrhythmia and diabetes mellitus	390-429, 440-449, 250	Cardiovascular drugs, low dose aspirin, antidiabetic	C*, B01AC06, A10*	
Cardiological visit	Suspicion of cardiovascular diseases, ambulatory cardiac monitoring, diabetes mellitus	390-429, 440-449, 250	Cardiovascular drugs, low dose aspirin, antidiabetic	C*, B01AC06, A10*	
Head and neck CT	Stroke, TIA (transient ischemic attack), headache/migraine, sinusitis, maxillofacial disorders, hemorrhage, aneurysm/arteriovenous malformation (AVM), ear disorders, traumas	290, 331, 294.1, 340, 320-326, 190,191, 192, 225, 380-389, 430-438, 461, 473, 346, 339, 800-804, 850-854, 959.0, 742.9	Antimigraine preparations, otological agents, decongestants and antiallergics, nasal preparations, anti-inflammatory agents, antineoplastic agents and immunomodulating agents	M01* R01A* R01B*, N02C*, L0*, S02*	

Abbreviations: ATC: Anatomical Therapeutic Chemical (ATC) classification system; ECG: Electrocardiogram; CT: computed tomography; International Classification of Disease, 9th Edition with Clinical Modification; CD 9-CM: MRI: magnetic resonance imaging.

Table 3: Demographic and clinical characteristics of new users of Ads and non-users of ADs.

	SSRIs N=2,681					Other ADs N=544					Non AD users N=6,205 (%)
	Low adherence N=1,371 (%)	Medium adherence N=850 (%)	High adherence N=460 (%)	p for trend[^]	p for general association[#]	Low adherence N=330 (%)	Medium adherence N=146 (%)	High adherence N=68 (%)	p for trend[^]	p for general association[#]	
Gender											
Male	450 (32.8)	281 (33.1)	156 (33.9)	0.687	0.912	125 (37.9)	52 (35.6)	30 (44.1)	0.558	0.489	2,156 (34.7)
Female	921 (67.2)	569 (66.9)	304 (66.1)			205 (62.1)	94 (64.4)	38 (55.9)			4,049 (65.3)
Age groups (mean ±SD, years)	54.9±17.3	56.6±18.1	54.6±18.5	0.290	0.048	60.4±17.8	59.2±18.7	59.8±16.4	0.561	0.831	56.9±15.5
<45	410 (29.9)	248 (29.2)	148 (32.2)	0.507	0.520	70 (21.2)	37 (25.3)	17 (25.0)	0.332	0.551	1,625 (26.2)
45-64	532 (38.8)	280 (32.9)	154 (33.5)	0.008	0.009	111 (33.6)	41 (28.1)	20 (29.4)	0.288	0.446	2,542 (41.0)
65-80	331 (24.1)	249 (29.3)	123 (26.7)	0.072	0.026	105 (31.8)	50 (34.2)	26 (38.2)	0.293	0.569	1,575 (25.4)
>80	98 (7.1)	73 (8.6)	35 (7.6)	0.501	0.464	44 (13.3)	18 (12.3)	5 (7.4)	0.215	0.394	463 (7.5)
Co-morbidities											
Arrhythmia	157 (11.5)	106 (12.5)	57 (12.4)	0.490	0.731	49 (14.8)	21 (14.4)	9 (13.2)	0.737	0.941	391 (6.3)
Cancer	118 (8.6)	69 (8.1)	45 (9.8)	0.595	0.590	22 (6.7)	11 (7.5)	3 (4.4)	0.685	0.692	337 (5.4)
Chronic kidney disease	37 (2.7)	28 (3.3)	11 (2.4)	0.978	0.585	16 (4.8)	6 (4.1)	2 (2.9)	0.471	0.767	118 (1.9)
Chronic liver disease	84 (6.1)	45 (5.3)	22 (4.8)	0.235	0.487	22 (6.7)	9 (6.2)	4 (5.9)	0.778	0.960	224 (3.6)
Congestive heart failure	63 (4.6)	47 (5.5)	20 (4.3)	0.889	0.524	31 (9.4)	8 (5.5)	3 (4.4)	0.078	0.185	219 (3.5)
COPD and asthma	415 (30.3)	251 (29.5)	116 (25.2)	0.061	0.115	120 (36.4)	49 (33.6)	16 (23.5)	0.057	0.126	1,284 (20.7)
Coronary disease	212 (15.5)	132 (15.5)	66 (14.3)	0.634	0.825	83 (25.2)	32 (21.9)	20 (29.4)	0.777	0.486	717 (11.6)
Dementia	13 (0.9)	21 (2.5)	11 (2.4)	0.008	0.011	13 (3.9)	6 (4.1)	3 (4.4)	0.855	0.983	36 (0.6)
Diabetes	180 (13.1)	102 (12.0)	56 (12.2)	0.480	0.704	52 (15.8)	31 (21.2)	9 (13.2)	0.832	0.234	622 (10.0)
Dyslipidemia	308 (22.5)	183 (21.5)	93 (20.2)	0.304	0.586	73 (22.1)	36 (24.7)	22 (32.4)	0.087	0.196	844 (13.6)
Hypertension	702 (51.2)	430 (50.6)	225 (48.9)	0.415	0.697	201 (60.9)	76 (52.1)	38 (55.9)	0.166	0.185	2,556 (41.2)
Ischemic brain disease	112 (8.2)	92 (10.8)	59 (12.8)	0.002	0.007	39 (11.8)	14 (9.6)	10 (14.7)	0.799	0.541	233 (3.8)
Obesity	29 (2.1)	24 (2.8)	12 (2.6)	0.397	0.551	11 (3.3)	4 (2.7)	0 (0.0)	0.162	0.349[§]	100 (1.6)
Osteoarthritis	765 (55.8)	445 (52.4)	216 (47.0)	0.001	0.004	213 (64.5)	83 (56.8)	45 (66.2)	0.637	0.227	2,741 (44.2)

Peripheral vasculopathy	101 (7.4)	83 (9.8)	35 (7.6)	0.431	0.119	40 (12.1)	14 (9.6)	4 (5.9)	0.113	0.280	334 (5.4)
Reumathoid arthitis	24 (1.8)	15 (1.8)	8 (1.7)	0.995	0.999	8 (2.4)	6 (4.1)	1 (1.5)	0.934	0.547[§]	62 (1.0)
Thyroid diseases	247 (18.0)	146 (17.2)	74 (16.1)	0.333	0.625	62 (18.8)	30 (20.5)	11 (16.2)	0.829	0.745	727 (11.7)
Number of co-morbidities: median (q$_1$-q$_3$)	2 (1-4)	2 (1-4)	2 (1-4)	0.096	0.162	3 (1-5)	3 (1-5)	2.5 (1-4)	0.420	0.651	1 (0-3)
0	240 (17.5)	174 (20.5)	109 (23.7)	0.003	0.010	43 (13.0)	28 (19.2)	7 (10.3)	0.717	0.110	1,903 (30.7)
1	261 (19.0)	162 (19.1)	90 (19.6)	0.863	0.948	62 (18.8)	24 (16.4)	12 (17.6)	0.602	0.781	1,350 (21.8)
2	249 (18.2)	134 (15.8)	75 (16.3)	0.194	0.310	49 (14.8)	17 (11.6)	15 (22.1)	0.336	0.098	1,075 (17.3)
3-4	373 (27.2)	218 (25.6)	98 (21.3)	0.012	0.031	85 (25.8)	39 (26.7)	19 (27.9)	0.698	0.924	1,247 (20.1)
>4	248 (18.1)	162 (19.1)	88 (19.1)	0.422	0.708	91 (27.6)	38 (26.0)	15 (22.1)	0.326	0.602	630 (10.2)
Concomitant use of drugs*											
Antiepileptic drugs	23 (1.7)	47 (5.5)	35 (7.6)	<0.001	<0.001	12 (3.6)	7 (4.8)	10 (14.7)	0.001	0.001	48 (0.8)
Cholinesterase inhibitor agents	2 (0.1)	2 (0.2)	2 (0.4)	0.269	0.400[§]	0 (0.0)	0 (0.0)	1 (1.5)	0.036	0.125[§]	0 (0.0)
Antiparkinson agents	16 (1.2)	30 (3.5)	25 (5.4)	<0.001	<0.001	8 (2.4)	5 (3.4)	3 (4.4)	0.332	0.488[§]	21 (0.3)
Antipsychotic drugs	8 (0.6)	20 (2.4)	10 (2.2)	0.001	0.001	6 (1.8)	3 (2.1)	2 (2.9)	0.576	0.744[§]	10 (0.2)
Opioids agents	26 (1.9)	22 (2.6)	6 (1.3)	0.763	0.261	6 (1.8)	3 (2.1)	2 (2.9)	0.576	0.744[§]	72 (1.2)
Antihypertensive agents	566 (41.3)	383 (45.1)	189 (41.1)	0.615	0.176	158 (47.9)	66 (45.2)	25 (36.8)	0.112	0.243	2,119 (34.1)
Antithrombotics	293 (21.4)	212 (24.9)	118 (25.7)	0.026	0.062	94 (28.5)	44 (30.1)	23 (33.8)	0.385	0.671	835 (13.5)
Antiplatelets	263 (19.2)	197 (23.2)	104 (22.6)	0.040	0.053	85 (25.8)	43 (29.5)	21 (30.9)	0.292	0.557	748 (12.1)
Corticosteroids	92 (6.7)	50 (5.9)	19 (4.1)	0.048	0.129	23 (7.0)	14 (9.6)	2 (2.9)	0.603		222 (3.6)
NSAIDs	286 (20.9)	190 (22.4)	72 (15.7)	0.077	0.014	69 (20.9)	26 (17.8)	12 (17.6)	0.405	0.665	936 (15.1)
Cardiac therapy excluding antihypertensive agents[1]	108 (7.9)	60 (7.1)	36 (7.8)	0.796	0.765	30 (9.1)	18 (12.3)	8 (11.8)	0.322	0.515	334 (5.4)
No. concomitant* drugs: median (q$_1$-q$_3$)	2 (1-5)	2 (1-5)	2 (1-5)	0.242	0.192	3 (1-5)	3 (1-5)	2 (1-6)	0.768	0.572	1 (0-3)
<3	751 (54.8)	439 (51.6)	256 (55.7)	0.851	0.256	158 (47.9)	69 (47.3)	36 (52.9)	0.572	0.715	4,294 (69.2)
3-5	359 (26.2)	245 (28.8)	109 (23.7)	0.654	0.119	103 (31.2)	41 (28.1)	14 (20.6)	0.085	0.205	1,244 (20.0)
6-8	174 (12.7)	103 (12.1)	63 (13.7)	0.727	0.715	45 (13.6)	25 (17.1)	14 (20.6)	0.113	0.284	489 (7.9)
>8	87 (6.3)	63 (7.4)	32 (7.0)	0.486	0.617	24 (7.3)	11 (7.5)	4 (5.9)	0.775	0.903	178 (2.9)

*within 90 days prior to the first AD prescription; ^p-values from Cochran-Mantel-Haenszel and Spearman correlation statistics for categorical and continuous variables, respectively;#p-values from Pearson Chi-Square and Kruskal-Wallis statistics for categorical and continuous variables, respectively; §p-values from Fisher exact test; 1Cardiac glycosides, antiarrhythmic, class I and III, cardiac stimulants excl. cardiac glycosides, vasodilators used in cardiac diseases, other cardiac preparations.

Abbreviations: NSAIDs: non-steroidal anti-inflammatory drugs;SD: standard deviation; SSRI: selective serotonin re-uptake inhibitor; q1-q3: first-third quartiles; other ADs: noradrenaline reuptake inhibitor, noradrenergic and specific serotonergic antidepressants, serotonin–norepinephrine reuptake inhibitors, serotonin antagonist and reuptake inhibitor, bupropion and ademetionine.Tricyclic antidepressants (n= 256) were not reported in this analysis, due to limited number of treated patients with high adherence (n=7). Adherence was classified as low (<20%), medium (20-80%) and high (≥80%) on the basis of proportion of days covered.

Table 4 : Frequency of diagnostic test requests for new users of AD and non-users during two years of follow-up.

	SSRIs N=2,681					Other ADs[a] N=544					Non-users of ADs N=6,205 (%)
	Low adherence N=1,371 (%)	Medium adherence N=850 (%)	High adherence N=460 (%)	p for trend ^	p for general association[#]	Low adherence N=330 (%)	Medium adherence N=146 (%)	High adherence N=68 (%)	p for trend ^	p for general association[#]	
Diagnostic test											
Ultrasound	481 (35.1)	277 (32.6)	133 (28.9)	0.014	0.046	108 (32.7)	50 (34.2)	16 (23.5)	0.287	0.265	1,302 (21.0)
CT	153 (11.1)	98 (11.5)	46 (10.0)	0.620	0.695	36 (10.9)	20 (13.6)	5 (7.3)	0.756	0.377	420 (6.8)
Nuclear medicine	66 (4.8)	58 (6.8)	18 (3.9)	0.977	0.042	14 (4.2)	6 (4.1)	4 (5.9)	0.646	0.818	181 (2.9)
Blood test	918 (66.9)	567 (66.7)	281 (61.1)	0.046	0.059	227 (68.8)	104 (71.2)	46 (67.6)	0.940	0.825	3,013 (48.6)
MRI	139 (10.1)	108 (12.7)	45 (9.8)	0.668	0.119	27 (8.2)	10 (6.8)	6 (8.8)	0.948	0.845	399 (6.4)
ECG	198 (14.4)	116 (13.6)	52 (11.1)	0.106	0.238	58 (17.6)	24 (16.4)	9 (13.2)	0.401	0.679	535 (8.6)
X-ray	279 (20.4)	165 (19.4)	88 (19.1)	0.511	0.792	70 (21.2)	29 (19.8)	9 (13.2)	0.172	0.325	759 (12.2)
Other tests[b]	828 (60.4)	493 (58.0)	260 (56.5)	0.109	0.270	208 (63.0)	93 (63.7)	44 (64.7)	0.786	0.963	2645 (42.6)
Total											
Patients who requested at least one test within two years of follow-up	1,055 (77.0)	661 (77.7)	336 (73.0)	0.189	0.137	264 (80.0)	119 (81.5)	50 (73.5)	0.412	0.387	3,652 (58.9)
Estimated number of patients which requested at least one test, adjusted by patients' number of comorbidities**	1081 (78.9)	683 (80.3)	353 (76.7)	0.549	0.309	264 (80.0)	122 (83.3)	49 (71.7)	0.433	0.197	4147 (66.8)
Median no tests requested by each patient who requested at least one diagnostic test, within two years of follow-up*	6 (3-12)	6 (3-12)	5.5 (3-10)	0.057	0.163	7 (3-12.5)	6 (2-12)	7 (3-13)	0.695	0.761	5 (2-9)

Legend: [a] noradrenaline reuptake inhibitor, noradrenergic and specific serotonergic antidepressants, serotonin–norepinephrine reuptake inhibitors, serotonin antagonist and reuptake inhibitor, bupropion and ademetionine; [b] other laboratory and diagnostic tests (e.g. urine test, magnetotherapy, dental panoramic radiograph, etc.).*median along with lower and upper quartiles (in brackets). [^] p-values from Cochran-Mantel-Haenszel and Spearman correlation statistics for categorical and continuous variables, respectively; [#] p-values from Pearson Chi-Square and Kruskal-Wallis statistics for categorical and continuous variables, respectively; **number of patients and proportion were estimated from logistic models. **Abbreviations:** SSRI: selective serotonin re-uptake inhibitors; CT: computerized tomography scan; MRI: magnetic resonance imaging; ECG: electrocardiogram; Tricyclic antidepressants (n=256) were not reported in this analysis, due to limited number of treated patients with high adherence (n=7).Adherence was classified as low (<20%), medium (20-80%) and high (≥80%) on the basis of proportion of days covered

Table 5: Median costs for new AD users compared to non-users who requested at least one diagnostic test during two years of follow-up.

	SSRIs N=2,681					Other ADs[a] N=544					Non-users of ADs N=6,205 (%)
	Low adherence N=1,371 (%)	Medium adherence N=850 (%)	High adherence N=460 (%)	p for trend^	p for general association#	Low adherence N=330 (%)	Medium adherence N=146 (%)	High adherence N=68 (%)	p for trend^	p for general association#	
Diagnostic test											
Ultrasound	481 (35.1)	277 (32.6)	133 (28.9)	0.014	0.046	108 (32.7)	50 (34.2)	16 (23.5)	0.287	0.265	1,302 (21.0)
CT	153 (11.1)	98 (11.5)	46 (10.0)	0.620	0.695	36 (10.9)	20 (13.6)	5 (7.3)	0.756	0.377	420 (6.8)
Nuclear medicine	66 (4.8)	58 (6.8)	18 (3.9)	0.977	0.042	14 (4.2)	6 (4.1)	4 (5.9)	0.646	0.818	181 (2.9)
Blood test	918 (66.9)	567 (66.7)	281 (61.1)	0.046	0.059	227 (68.8)	104 (71.2)	46 (67.6)	0.940	0.825	3,013 (48.6)
MRI	139 (10.1)	108 (12.7)	45 (9.8)	0.668	0.119	27 (8.2)	10 (6.8)	6 (8.8)	0.948	0.845	399 (6.4)
ECG	198 (14.4)	116 (13.6)	52 (11.1)	0.106	0.238	58 (17.6)	24 (16.4)	9 (13.2)	0.401	0.679	535 (8.6)
X-ray	279 (20.4)	165 (19.4)	88 (19.1)	0.511	0.792	70 (21.2)	29 (19.8)	9 (13.2)	0.172	0.325	759 (12.2)
Other tests[b]	828 (60.4)	493 (58.0)	260 (56.5)	0.109	0.270	208 (63.0)	93 (63.7)	44 (64.7)	0.786	0.963	2645 (42.6)
Total											
Patients who requested at least one test within two years of follow-up	1,055 (77.0)	661 (77.7)	336 (73.0)	0.189	0.137	264 (80.0)	119 (81.5)	50 (73.5)	0.412	0.387	3,652 (58.9)
Estimated number of patients which requested at least one test, adjusted by patients' number of comorbidities**	1081 (78.9)	683 (80.3)	353 (76.7)	0.549	0.309	264 (80.0)	122 (83.3)	49 (71.7)	0.433	0.197	4147 (66.8)
Median no tests requested by each patient who requested at least one diagnostic test, within two years of follow-up*	6 (3-12)	6 (3-12)	5.5 (3-10)	0.057	0.163	7 (3-12.5)	6 (2-12)	7 (3-13)	0.695	0.761	5 (2-9)

[a]Noradrenaline reuptake inhibitor, noradrenergic and specific serotonergic antidepressants, serotonin–norepinephrine reuptake inhibitors, serotonin antagonist and reuptake inhibitor, bupropion and ademetionine; [b]other laboratory and diagnostic tests (e.g. urine test, magnetotherapy, dental panoramic radiograph, etc.). *median along with lower and upper quartiles (in brackets). [^]p-values from Cochran-Mantel-Haenszel and Spearman correlation statistics for categorical and continuous variables, respectively; [#]p-values from Pearson Chi-Square and Kruskal-Wallis statistics for categorical and continuous variables, respectively; **means (along with 95% confidence intervals) were estimated from ANOVA models using log-transformation of costs as outcome and both class number of comorbidities and adherence treatment as covariates.

Abbreviations: SSRI: selective serotonin re-uptake inhibitors; CT: computed tomography; MRI: magnetic resonance imaging; ECG: electrocardiogram; the price cost is reported in euro currency (€).Tricyclic antidepressants (n=256) were not reported in this analysis, due to limited number of treated patients with high adherence (n=7).Adherence was classified as low (<20%), medium (20-80%) and high (≥80%) on the basis of proportion of days covered.

Table 6: Frequency of inappropriate diagnostic tests during two years of follow-up for AD users and non-AD users.

Inappropriate request for diagnostic test/visit	SSRI N=2,681			Other ADs* N= 546			Non-users of ADs N=6,205
	Low adherence N=1,371	Medium adherence N=850	High adherence N=460	Low adherence N=330	Medium adherence N=146	High adherence N=68	
ECG							
Patients with inappropriate tests among those who requested at least one test	27/198 (13.6%; 95%CI: 9.2-19.2%)	13/116 (11.2%; 95%CI: 6.1-18.4%)	7/52 (13.5%; 95%CI: 5.6-25.8%)	8/58 (13.8%; 95%CI: 6.2-25.4%)	1/24 (4.2%; 95%CI: 0.1-21.1%)	0/9 (0.0%)	61/535 (11.4%; 95%CI: 8.8-14.4%)
Number of inappropriate tests among the total number of requested tests	33/301 (11.0%)	22/191 (11.5%)	7/82 (8.5%)	12/94 (12.8%)	1/39 (2.6%)	0/13 (0.0%)	73/873 (8.4%)
Cardiac ultrasound							
Patients with inappropriate tests among those who requested at least one test	11/144 (7.6%; 95%CI: 3.9-13.3%)	10/91 (11.0%; 95%CI: 5.4-19.3%)	4/46 (8.7%; 95%CI: 2.4-20.8%)	5/41 (12.2%; 95%CI: 4.1-26.2%)	2/17 (11.8%; 95%CI: 1.5-36.4%)	0/6 (0.0%)	32/379 (8.4%; 95%CI: 5.9-11.7%)
Number of inappropriate tests among the total number of requested tests	14/256 (5.5%)	20/172 (11.6%)	5/82 (6.1%)	10/77 (13.0%)	5/34 (14.7%)	0/8 (0.0%)	55/769 (7.2%)
Cardiological visit							
Patients with inappropriate tests among those who requested at least one test	19/116 (16.4%; 95%CI: 10.2-24.4%)	9/67 (13.4%; 95%CI: 6.3-24%)	5/31 (16.1%; 95%CI: 5.5-33.7%)	7/38 (18.4%; 95%CI: 7.7-34.3%)	1/12 (8.3%; 95%CI: 0.2-38.5%)	0/5 (0.0%)	32/289 (11.1%; 95%CI: 7.7-15.3%)
Number of inappropriate tests among the total number of requested tests	20/158 (12.7%)	13/98 (13.3%)	5/64 (7.8%)	8/56 (14.3%)	1/21 (4.8%)	0/7 (0.0%)	34/434 (7.8%)
Head and neck CT							
Patients with inappropriate tests among those who	26/70 (37.1%; 95%CI: 25.9-49.5%)	24/58 (41.4%; 95%CI: 28.6-	7/26 (26.9%; 95%CI: 11.6-	10/25 (40.0%; 95%CI: 21.1-	3/9 (33.3%; 95%CI: 7.5-	3/5 (60.0% 95%CI: 14.7-	77/154 (50.0%; 95%CI: 41.9-

requested at least one test		55.1%)	47.8%)	61.3%)	70.1%)	94.7%)	58.2%)
Number of inappropriate tests among the total number of requested tests	38/102 (37.3%)	41/81 (50.6%)	9/35 (25.7%)	13/32 (40.6%)	3/10 (30.0%)	3/5 (60.0%)	108/212 (50.9%)

Legend: * noradrenaline reuptake inhibitor, noradrenergic and specific serotonergic antidepressants, serotonin–norepinephrine reuptake inhibitors, serotonin antagonist and reuptake inhibitor, bupropion and ademetionine.

Abbreviations: SSRI: selective serotonin re-uptake inhibitors; ECG: electrocardiogram; CT: computed tomography. Tricyclic antidepressants (n=256) were not reported in this analysis, due to limited number of treated patients with high adherence (N=7). Adherence was classified in low (<20%), medium (20-80%) and high (≥80%) on the basis of proportion of days covered.