



Table S1. Equivalences between names used in ADRs classification and ATC codes.

Name	ATC Code
Analgesic	M01A
Angiotensin-converting enzyme (ACE) inhibitor	C09A
Angiotensin II receptor blocker	C09C
Antiarrhythmic	C01
Antibiotic	J01
Anticoagulant	B01AB
Antidepressant	N06A
Antiepileptic	N03A
Antiplatelet	B01AC
Antivitamin K	B01AA
Benzodiazepine	N05BA
Beta blocker	C07
Bronchodilator	R03
Corticoid	H02A
Loop diuretic	C03C
Hypnotic	N05C
Insulin	A10A
Neuroleptic	N05A
Opioid	N02A
Oral anticoagulant	B01AE, B01AF
Oral antidiabetic	A10B
Potassium sparing diuretic	C03D
Proton pump inhibitor	A02BC
Statin	C10AA
Thiazide diuretic	C03A

ATC: Anatomical Therapeutic Chemical.

Table S2. Number and percentage of patients with each chronic condition or geriatric syndrome registered according to the assigned multimorbidity cluster.

Chronic Condition or Geriatric Syndrome	Osteo- Articular	Psycho- Geriatric	Minor Chronic Disease	Cardio- Respiratory
Acute confusional syndrome/delirium	51 (37.2)	102 (67.5)	29 (22.8)	53 (16.3)
Amputation	7 (5.1)	2 (1.3)	4 (3.1)	3 (0.9)
Anaemia	77 (56.2)	64 (42.4)	76 (59.8)	117 (36.0)
Asthma	32 (23.4)	11 (7.3)	10 (7.9)	29 (8.9)
Cardiac arrhythmia	86 (62.8)	77 (51.0)	77 (60.6)	183 (56.3)
Cerebrovascular disease	40 (29.2)	53 (35.1)	36 (28.3)	59 (18.2)
Chronic gastritis or gastro-oesophageal reflux	25 (18.2)	11 (7.3)	19 (15.0)	39 (12.0)
Chronic pain	127 (92.7)	82 (54.3)	88 (69.3)	105 (32.3)
Chronic renal insufficiency	81 (59.1)	50 (33.1)	73 (57.5)	116 (35.7)
Chronic thyroid disease	44 (32.1)	19 (12.6)	23 (18.1)	49 (15.1)
Cognitive/Intellectual impairment	32 (23.4)	130 (86.1)	35 (27.6)	32 (9.8)
Constipation	78 (56.9)	88 (58.3)	41 (32.3)	133 (40.9)
COPD	41 (29.9)	38 (25.2)	49 (38.6)	145 (44.6)
Degenerative arthropathy	111 (81.0)	79 (52.3)	81 (63.8)	114 (35.1)
Dementia	17 (12.4)	98 (64.9)	24 (18.9)	40 (12.3)

Depression or anxiety	84 (61.3)	52 (34.4)	37 (29.1)	95 (29.2)
Diabetes mellitus with organ damage	28 (20.4)	21 (13.9)	34 (26.8)	50 (15.4)
Diabetes mellitus without organ damage	27 (19.7)	57 (37.7)	36 (28.3)	81 (24.9)
Drug-related conditions	22 (16.1)	19 (12.6)	7 (5.5)	19 (5.8)
Dyslipidaemia	89 (65.0)	50 (33.1)	88 (69.3)	133 (40.9)
Dysphagia	36 (26.3)	78 (51.7)	28 (22.0)	17 (5.2)
Frailty	115 (83.9)	138 (91.4)	59 (46.5)	145 (44.6)
Gallstones (previous hepatic colic)	18 (13.1)	12 (7.9)	16 (12.6)	33 (10.2)
Gout	30 (21.9)	14 (9.3)	54 (42.5)	39 (12.0)
Heart failure	89 (65.0)	79 (52.3)	71 (55.9)	204 (62.8)
Hematologic disorders	8 (5.8)	3 (2.0)	14 (11.0)	11 (3.4)
Hypertension	121 (88.3)	119 (78.8)	111 (87.4)	252 (77.5)
Immobility	101 (73.7)	143 (94.7)	55 (43.3)	131 (40.3)
Incontinence (urinary/fecal)	33 (24.1)	112 (74.2)	16 (12.6)	31 (9.5)
Inflammatory osteoarticular disease	19 (13.9)	4 (2.6)	12 (9.4)	14 (4.3)
Instability/falls	93 (67.9)	59 (39.1)	51 (40.2)	83 (25.5)
Ischemic heart disease without infarction	38 (27.7)	17 (11.3)	27 (21.3)	38 (11.7)
Malnutrition	12 (8.8)	65 (43.0)	5 (3.9)	65 (20.0)
Mild liver disease	5 (3.6)	7 (4.6)	7 (5.5)	13 (4.0)
Moderate or severe liver disease	3 (2.2)	3 (2.0)	1 (0.8)	12 (3.7)
Myocardial infarction	28 (20.4)	11 (7.3)	26 (20.5)	46 (14.2)
Neoplasia	16 (11.7)	18 (11.9)	25 (19.7)	52 (16.0)
Neurologic disorder of the central nervous system	11 (8.0)	9 (6.0)	4 (3.1)	8 (2.5)
Non-ischemic heart disease	58 (42.3)	31 (20.5)	58 (45.7)	91 (28.0)
Obesity	58 (42.3)	24 (15.9)	43 (33.9)	68 (20.9)
Osteoporosis	49 (35.8)	13 (8.6)	12 (9.4)	29 (8.9)
Parkinson's disease	10 (7.3)	9 (6.0)	5 (3.9)	10 (3.1)
Peptic ulcer disease	10 (7.3)	8 (5.3)	12 (9.4)	16 (4.9)
Peripheral neuropathy or neuritis	21 (15.3)	9 (6.0)	18 (14.2)	13 (4.0)
Peripheral vascular disease	21 (15.3)	13 (8.6)	22 (17.3)	49 (15.1)
Polypharmacy	133 (97.1)	115 (76.2)	123 (96.9)	220 (67.7)
Pressure ulcers	10 (7.3)	60 (39.7)	10 (7.9)	15 (4.6)
Previous fractures (not hip)	57 (41.6)	28 (18.5)	19 (15.0)	35 (10.8)
Previous hip fracture	22 (16.1)	14 (9.3)	4 (3.1)	27 (8.3)
Rheumatologic disease	8 (5.8)	3 (2.0)	5 (3.9)	16 (4.9)
Sensory deficit	58 (42.3)	70 (46.4)	49 (38.6)	137 (42.2)
Sleep apnoea	29 (21.2)	7 (4.6)	18 (14.2)	12 (3.7)
Sleep disorders/Insomnia	90 (65.7)	86 (57.0)	51 (40.2)	106 (32.6)
Varicose veins	59 (43.1)	25 (16.6)	43 (33.9)	37 (11.4)
Vertigo	42 (30.7)	13 (8.6)	7 (5.5)	15 (4.6)

COPD: chronic obstructive pulmonary disease.

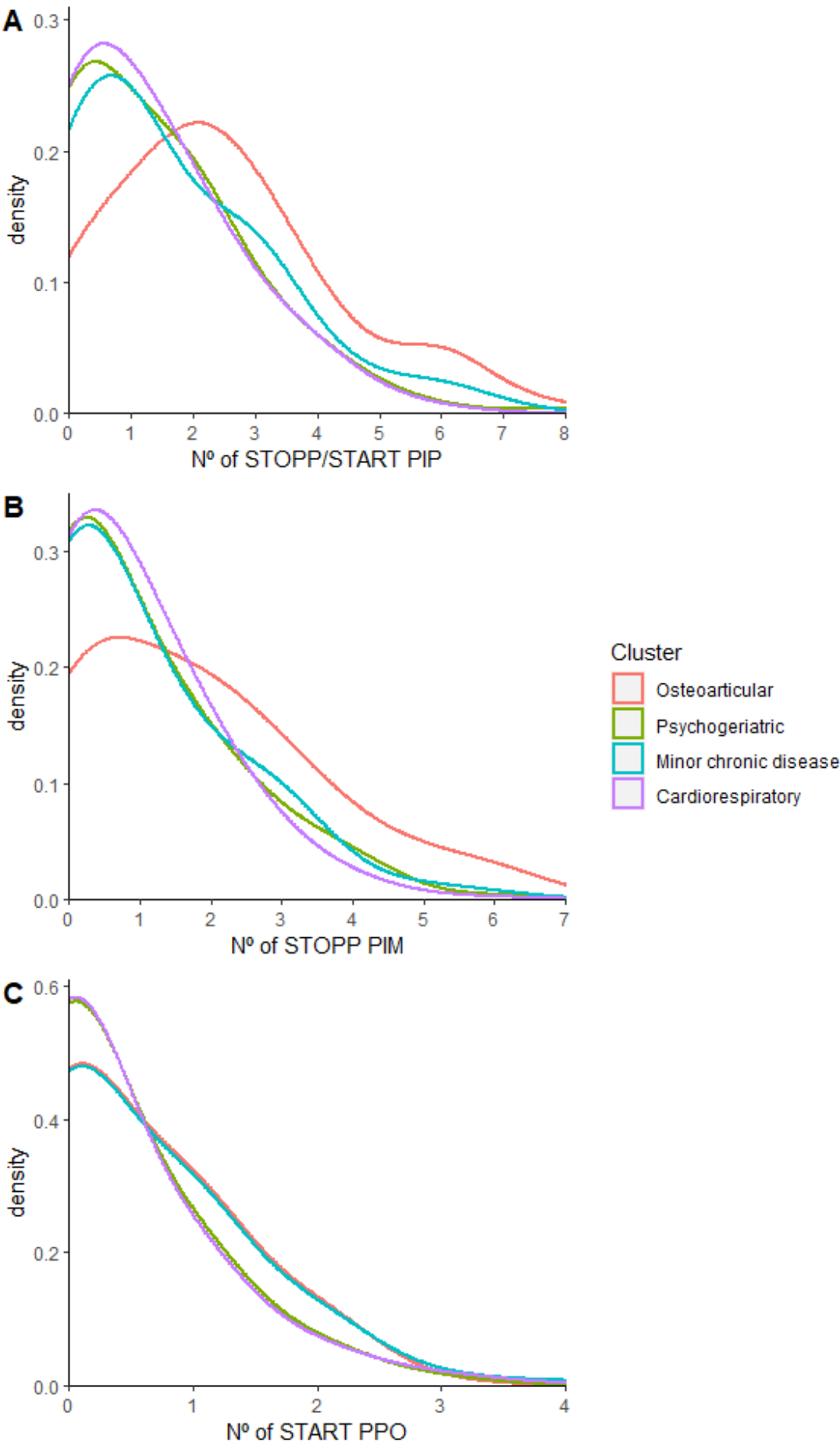


Figure S1. **A:** Distribution of the number of STOPP/START PIP according to the assigned multimorbidity cluster. Pairwise comparisons between cluster distributions performed with the Kolmogorov-Smirnov test showed significant differences between the osteoarticular cluster and the rest ($p < 0.001$). PIP: Potentially inappropriate prescribing. **B:** Distribution of the number of STOPP PIM according to the assigned multimorbidity cluster. Pairwise comparisons between cluster distributions performed with the Kolmogorov-Smirnov test showed significant differences between the osteoarticular cluster and the rest ($p < 0.005$). PIM: potentially inappropriate medication. **C:** Distribution of the number of START PPO according to the assigned multimorbidity cluster. Pairwise comparisons between cluster distributions performed with the Kolmogorov-Smirnov test showed no significant differences ($p > 0.05$). PPO: potential prescribing omission.

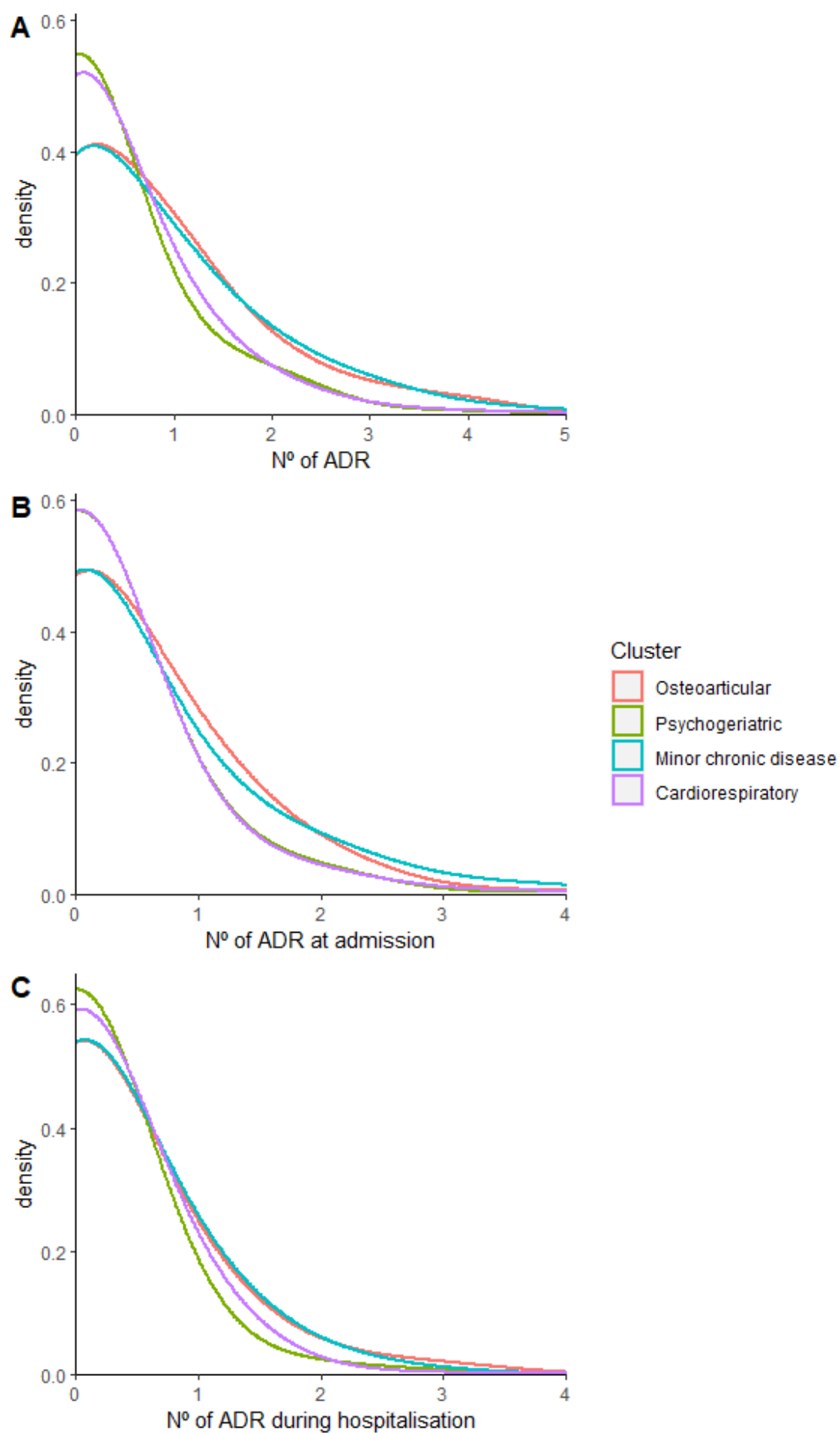


Figure S2. A: Distribution of the number of ADRs according to the assigned multimorbidity cluster. Pairwise comparisons between cluster distributions performed with the Kolmogorov-Smirnov test showed significant differences between the osteoarticular and the minor chronic disease clusters and the rest ($p < 0.001$). **B:** Distribution of the number of ADRs at admission according to the assigned multimorbidity cluster. Pairwise comparisons between cluster distributions performed with the Kolmogorov-Smirnov test showed significant differences between the osteoarticular cluster and the minor chronic disease clusters and the rest ($p < 0.05$). **C:** Distribution of the number of ADRs during admission according to the assigned multimorbidity cluster. Pairwise comparisons between cluster distributions performed with the Kolmogorov-Smirnov test showed no significant differences ($p > 0.05$). ADR: adverse drug reaction.

Table S3. p -values of post-hoc pairwise.

	Osteoarticular vs. Psychogeriatric	Osteoarticular vs. Minor Chronic Disease	Osteoarticular vs. Cardiorespiratory	Psychogeriatric vs. Minor Chronic Disease	Psychogeriatric vs. Cardiorespiratory	Cardiorespiratory vs. Minor Chronic Disease
Any PIP	<0.001	0.009	<0.001	0.347	0.815	0.19
Any PIM	0.014	0.014	0.002	1	0.779	0.779
Any PPO	0.037	1	0.012	0.037	0.998	0.012

Fisher's exact test assessing for association between the presence of any potentially inappropriate prescribing (PIP), potentially inappropriate medication (PIM) or potential prescribing omission (PPO), according to STOPP/START criteria, and multimorbidity cluster belonging (osteoarticular, psychogeriatric, minor chronic disease or cardiorespiratory). Benjamini-Hochberg correction was applied at a false discovery rate of 5%. $p < 0.05$ are shown in bold.

Table S4. p -values of post-hoc pairwise.

	Osteoarticular vs. Psychogeriatric	Osteoarticular vs. Minor Chronic Disease	Osteoarticular vs. Cardiorespiratory	Psychogeriatric vs. Minor Chronic Disease	Psychogeriatric vs. Cardiorespiratory	Cardiorespiratory vs. Minor Chronic Disease
Any STOPP A1: Acetylsalicylic acid	0.103	0.044	0.102	0.602	1	0.287
Any STOPP A1: Proton pump inhibitor	0.519	0.519	0.001	0.213	<0.001	0.022
Any STOPP A2	0.641	0.643	0.198	0.266	0.643	0.06
Any STOPP B11	0.013	0.112	<0.001	0.444	0.311	0.055
Any STOPP D5	<0.001	0.003	0.003	0.568	0.192	0.568
Any STOPP G5	0.004	0.088	0.007	0.4	0.436	0.823
Any STOPP I1	0.571	0.061	1	0.023	0.469	0.042
Any STOPP K1	<0.001	<0.001	<0.001	0.866	0.086	0.146
Any STOPP K2	0.103	0.771	0.003	0.04	<0.001	0.015
Any STOPP L2	0.047	0.356	0.047	0.522	1	0.522

Fisher's exact test assessing for association between the presence of any STOPP criteria previously significantly associated, and multimorbidity cluster belonging (osteoarticular, psychogeriatric, minor chronic disease or cardiorespiratory). Benjamini-Hochberg correction was applied at a false discovery rate of 5%. $p < 0.05$ are shown in bold.

Table S5. p -values of post-hoc pairwise.

	Osteoarticular vs. Psychogeriatric	Osteoarticular vs. Minor Chronic Disease	Osteoarticular vs. Psychogeriatric Cardiorespiratory vs. Minor	Psychogeriatric vs. Cardiorespiratory	Cardiorespiratory vs. Minor Chronic Disease
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		Chronic Disease		Chronic Disease		
Any START A8	0.854	0.854	0.037	1	0.01	0.01
Any START C2	0.112	1	0.06	0.144	1	0.062
Any START C3	0.138	0.165	1	0.877	0.082	0.138
Any START E2	0.169	0.427	0.02	0.594	0.594	0.384
Any START E5	0.506	0.506	0.003	0.185	0.037	<0.001
Any START H2	0.007	0.68	0.007	0.039	0.802	0.039

Fisher's exact test assessing for association between the presence of any START criteria previously significantly associated, and multimorbidity cluster belonging (osteoarticular, psychogeriatric, minor chronic disease or cardiorespiratory). Benjamini-Hochberg correction was applied at a false discovery rate of 5%. $p < 0.05$ are shown in bold.

Table S6. p -values of post-hoc pairwise.

	Osteoarticular vs. Psychogeriatric	Osteoarticular vs. Minor Chronic Disease	Osteoarticular vs. Cardiorespiratory	Psychogeriatric vs. Minor Chronic Disease	Psychogeriatric vs. Cardiorespiratory	Cardiorespiratory vs. Minor Chronic Disease
Any ADR	<0.001	0.902	<0.001	<0.001	0.168	<0.001
Any ADR at admission	0.001	0.95	<0.001	0.002	1	<0.001
Any ADR during admission	0.001	1	0.041	0.001	0.041	0.041

Fisher's exact test assessing for association between the presence of any adverse drug reaction (ADR), detected at the time of admission or during admission, and multimorbidity cluster belonging (osteoarticular, psychogeriatric, minor chronic disease or cardiorespiratory). Benjamini-Hochberg correction was applied at a false discovery rate of 5%. $p < 0.05$ are shown in bold.

Table S7. p -values of post-hoc pairwise.

	Osteoarticular vs. Psychogeriatric	Osteoarticular vs. Minor Chronic Disease	Osteoarticular vs. Cardiorespiratory	Psychogeriatric vs. Minor Chronic Disease	Psychogeriatric vs. Cardiorespiratory	Cardiorespiratory vs. Minor Chronic Disease
Any ADR ACE inhibitor	0.093	0.169	0.01	0.788	0.727	0.442
Any ADR Neuroleptic	0.371	0.732	1	0.472	0.087	0.472
Any ADR ARB	0.059	0.609	0.099	0.038	0.528	0.045
Any ADR Insulin	0.727	0.106	0.727	0.039	1	0.005
Any ADR Loop diuretic	0.094	0.446	0.145	0.296	0.446	0.446
Any ADR Thiazide diuretic	0.412	0.412	0.54	0.083	0.54	0.083

Fisher's exact test assessing for association between the presence of any adverse drug reaction (ADR) previously significantly associated, and multimorbidity cluster belonging (osteoarticular, psychogeriatric, minor chronic disease or cardiorespiratory). Benjamini-Hochberg correction was applied at a false discovery rate of 5%. $p < 0.05$ are shown in bold. ACE: angiotensin-converting enzyme. ARB: angiotensin II receptor blocker.