Drug Prescription and Delirium in Older Inpatients:
Results From the Nationwide Multicenter Italian Delirium Day 2015–2016

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ABSTRACT

Objective: This study aimed to evaluate the association between polypharmacy and delirium, the association of specific drug categories with delirium, and the differences in drug-delirium association between medical and surgical units and according to dementia diagnosis.

Methods: Data were collected during 2 waves of Delirium Day, a multicenter delirium prevalence study including patients (aged 65 years or older) admitted to acute and long-term care wards in Italy (2015–2016); in this study, only patients enrolled in acute hospital wards were selected (n = 4,133). Delirium was assessed according to score on the 4 "A's" Test. Prescriptions were classified by main drug categories; polypharmacy was defined as a prescription of drugs from 5 or more classes.

Results: Of 4,133 participants, 969 (23.4%) had delirium. The general prevalence of polypharmacy was higher in patients with delirium (67.6% vs 63.0%, $P = .009$) but varied according to clinical settings. After adjustment for confounders, polypharmacy was associated with delirium only in patients admitted to surgical units (OR = 2.9; 95% CI, 1.4–6.1). Insulin, antibiotics, antiepileptics, antipsychotics, and atypical antidepressants were associated with delirium, whereas statins and angiotensin receptor blockers exhibited an inverse association. A stronger association was seen between typical and atypical antipsychotics and delirium in subjects free from dementia compared to individuals with dementia (typical: OR = 4.31; 95% CI, 2.94–6.31 without dementia vs OR = 1.64; 95% CI, 1.19–2.26 with dementia; atypical: OR = 5.32; 95% CI, 3.44–8.22 without dementia vs OR = 1.74; 95% CI, 1.26–2.40 with dementia). The absence of antipsychotics among the prescribed drugs was inversely associated with delirium in the whole sample and in both of the hospital settings, but only in patients without dementia.

Conclusions: Polypharmacy is significantly associated with delirium only in surgical units, raising the issue of the relevance of medication review in different clinical settings. Specific drug classes are associated with delirium depending on the clinical setting and dementia diagnosis, suggesting the need to further explore this relationship.

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Delirium is an acute and fluctuating disorder of attention and cognitive functioning often affecting older people.[1] One-third of general medical inpatients who are 70 years of age or older experience delirium; this syndrome is present at hospital admission in half of these inpatients and develops during hospitalization in the other half.[2,3] Delirium is also the most common surgical complication among older adults; postoperative delirium rates among seniors are highly variable, ranging between 15% and 25% after elective surgery, such as total joint replacement,[4] and reaching 50% after high-risk procedures, such as hip fracture repair and cardiac surgery.[5,6]

Clinical Points

- Dementia represents the main risk factor for delirium, though delirium induced by drugs, especially those prescribed in surgical settings, is also common in older patients.
- Polypharmacy is significantly associated with delirium only in surgical units, and specific drug classes are associated with delirium depending on the clinical setting and dementia diagnosis, suggesting the need to further explore these relationships.

Delirium is associated with many negative outcomes, including increased mortality rates, prolonged hospital stays, decreased physical recovery, and higher rates of institutionalization,[7–9] finally resulting in a great increase in health care costs.[10–13]

There is substantial evidence that delirium is often related to underlying medical causes. Dementia, for instance, represents the main risk factor for delirium, and "delirium superimposed on dementia" is considered a separate diagnostic entity by some authors,[14–16] with worse outcomes than delirium or dementia alone.[17–19] Other risk factors, such as immobility, dehydration, malnutrition, and infections, are frequent, and their avoidance might prevent 30%–40% of delirium cases.[20–22] Moreover, some authors[23–30] hypothesize that specific drug categories and polypharmacy represent the most common reversible cause of this syndrome and, as such, that they can be the target of delirium prevention. The incidence of drug-induced delirium seems to be particularly high among very old patients due to aging-related changes in pharmacokinetics and pharmacodynamics and the high prevalence of polypharmacy and inappropriate prescribing.[31] In a systematic review[32] of prospective studies evaluating the relationship between drugs and the risk of delirium, psychoactive agents, such as benzodiazepines, opioids, and antihistamines, were most often associated with delirium; the evidence was less clear regarding histamine H_2 receptor antagonists, tricyclic antidepressants, antiparkinsonian medications, corticosteroids, and anticholinergics. Other studies[33,34] showed that benzodiazepines, narcotic analgesics, and drugs with anticholinergic effects are associated with delirium. However, the mechanisms through which drugs act as triggers of delirium are still debated and mainly unknown.[21,35] Delirium in surgical setting shows the prescription of specific drugs as pre-, intra-, and post-operative risk factors.[36,37]

The aims of this study are to evaluate the association of polypharmacy and specific drug categories with delirium in Italian hospitalized patients and to analyze differences in drug-delirium association between medical and surgical units and according to dementia.

METHODS

Delirium Day is an Italian multicenter point-prevalence study held in hospital wards, emergency rooms, rehabilitation units, nursing homes, and hospices; physicians affiliated with 10 Italian scientific societies were involved (Italian Association of Psychogeriatrics, Italian Society of Gerontology and Geriatrics, Italian Society of Hospital and Territory Geriatricians, Extrahospital Geriatrics Association, Italian Society of Internal Medicine, Federazione Associazione Dirigenti Ospedalieri Internisti, Italian Society of Neurology, Italian Society of Neurology for Dementia, Italian Society of Surgery, and Italian Society of Palliative Care). So far, 3 waves of the study have been carried out: the first took place on September 30, 2015, and the second on September 28, 2016. Data of the third wave held in 2017 are currently under quality control review. During each wave, data on older patients (aged 65 years or older) admitted to the participating centers were collected from midnight to 11:59 PM of Delirium Day. Patients with coma, aphasia, blindness, and deafness or at the end of life were excluded. Overall, 161 centers in 2015 and 276 in 2016 from all around Italy participated.

Study Sample

Three thousand three hundred forty patients were admitted to the participating wards in 2015 and 4,810 in 2016. For the purpose of this study, patients in palliative care settings, intensive care units, and long-term wards, including nursing homes and rehabilitation facilities, were excluded. Thus, a sample of 4,133 patients was analyzed: 3,770 were admitted to medical wards, and 363 were admitted to surgical units. Medical wards included geriatrics (n = 2,267), internal medicine (n = 1,126), neurology (n = 319), cardiology (n = 43), and infectious diseases (n = 15). Surgical wards included patients hospitalized in orthopedic (n = 241), neurosurgery (n = 17), and general surgery (n = 105).

Data Collection and Ethical Procedures

The Ethical Committee of the IRCSS Fondazione Santa Lucia, Rome, in 2015 and the Ethical Committee of Monza Brianza Province in 2016 approved the study protocols. All patients enrolled were able to speak Italian and provided a written informed consent (if patients were affected by severe cognitive impairment, a proxy signed the informed consent). The data were recorded using a web-based electronic case report form (e-CRF). Each participating center received a username and password to access the system and insert data. The data were anonymous, and patient identification was not possible.

Delirium Assessment

Delirium was assessed in all centers using the 4 "A's" Test (4AT), a rapid (ie, less than 2 minutes) clinical instrument to detect delirium. Previous validation studies showed a sensitivity of 89.7% and a specificity of 84.1% for delirium diagnosis.[38] The likelihood of delirium is scored according to 4 questions asked to the patient or caregiver to investigate acute changes of alertness, attention, and cognition. The final score is used for the diagnosis of delirium as follows: 0 points: absence of delirium; 1–3 points: delirium unlikely;

4+ points: probable delirium. A score of 4 or more on the 4AT instrument identified delirium in this study.

Assessment of Pharmacologic Therapy

Patients' therapy history was retrieved from medical records and grouped according to the following categories: laxatives, antiulcer drugs, antiplatelet drugs, diuretics, angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), β-blockers, calcium channel blockers, other antiarrhythmic drugs, statins and lipid-lowering drugs, oral hypoglycemic drugs, insulin, antiosteoporotic drugs, antibiotics, glucocorticoids, benzodiazepines, first- and second-generation antipsychotics, selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), atypical antidepressants, antiepileptics, and antidementia drugs (acetylcholinesterase inhibitors [AChE-Is] and memantine). Antiosteoporotic drugs were not evaluated separately due to the inclusion in this class of both biphosphonates and vitamin D. In addition, opioid prescription records were collected in 2016. Polypharmacy was defined as the simultaneous prescription of 5 or more drug classes.

Clinical Assessment

Data on sociodemographic characteristics and medical history were collected through interview and clinical records. Comorbidities were scored according to the Charlson Comorbidity Index.[39] Patients were deemed to have dementia if they either had dementia diagnosis in medical records (reported in the Charlson Comorbidity Index score), or were prescribed any antidementia drug prior to admission.

Statistical Analysis

Main characteristics of the sample were described using mean, standard deviation, and frequency, as appropriate. Fisher exact tests, *t* test, and χ^2 test, and were used to investigate significant differences within the study population. The association between delirium and polypharmacy was investigated through logistic regression analysis, with adjustment for age, sex, education, Charlson Comorbidity Index score, and the diagnosis of dementia. Analyses were further stratified by ward of admission (ie, surgical and medical) and diagnosis of dementia. Logistic regression analyses were also performed to assess the association between specific drug categories and delirium. All analyses were conducted with α-level set at .05 and using Stata 15 (StataCorp LLC, College Station, Texas).

Table 1. Sociodemographics and Clinical Characteristics of the Whole Sample and According to Presence of Absence of Delirium Diagnosis[a,b]

Variable	Total	Delirium		*P* Value
		No	Yes	
n (%)	4,133 (100)	3,164 (76.6)	969 (23.4)	
Age, mean (SD), y	81.6 (7.6)	80.8 (7.6)	84.4 (7.0)	<.001
Female	2,284 (55.2)	1,774 (55.1)	540 (55.7)	.739
Education, mean (SD), y	6.6 (3.7)	6.9 (3.8)	5.9 (3.2)	<.001
Surgical wards	363 (8.8)	300 (9.5)	63 (6.5)	.004
Medical wards	3,770 (91.2)	2,864 (90.5)	906 (93.5)	
Charlson Comorbidity Index score, median (SD)	6.4 (2.4)	6.33 (2.5)	6.71 (2.4)	<.001
Dementia	977 (23.6)	505 (16.0)	566 (58.4)	<.001
No. of drugs, median (SD)	5.3 (2.2)	5.3 (2.2)	5.6 (2.2)	.001
Polypharmacy (5+ drugs)	2,649 (64.1)	1,994 (63.0)	655 (67.6)	.009
Drug classes				
Laxatives	934 (22.6)	724 (22.9)	210 (21.7)	.430
Antiulcer drugs	2,912 (70.5)	2,237 (70.7)	675 (69.7)	.534
Antiplatelet drugs	1,869 (45.2)	1,438 (45.4)	431 (44.5)	.596
Diuretics	2,106 (50.7)	1,604 (50.7)	502 (51.8)	.545
ACE inhibitors	1,105 (26.7)	873 (27.6)	232 (23.9)	.025
ARBs	500 (12.1)	415 (13.1)	85 (8.8)	<.001
β-Blockers	1,546 (37.4)	1,194 (37.7)	352 (36.3)	.427
Calcium channel blockers	749 (18.1)	582 (18.4)	167 (17.2)	.412
Antiarrhythmic drugs	475 (11.5)	371 (11.7)	104 (10.7)	.396
Statins/lipid-lowering drugs	871 (21.1)	725 (22.9)	146 (15.1)	<.001
Oral hypoglycemics	407 (9.9)	329 (10.4)	78 (8.1)	.032
Insulin	556 (13.4)	408 (13.0)	148 (15.3)	.058
Antibiotics	1,641 (39.7)	1,179 (37.3)	462 (47.7)	<.001
Glucocorticoids	724 (17.5)	565 (17.9)	159 (16.4)	.299
Benzodiazepines	1,014 (24.5)	772 (24.4)	242 (25.0)	.716
Typical antipsychotics	335 (8.1)	158 (5.0)	177 (18.3)	<.001
Atypical antipsychotics	310 (7.5)	133 (4.2)	177 (18.3)	<.001
SSRIs	532 (12.9)	408 (12.9)	124 (12.8)	.936
SNRIs	74 (1.8)	59 (1.9)	15 (1.6)	.515
Atypical antidepressants	318 (7.7)	184 (5.8)	134 (13.8)	<.001
Antiepileptics	262 (6.3)	186 (5.9)	76 (7.8)	.0228
AChE-I/memantine	84 (2.03)	45 (1.4)	39 (4.0)	<.001

[a]Values shown as n (%) unless otherwise noted.
[b]Values for 78 and 50 patients were missing for education for medical ward and surgical ward patients, respectively.
Abbreviations: ACE = angiotensin-converting enzyme, AChE-I = acetylcholinesterase inhibitor, ARB = angiotensin II receptor blocker, SNRI = serotonin-norepinephrine reuptake inhibitor, SSRI = selective serotonin reuptake inhibitor.

RESULTS

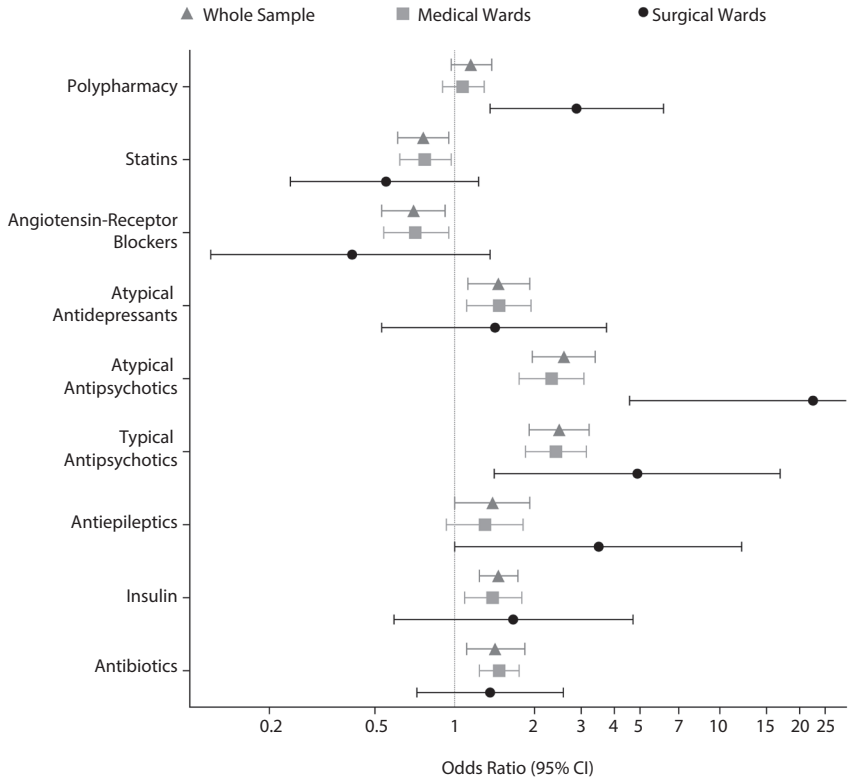
Whole Sample

The mean age of the sample was 81.6 years, and 55.3% were female. A total of 969 patients (23.4%) were diagnosed with delirium. Patients with delirium were older and more frequently affected by cerebrovascular diseases and dementia; they had a higher mean Charlson Comorbidity Index score and a higher number of prescribed medications than those without delirium (Table 1). Antibiotics, insulin, typical and atypical antipsychotics, atypical antidepressants, antiepileptics, and antidementia drugs were more frequently prescribed in patients with delirium, whereas oral hypoglycemics, statins, ARBs, and ACE inhibitors were less prescribed (Table 1). After multiadjustment, specific drug categories were directly (antibiotics, insulin, typical and atypical antipsychotics, atypical antidepressants, antiepileptics) or inversely (statins and ARBs) associated with delirium, but polypharmacy was not (Figure 1).

Medical and Surgical Units

Prevalence of delirium was 24.0% in medical units and 17.4% in surgical units. Among patients with delirium, only those admitted

Figure 1. Multivariate Logistic Regression Models Testing the Association of Specific Drug Categories and Polypharmacy With Delirium in the Whole Sample and in Medical and Surgical Wards[a]



[a]Models were adjusted for age, sex, education, dementia diagnosis, and Charlson Comorbidity Index score.

to surgical units were prescribed with a higher number of drug classes (Table 2 and Figure 1). Typical and atypical antipsychotics and atypical antidepressants were more frequently prescribed in patients with delirium in both medical and surgical units. Antibiotics and antidementia drugs were more frequently prescribed among patients with delirium in medical units, as opposed to insulin, laxatives, diuretics, and antiarrhythmics among those admitted to surgical units (Table 2). ACE inhibitors, ARBs, and statins were less prescribed among medical inpatients with delirium. Comparison of prescriptions only in patients with delirium in medical and surgical units showed that benzodiazepines were more prescribed in surgical compared to medical settings (38.1% vs 24.1%, $P = .013$); moreover, the percentage of patients with delirium not prescribed any antipsychotic drug was higher in medical versus surgical units (33.5% vs 20.6%, $P = .035$).

After adjustment, antibiotics, insulin, and atypical antidepressants were significantly associated with delirium in medical but not surgical units, whereas typical and atypical antipsychotics were associated with delirium in both medical and surgical units (Figure 1). Polypharmacy and delirium were associated in surgical but not medical wards (OR = 2.9; 95% CI, 1.4–6.1). Statins and ARBs were still inversely associated with delirium, but only in medical units (Figure 1).

Stratification for Dementia

Prevalence of delirium in dementia patients was 52.8%. Supplementary Table 1 describes sample characteristics according to both dementia and delirium. In multivariate analysis, a similar association between antibiotics and delirium was observed in patients with and without dementia (data not shown), and a more powerful association between typical and atypical antipsychotics and delirium was found in the stratum without dementia compared to the one with dementia (typical antipsychotics: OR = 4.31; 95% CI, 2.94–6.31 without dementia vs OR = 1.64; 95% CI, 1.19–2.26 with dementia; atypical antipsychotics: OR = 5.32; 95% CI, 3.44–8.22 without dementia vs OR = 1.74; 95% CI, 1.26–2.40 with dementia).

The absence of antipsychotic prescription was inversely associated with delirium in the whole sample and in both medical and surgical units, but only among patients without dementia (Table 3).

DISCUSSION

Polypharmacy is associated with delirium only in patients admitted to surgical units. Antipsychotics—both typical and atypical—atypical antidepressants, insulin, and antibiotics are directly associated whereas statins and ARBs are

Table 2. Drug Prescriptions in Medical and Surgical Wards According to Presence or Absence of Delirium Diagnosis[a]

	Medical Wards			Surgical Wards		
	Delirium			Delirium		
Variable	No	Yes	*P*	No	Yes	*P*
n (%)	2,864 (76.0)	906 (24.0)		300 (82.6)	63 (17.4)	
No. of drugs, median (SD)	5.4 (2.2)	5.5 (2.1)	.095	4.7 (2.3)	6.3 (2.8)	<.001
Polypharmacy (5+ drugs)	1,848 (64.5)	606 (66.9)	.194	146 (48.7)	49 (77.8)	<.001
Drug classes						
Laxatives	681 (23.8)	194 (21.4)	.142	43 (14.3)	16 (25.4)	.030
Antiulcer drugs	2,022 (70.6)	625 (69.0)	.354	215 (71.7)	50 (79.4)	.211
Antiplatelet drugs	1,313 (45.8)	398 (43.9)	.313	125 (41.7)	33 (52.4)	.119
Diuretics	1,504 (52.5)	471 (52.0)	.782	100 (33.3)	31 (49.2)	.017
ACE inhibitors	785 (27.4)	212 (23.4)	.017	88 (29.3)	20 (31.7)	.703
ARBs	381 (13.3)	80 (8.8)	<.001	34 (11.3)	5 (7.9)	.509
β-Blockers	1,106 (38.6)	332 (36.6)	.287	88 (29.3)	20 (31.7)	.703
Calcium channel blockers	535 (18.7)	155 (17.1)	.286	47 (15.7)	12 (19.0)	.508
Antiarrhythmic drugs	346 (12.1)	92 (10.1)	.115	25 (8.3)	12 (19.0)	.011
Statins/lipid-lowering drugs	649 (22.7)	134 (14.8)	<.001	76 (25.3)	12 (19.0)	.290
Oral hypoglycemics	285 (10.0)	71 (7.8)	.058	44 (14.7)	7 (11.1)	.460
Insulin	391 (13.7)	137 (15.1)	.267	17 (5.7)	11 (17.5)	.001
Antibiotics	1,071 (37.4)	433 (47.8)	<.001	108 (36.0)	29 (46.0)	.135
Glucocorticoids	546 (19.1)	154 (17.0)	.163	19 (6.3)	5 (7.9)	.584
Benzodiazepines	687 (24.0)	218 (24.1)	.964	85 (28.3)	24 (38.1)	.124
Typical antipsychotics	151 (5.3)	169 (18.6)	<.001	7 (2.3)	8 (12.7)	<.001
Atypical antipsychotics	131 (4.6)	164 (18.1)	<.001	2 (0.7)	13 (20.6)	<.001
SSRIs	379 (13.2)	112 (12.4)	.497	29 (9.7)	12 (19.0)	.032
SNRIs	54 (1.9)	12 (1.3)	.262	5 (1.7)	3 (4.8)	.146
Atypical antidepressants	169 (5.9)	123 (13.6)	<.001	15 (5.0)	11 (17.5)	<.001
Antiepileptics	177 (6.2)	71 (7.8)	.080	9 (3.0)	5 (7.9)	.076
AChE-I/memantine	42 (1.5)	39 (4.3)	<.001	3 (1.0)	0 (0.0)	1.000

[a]Values shown as n (%) unless otherwise noted.
Abbreviations: ACE = angiotensin-converting enzyme, AChE-I = acetylcholinesterase inhibitor, ARB = angiotensin II receptor blocker, SNRI = serotonin-norepinephrine reuptake inhibitor, SSRI = selective serotonin reuptake inhibitor.

Table 3. Multivariate Logistic Regression Models Testing the Association of No Prescription of Any Antipsychotic and Delirium in Subjects With and Without Dementia[a]

	Whole Sample (n = 4,133)		Medical Wards (n = 3,770)		Surgical Wards (n = 363)	
Dementia Diagnosis	OR	95% CI	OR	95% CI	OR	95% CI
Yes	0.92	0.77–1.11	0.93	0.96–1.23	0.60	0.16–2.24
No	0.54	0.45–0.64	0.54	0.43–0.68	0.13	0.05–0.33

[a]Models were adjusted for age, sex, education, and Charlson Comorbidity Index score.
Abbreviation: OR = odds ratio.

inversely associated with delirium. The association between antipsychotics and delirium varies according to dementia diagnosis, being stronger in patients without dementia.

The main strengths of the study are the high participation rate of Italian wards[40] and the large number of prescriptions evaluated. The main limitation is that drug collection was done on the day of delirium assessment, restraining the interpretation of the cause-effect relationship between drugs and delirium. Thus, future longitudinal studies are needed to disentangle the effect of polypharmacy and especially antipsychotic drugs on delirium onset.

Drugs have been widely associated with the development of delirium, with controversial results.[20,21,26,32,41–43] Polypharmacy often means a high number of drug-drug interactions,[12,44–49] potentially inappropriate drugs,[50–53] and drug duplicates.[54–56] Further, the sum of the anticholinergic load of a number of drugs is often higher than that of specific drugs.[57–59] Anticholinergic effect has been studied as a possible trigger of delirium,[24,35,60–62] but the lack of information regarding single drugs prevented us from testing this hypothesis. Polypharmacy was associated with delirium only in surgical units. One hypothesis for this finding is that elderly individuals with delirium could be overtreated with psychoactive drugs in surgical units, where health care professionals are not trained in geriatric care. This hypothesis is strengthened by the higher prescription of benzodiazepines and the lower number of patients with delirium not treated with any antipsychotic in surgical units compared to medical units.

Typical and atypical antipsychotics, atypical antidepressants, insulin, and antibiotics were associated with delirium. The role of antibiotics has been discussed,[63–68] but the presence of an infection limits the interpretation, as infection per se can trigger delirium. The association between insulin and delirium may be explained by possible hypoglycemic events, which may have triggered delirium. The association between antipsychotics and atypical antidepressants with delirium is not surprising given the cross-sectional study and the high prevalence of delirium in dementia.

ARBs and statins were less prescribed in patients with delirium. The role of statins in preventing delirium has been debated, but clinical trials failed to show a benefit.[69] This

study is the first showing a possible protective effect of ARBs; thus, this finding needs to be replicated.

An interesting result is the inverse association between absence of antipsychotic prescription and delirium in the whole sample and in both medical and surgical units, but only in dementia-free patients. In patients with dementia, the absence of antipsychotic prescription is no longer a protective factor for delirium. This finding may underline the use of antipsychotics in treating other conditions (eg, neuropsychiatric symptoms in depression) and that the association between dementia and delirium is present even in the absence of antipsychotic prescription.

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Supplementary Material

Article Title: Drug Prescription and Delirium in Older Inpatients: Results From the Nationwide Multicenter Italian Delirium Day 2015–2016

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List of Supplementary Material for the article

1. Appendix 1 Complete list of authors and members of the Italian Study Group on Delirium (ISGoD)
2. Table 1 Drug prescriptions according to delirium diagnosis after stratification for dementia

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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.

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Supplementary Table 1. Drug prescriptions according to delirium diagnosis after stratification for dementia.

	Patients without dementia diagnosis N= 3062			**Patients with dementia diagnosis N=1071**		
	Delirium			**Delirium**		
	No	**Yes**		**No**	**Yes**	
	N 2659 (87%)	**N 403 (13%)**	**p**	**N 505 (47%)**	**N 566 (53%)**	**p**
Drugs categories						
Laxatives, n (%)	573 (22)	85 (21)	0,835	151 (30)	125 (22)	0,004
Antiulcer drugs, n (%)	1891 (71)	284 (70)	0,790	346 (69)	391 (69)	0,842
Antiplatelet drugs, n (%)	1188 (45)	180 (45)	0,996	250 (50)	251 (44)	0,091
Diuretics, n (%)	1358 (51)	219 (54)	0,221	246 (49)	283 (50)	0,674
ACE inhibitors, n (%)	768 (29)	111 (28)	0,580	105 (21)	121 (21)	0,815
ARBs, n (%)	359 (14)	39 (10)	0,033	56 (11)	46 (8)	0,099
Beta blockers, n (%)	1036 (39)	159 (39)	0,850	158 (31)	193 (34)	0,328
Calcium channel blockers, n (%)	482 (18)	64 (16)	0,272	100 (20)	103 (18)	0,504
Antiarrhythmic drugs, n (%)	328 (12)	54 (13)	0,547	43 (9)	50 (9)	0,853
Statins/lipid lowering drugs, n (%)	636 (24)	82 (20)	0,115	89 (18)	64 (11)	0,003
Oral hypoglycemics, n (%)	284 (11)	37 (9)	0,360	45 (9)	41 (7)	0,316
Insulin, n (%)	354 (13)	75 (19)	0,004	54 (11)	73 (13)	0,265
Anti-osteoporotic drugs, n (%)	289 (11)	37 (9)	0,306	64 (13)	47 (8)	0,019
Antibiotics, n (%)	993 (37)	185 (46)	0,001	186 (37)	277 (49)	<0,001
Glucocorticoids, n (%)	502 (19)	81 (20)	0,561	63 (12)	78 (14)	0,528
Benzodiazepines, n (%)	643 (24)	109 (27)	0,213	129 (26)	133 (23)	0,437
Typical antipsychotics, n (%)	81 (3)	51 (13)	<0,001	77 (15)	126 (22)	0,003
Atypical antipsychotics, n (%)	56 (2)	39 (10)	<0,001	77 (15)	138 (24)	<0,001
SSRIs, n (%)	302 (11)	40 (10)	0,395	106 (21)	84 (15)	0,009
SNRIs, n (%)	40 (2)	10 (2)	0,149	19 (4)	5 (1)	0,001
Atypical antidepressants, n (%)	113 (4)	29 (7)	0,009	71 (14)	105 (19)	0,048
Antiepileptics, n (%)	141 (5)	36 (9)	0,004	45 (9)	40 (7)	0,265
No prescription of any antipsychotic, n (%)	1557 (59)	168 (42)	<0,001	139 (28)	149 (26)	0,658