



ORDINE DEI MEDICI CHIRURGHI E DEGLI ODONTOIATRI DELLA PROVINCIA DI PARMA



Farmaci ed urgenze mediche.

Gianfranco Cervellin

Ex...

Cardiovascular Risk of Nonsteroidal Anti-Inflammatory Drugs: An Under-Recognized Public Health Issue

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ORIGINAL INVESTIGATION

Consumption of NSAIDs and the Development of Congestive Heart Failure in Elderly Patients

An Underrecognized Public Health Problem

John Page, MBBS(Hons); David Henry, MBChB

Archives of Internal Medicine, 2000

FANS come causa scatenante di HF

- **Inibizione prostaglandine renali → rischio di scatenamento HF massimo in pazienti già trattati con diuretici.**
- **L'uso di FANS (escluso ASA a basso dosaggio) nella settimana precedente è associato ad un rischio doppio di ricovero ospedaliero per scompenso cardiaco.**
- **Il carico di morbidità associato alla scompenso cardiaco FANS-correlato eccede quello risultante dalle lesioni gastrointestinali.**
- **I FANS devono essere usati con la massima cautela nei pazienti con storia di malattia cardiovascolare.**



Drug-Related Orthostatic Hypotension: Beyond Anti-Hypertensive Medications

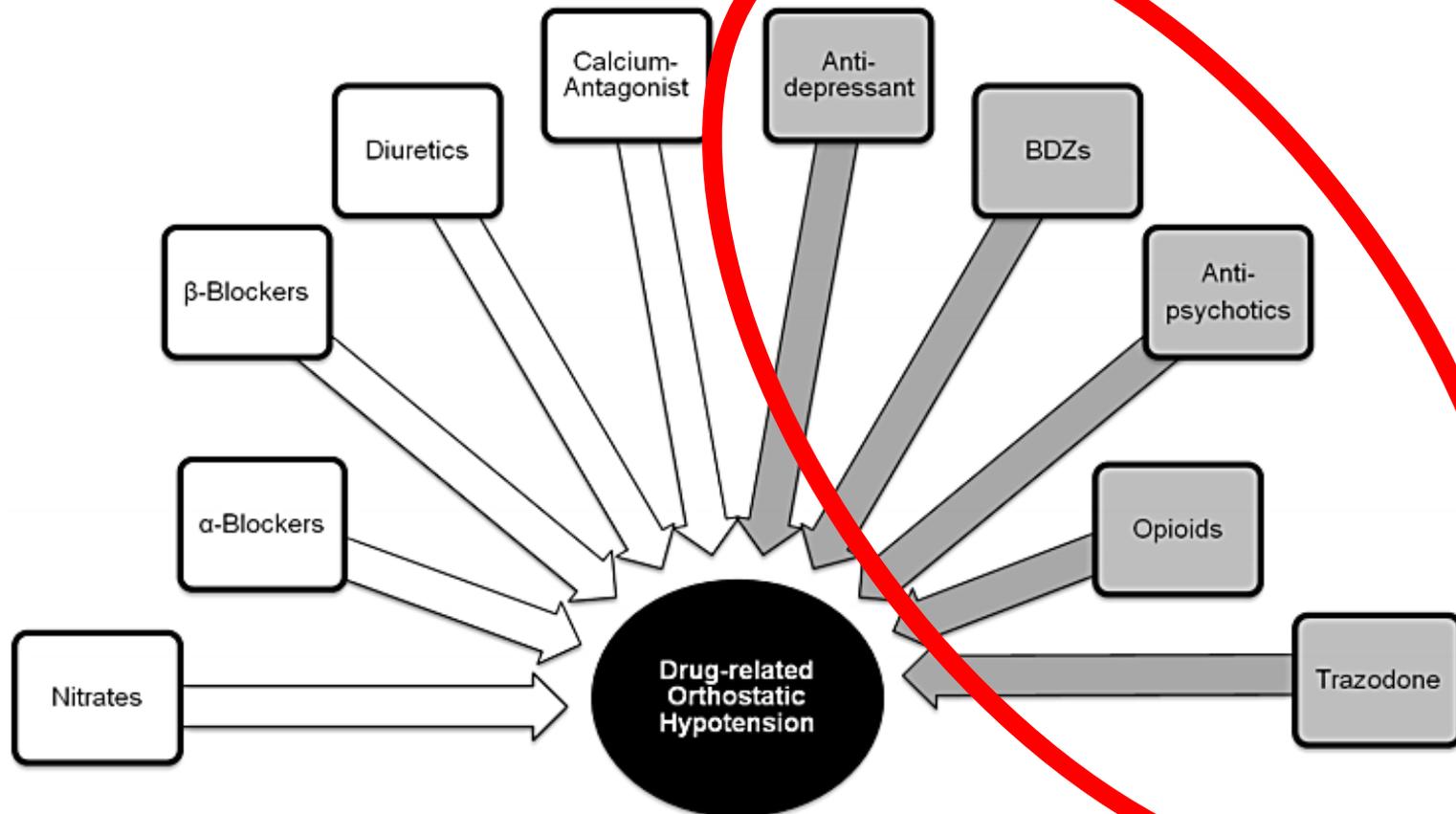
Giulia Rivasi¹ · Martina Rafanelli¹ · Enrico Mossello¹ · Michele Brignole² · Andrea Ungar¹

- **With standing, the force of gravity rapidly displaces approximately 10% of the circulating blood volume (300–800 mL) to the lower body, particularly to the lower extremities and splanchnic venous capacitance vessels. As a consequence, venous return and cardiac output are reduced and an ensemble of compensatory responses is activated to prevent a BP fall.**
- **Increase in sympathetic outflow and a decrease in vagal nerve activity, leading to an increase in peripheral vascular resistance, heart rate, and cardiac contractility aimed to preserve organ perfusion. Additionally, contractions of lower body muscles (the so-called ‘muscle pump’) prevent excessive blood pooling in venous vessels and favor venous return to the heart.**
- **OH derives from a failure of the aforementioned compensatory responses, which determines a fall in cardiac output and/or inadequate vasoconstriction.**



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- **Diuretics** are considered to be one of the main determinants of drug-related OH.
- Significant association with OH (**OR 10.44 for loop diuretics**; OR 1.25 for thiazide diuretics)
- **Loop diuretics should be avoided as treatment of hypertension** in frailer and older patients, unless specifically indicated (e.g., glomerular filtration rate < 30 mL/min)



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- **α -Receptor blockers** are a known risk factor for OH, which mainly derives from reduced vascular resistance
- **Three different α 1-adrenergic receptors** subtypes exist, classified as α 1A, α 1B, and α 1D. α 1B-receptors are located in the vessels, and α 1D receptors are located in the detrusor muscle, in the spinal cord, and in afferent nerves originating in the bladder.
- **Silodosin and tamsulosin has the highest selectivity** for urinary α -adrenergic receptors with α 1A affinity > α 1D > α 1B
- Their hypotensive effect may be potentiated by the concomitant administration of phosphodiesterase type 5 inhibitors
- Given all of the above, **α -blockers should be avoided as a treatment for high BP in older hypertensive subjects**, as the European guidelines on hypertension recommend



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- Data on **calcium channel blockers** as a risk factor for OH are **conflicting**.
- **Dihydropyridine calcium channel blockers** frequently induce a compensatory heart rate increase, which may counteract a BP fall after standing, thus suggesting a potential explanation for their neutral/protective effect.
- Conversely, **non-dihydropyridine calcium channel blockers** have negative chronotropic and inotropic effects, which probably interfere with compensatory cardiac responses to standing



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- The chronic use of **ACE inhibitors** (ACE-I) and angiotensin II receptor blockers does not seem to be associated with OH



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- OH is the most common cardiovascular adverse effect of **tricyclic antidepressants** (TCA), occurring in 10–50% of treated patients (→ higher for amitriptyline and clomipramine)
- **Serotonin-selective reuptake inhibitors (SSRI)** are reported to cause OH **less frequently** than TCA
- It is well known that serotonin-norepinephrine reuptake inhibitors (SNRI) may induce BP and heart rate increase. Nevertheless, a strong association between SNRI and OH has been described in a sample of older adults at high risk of falling



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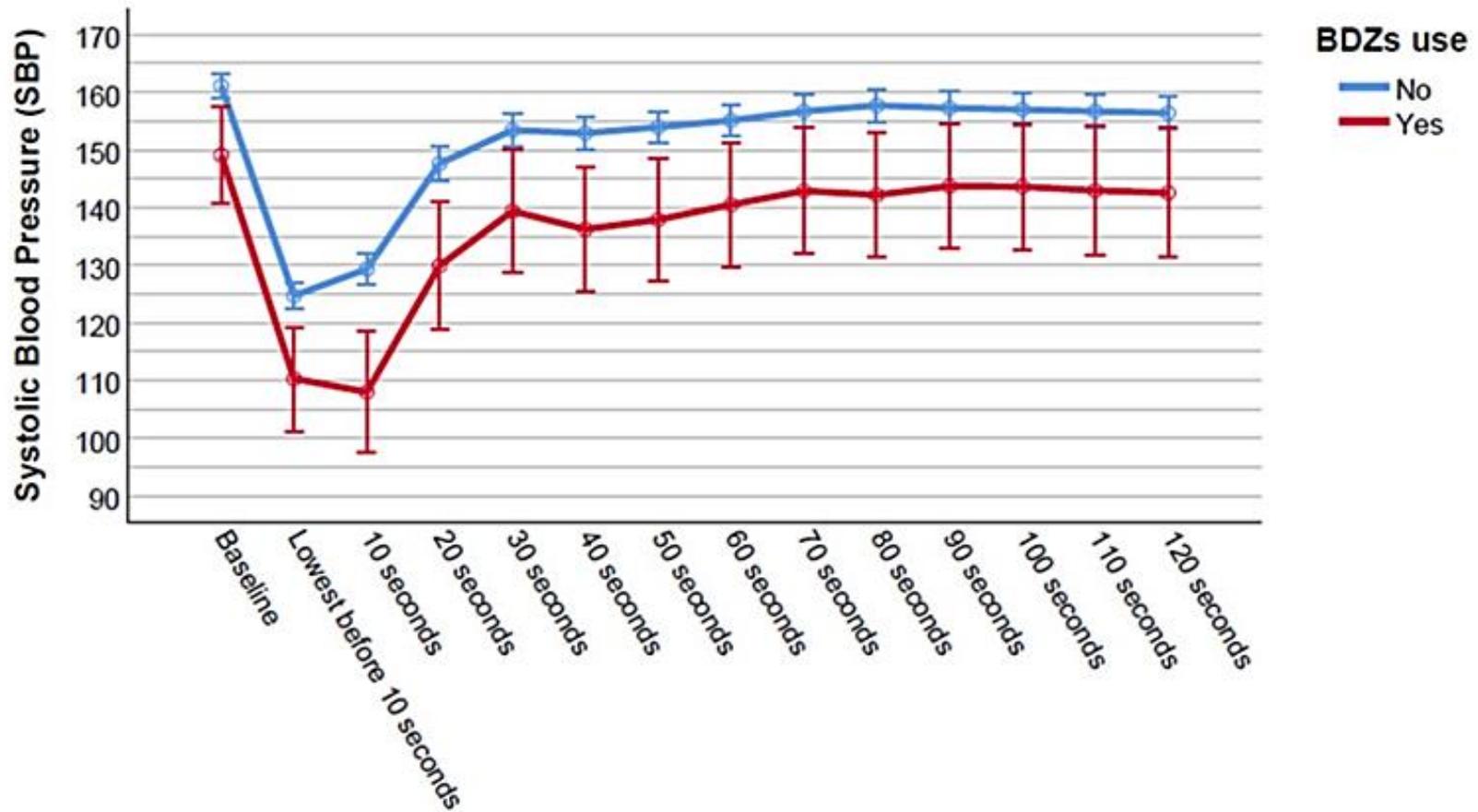
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- OH develops in up to 40% of patients taking **antipsychotics**, with a higher incidence at advanced age.
- **Clozapine and quetiapine show the highest risk**, with an OH incidence of 24% and 27%, respectively; a similar incidence is reported for **chlorpromazine**. Conversely, OH risk is lowest for haloperidol and olanzapine
- **→ QTc only???**



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Drug-Related Orthostatic Hypotension: Beyond Anti-Hypertensive Medications

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- **Dopaminergic drugs** may cause OH through the activation of dopamine receptors, leading to cutaneous, mesenteric, and renal vasodilation. Therefore, levodopa significantly contributes to OH associated with Parkinson disease, irrespective of the presence of autonomic dysfunction.
- **Memantine**, was found to be significantly associated with OH in geriatric ward patients

Do Emergency Physicians Attribute Drug-Related Emergency Department Visits to Medication-Related Problems?

Ann Emerg Med. 2010;55:493-502

- **A significant proportion of drug-related visits are not deemed medication related by emergency physicians.**
- **Drug-related visits not attributed to medication-related problems by emergency physicians may be missed in ongoing outpatient adverse drug event surveillance programs.**

ADVERSE DRUG EVENT NONRECOGNITION IN EMERGENCY DEPARTMENTS: AN EXPLORATORY STUDY ON FACTORS RELATED TO PATIENTS AND DRUGS

Lucien Roulet, PHARM.D, PH.D,^{*†} Françoise Ballereau, PHARM.D, PH.D,^{†‡} Jean-Benoît Hardouin, PH.D,^{§||}
Anne Chiffolleau, MD,[¶] Gilles Potel, MD, PH.D,^{*†} and Nathalie Asseray, MD, PH.D^{†#}

J Emerg Med 2014;46:857–864

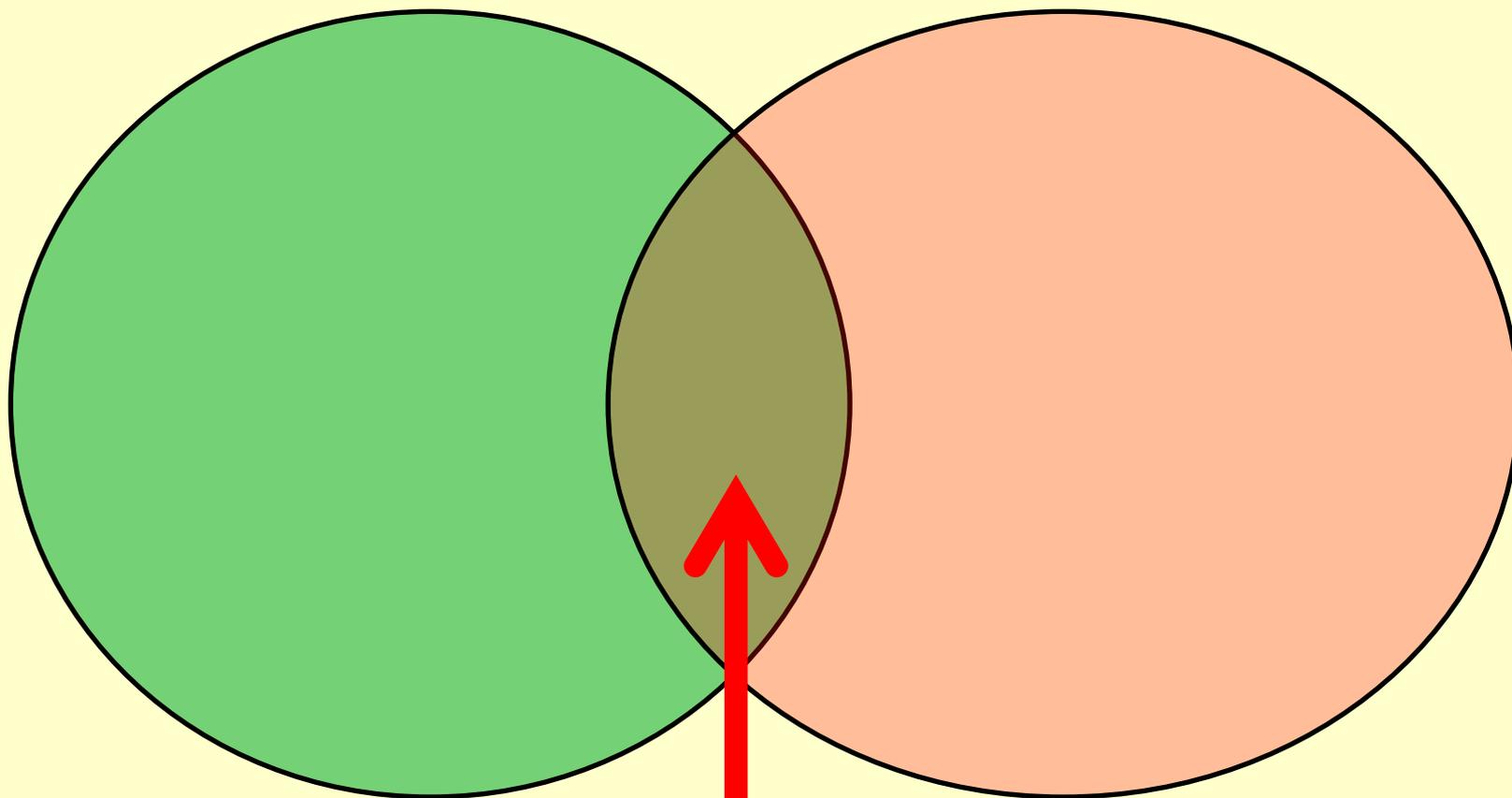
- **19.4%** of patients experienced an ADE at ED visit.
- Emergency physicians correctly recognized **40.0%** of these cases.
- Our results emphasize the importance of searching for ADEs in patients with daily polypharmacy or whose chief complaint does not seem to be drug related.

- **Diakonhjemmet Hospital, Oslo, anni 2017-2018. Tutti gli accessi al PS.**
- **Farmacista clinico in PS ore 9-22 → identificati tutti i pazienti per i quali era disponibile una storia farmacologica.**
- **Età mediana 67 anni (range 19-96), femmine 49%.**
- **19.7%** degli accessi risultava correlato a farmaci (2.5% degli accessi non classificabile).
- **Di questi: 71% reazione avverse, 16% mancata aderenza alla terapia; 8% errori di dosaggio.**
- **Farmaci antitrombotici il gruppo più rappresentato, seguiti da FANS, farmaci del RAS...**

**Nymoén LD, Björk M, Flatebø TE, et al. Drug-related emergency department visits. Prevalence and risk factors.
Intern Emerg Med, 2021. In Press**

Cadute

Sincopi



Percentuale sconosciuta

Caduta/sincope

Nel 40 - 60% dei casi le cadute avvengono in assenza di testimoni

- **Seconda causa di morte traumatica accidentale, preceduta solo dagli incidenti stradali.**
- **Anche quando non letali, le cadute sono associate con effetti negativi sulla salute, essendo causa del 20-30% di tutti i traumi moderati-severi, dalle lesioni dei tessuti molli alle fratture.**

A multicenter retrospective study on falls in elderly population. Epidemiology and impact on hospital workload in two Emergency Departments of Northern Italy

Gianfranco Cervellin,¹ Francesca Montali,²
Giovanna Campaniello,² Mario Benatti,¹
Roberto Fiorini,³ Gianni Rastelli³

- A total number of **129,898 ED visits** was recorded during 2013, of whom 92,981 in the University Hospital, and 37,007 in the Community Hospital.
- Males accounted for 52.1% and females for 47.9% of the whole sample.
- During the same study period, **3720 ED visits were related to domestic falls in patients aged ≥ 65 years (i.e., 2.9% of the total visits).**

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A total number of 963 (i.e., 25.9%) of patients needed to be hospitalized:

- 605 in Orthopaedic ward
- 342 in Medical wards (including Geriatrics, Cardiology, and Neurology)
- 10 in the Neurosurgical unit
- 2 in the Maxillo-facial Surgery
- 2 in the Thoracic Surgery
- 2 in the Intensive Care Unit

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Conclusions:

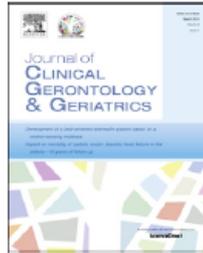
- **Falls represent an important cause of morbidity in the elderly population, representing up to **2.9%** of the whole ED workload, and up to 13.3% of the visits for patients aged ≥ 65 .**
- **The hospital workload induced by falls is globally impressive, roughly corresponding to the whole activity of a medical or orthopaedic ward, in terms of number of admitted patients per year.**



Contents lists available at [ScienceDirect](#)

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Original article

Impact of different drug classes on clinical severity of falls in an elderly population: Epidemiological survey in a trauma center

Francesca Montali, PhD ^a, Giovanna Campaniello, MD ^a, Mario Benatti, MD ^b,
Gianni Rastelli, MD ^c, Mario Pedrazzoni, MD ^d, Gianfranco Cervellin, MD ^{b,*}

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Original article

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^d Department of Internal Medicine, University of Parma, Parma, Italy

- A total of 93,029 ED visits were recorded during the year 2013.
- During the study period, **2533 visits were related to trivial falls** in 2377 patients aged 65 years or older (i.e., 2.7% of the total visits), occurring at home or in nursing home.
- During the same period, 2229 patients (87.4%) visited the ED for a fall only once, whereas 139 patients visited two times (5.5%), eight patients three times (0.3%), and one patient four times.
- Accordingly, the ED recorded 2533 visits for 2377 patients.
- For **1280 cases**, a thorough drug therapy history was available.

~50%



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- **A total number of 756 (i.e., 28.1%) patients needed hospitalization.**
- **Eight patients (1.1%) fell once more during the hospital stay.**



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Impact of different drug classes on clinical severity of falls in an elderly population: Epidemiological survey in a trauma center

Francesca Montali, PhD ^a, Giovanna Campaniello, MD ^a, Mario Benatti, MD ^b, Gianni Rastelli, MD ^c, Mario Pedrazzoni, MD ^d, Gianfranco Cervellin, MD ^{b,*}^a Clinical Governance, Risk Management, Quality and Accreditation Unit, Academic Hospital of Parma, Parma, Italy^b Emergency Department, Academic Hospital of Parma, Parma, Italy^c Emergency Department, Hospital of Vaio, Fidenza, Italy^d Department of Internal Medicine, University of Parma, Parma, Italy**Table 4**
Relation between drugs use and hospital admission.

Drugs use, N (%)	Outcome: Hospital admissions				
		Falls leading to hospital admission (n = 712)	Falls not leading to hospital admission (n = 1821)	p	Adjusted OR
		N (%)	N (%)		
Anticoagulants	Yes	116 (16.3)	191 (10.5)	0.001	1.592
	No	596 (83.7)	1630 (89.5)		
Antiplatelets drugs	Yes	178 (25.0)	335 (18.4)	0.004	1.411
	No	534 (75.0)	1486 (81.6)		
Narcotic analgesics	Yes	21 (2.9)	19 (1.0)	0.010	2.379
	No	691 (97.1)	1802 (99)		

CI = confidence interval; OR = odds ratio.



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Relation between drugs use and traumatic brain injuries.

Outcome: Traumatic brain injuries

Drugs, N (%)		Brain injury (n = 453)		Other (n = 2080)		p	Adjusted OR
		N		N			
Antiplatelets drugs	Yes	143	(31.6)	370	(17.8)	0.000	1.941
	No	310	(68.4)	1710	(82.2)		
Anticoagulants	Yes	76	(16.8)	231	(11.1)	0.000	1.794
	No	377	(83.2)	1849	(88.9)		
Antihypertensive	Yes	147	(32.5)	423	(20.3)	0.011	1.453
	No	306	(67.5)	1657	(79.7)		
Psychotropic drugs	Yes	81	(17.9)	226	(10.9)	0.041	1.404
	No	372	(82.1)	1854	(89.1)		

CI = confidence interval; OR = odds ratio.

Lo riconosciamo poco...

**...e spesso lo
causiamo/peggioriamo noi**

Identifying frequent drug combinations associated with **delirium** in older adults: application of association rules method to a case-time-control design

Pharmacoepid Drug Safety, 2021, in press

- **28503** individuals (mean age 84.1 years) from 2005 to 2015 with delirium
- Identified frequently used drug combinations associated with delirium.
- Examples include combined exposures to quetiapine and furosemide (OR=6.17), haloperidol (OR=4.81), combined exposures to furosemide, omeprazole and lorazepam (OR=3.94), and fentanyl (OR=3.46).

