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Depression is often under-recognized in older patients, even if antidepressants (AD) are commonly prescribed, with a prevalence of use that increase with ageing [1]. Nevertheless, even if a diagnosis of depression is established, inappropriate treatment can occur [2]. Beers criteria are the most widely screening tools used to detect inappropriate prescription of drugs in people aged 65 years or more [3]. Since 2010, attempts to adapt the Beers' criteria have been made in Europe [4,5]. Tricyclic drugs are the ADs to be always avoided in the elderly, owing to their anticholinergic side effects, such as cognitive impairment, delirium, urinary retention and falls [3]. Selective serotonin reuptake inhibitors (SSRIs) should be used with caution because they can cause or exacerbate hyponatraemia [3]. To our knowledge no studies have been conducted on recent data collected in hospitalized older patients in order to assess the appropriateness of prescription of ADs. With this background, the objectives of this study were to investigate the prevalence of AD use and prescription appropriateness, according to the above-cited criteria, in a large cohort of older patients hospitalized in Italian internal medicine and geriatric wards from 2010 to 2017.Data were obtained from the register REgistro POliterapie –Società Italiana Medicina Interna (REPOSI), an ongoing collaboration between the Italian Society of Internal Medicine (SIMI), IRCCS Fondazione Ca` Granda Ospedale Maggiore Policlinico and the Istituto di Ricerche Farmacologiche Mario Negri IRCCS. The REPOSI is a multicenter register in order to collect clinical and therapeutic information on patients aged 65 or older acutely admitted to >100 internal medicine and geriatric wards in Italy. More details are available elsewhere [6]. For this analysis, we included all patients enrolled in REPOSI from 2010 to 2017 and prescribed with at least one antidepressant. Prescription appropriateness was assessed according to the American Geriatrics Society Beers Criteria (version 2015) and to the criteria developed in Europe [4,5]. We divided antidepressants in groups and considered them inappropriately prescribed, because 1) they should be always avoided in older people (e.g. TCA, paroxetine in 2017, fluoxetine from 2014), 2) prescribed to patients with a Glomerular Filtration Rate (GFR) < 30 ml/min (duloxetine), 3) prescribed to patients with a history of falls, 4) co-prescribed with at least other two additional drugs active on the central nervous system (CNS). Furthermore, for the first 3 mostly prescribed SSRIs (sertraline, paroxetine, escitalopram) we also assessed the most clinically relevant potential drug-drug interactions (DDIs) with antithrombotic agents, nonsteroidal anti-inflammatory drugs,fluorochinolone and macrolide antibiotics and amiodarone.

All in all, 4681 were eligible for the analysis. At hospital discharge, 616 patients (13.2%, 95% CI: 12.2%–14.2%) were prescribed antidepressants, 39 taking two of them and 2 even three. These were mostly females (64.8%), aged 75 years or more (75%), living in Northern Italy (67.4%), living with family members (59.4%), taking several concomitant drugs (79.1%), and being affected by depression (N = 187, 30.4%), cerebrovascular diseases (N = 169,27.4%) and delirium (N = 143,23.2%). In the face of a decreasing trend of SSRIs from 64.9% in 2010 to 52.9% in 2017, other antidepressants (SNRI) increased from 30.4% to 43.4%. The most prescribed class of AD was that of SSRI (n = 361), followed by other ADs (i.e. SNRIs; n = 210) and then TCA (n = 33). The most prescribed AD (alone or in combination) was sertraline (N = 139, 22.6%), followed by trazodone (N = 130, 21.1%), paroxetine (N = 89, 14.5%) and escitalopram (N = 65, 10.5%). Table 1 shows the profiles of prescription inappropriateness in AD users. At hospital discharge, 158 patients (26.9%, 95% CI: 22.4%–29.2%) were inappropriately prescribed: 39.9% of them (N = 63) prescribed with AD in combination with other CNS - active drugs, 31.6% (n = 50) with AD always to be avoided in the elderly and 25.3% (n = 40) with a history of falls. Among patients prescribed with sertraline, alone or in combination, 103 (/139,74.1%) had at least a potential DDI: the antithrombotic agents were the most co-prescribed drugs at risk of DDI (N = 96), followed by antibiotics (N = 15). The same pattern of potential DDI risk was found for paroxetine (N = 66/89,74.2% patients with at least one DDI) and escitalopram (N = 51/65, 78.5%).

At hospital admission, 564 patients (12.0%, 95% CI: 11.1%–13.0%) were prescribed with ADs, being 140 patients (24.8%, 95% CI: 21.4%–28.6%) inappropriately prescribed (Table 1). Also at admission the majority of patients (N = 52, 37.1%) were inappropriately co-prescribed with at least two other CNS drugs, but in this instance there were more patients prescribed with AD always to be avoided in the elderly. Among 564 patients prescribed ADs at hospital admission, 88 (15.6%, 95% CI: 12.8%–18.8%) stopped them at discharge, while 140/4117 patients (3.4%, 95%CI: 2.9%–4.0%) were first prescribed at discharge. Of the latter, 26 (18.6%) were inappropriately prescribed. Among 476 patients prescribed both at admission and discharge, 104/121 (85.9%, 95%CI: 78.6% - 91.0%) continued to be inappropriately prescribed and 327/355 (92.1%, 95% CI: 88.8% - 94.5%) were still appropriately prescribed from admission to discharge. In conclusion, this study shows an overall appropriate use of ADs in acutely hospitalized older people in internal medicine and geriatric wards from 2010 to 2017, but still some critical aspects were highlighted: an increasing number of patients prescribed ADs despite their history of falls, the frequent combinations between ADs and

drugs acting on CNS and the concomitant use of other drugs that can cause potential drug-drug interactions. The hospital setting should represent an important opportunity to improve the quality of drug prescription for frail, multimorbid and polytreated older patients. In our previous studies we pointed out that hospitalization did fail in this goal [[7], [8], [9], [10]]. With reference to ADs, even if the overall use was often mainly appropriate, physicians should improve their knowledge on the risks related to potential DDI and on the concomitant use of drugs that may increase the risk of falls in the elderly, in order to avoid harmful adverse events for patients and unnecessary direct and indirect costs for National Health Service.The authors declare that they have no conflicts of interest.

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Table 1. Patients inappropriately prescribed with antidepressants.

	Hospital discharge		Hospital admission	
	Antidepressant users	**N (%)**	**Antidepressant users**	**N (%)**
		616		564
Not appropriate		158 (26.9)		140 (24.8)
Always		*50 (31.6)*		*52 (37.1)*
Amitriptyline	24		25	
Amoxapine	0		0	
Clomipramine	4		4	
Desipramine	0		0	
Doxepin > 6 mg/d	0		0	
Imipramine	1		2	
Nortriptyline	2		2	
Protriptyline	0		0	
Trimipramine	0		0	
Paroxetine*	15		13	
Fluoxetine#	4		3	
Tranylcypromine	0		0	
Amitriptyline and psycholeptics	0		3	
Fluoxetine and psycholeptics	0		0	
If GFR < 30 ml/min		*5 (3.2)*		*4 (2.9)*
Duloxetine	5		4	
If co-prescribed with ≥ 2 CNS active-drugs*		*63 (39.9)*		*52 (37.1)*
If there are previous falls and fractures		40 (25.3)		32 (22.9)
NOT ASSESSABLE		1		1

Legend: CNS = Central Nervous System. International Classification of Diseases, 9th Revision. ICD-9 codes considered for falls/ fractures/prosthesis: V15.88, V43.6, 800–829.* We considered it inappropriately prescribed only in REPOSI 2017 since it has been included in the Beers 2015 version. # We considered it inappropriately prescribed from REPOSI 2014. **Antipsychotics (Anatomical Therapeutic Chemical classification system -ATC: N05A), benzodiazepines, nonbenzodiazepine, benzodiazepine receptor agonist hypnotics (ATC: N05B and N05C), tricyclic antidepressants (ATC: N06AA), selective serotonin reuptake inhibitors (SSRIs) (ATC: N06AB), others antidepressants (ATC: N06AX) and opiods (ATC: N02A).