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The stigma of low opioid prescription in the hospitalized multimorbid elderly in Italy

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Abstract The primary aim of this study was to evaluate the prevalence of opioid prescriptions in hospitalized geriatric patients. Other aims were to evaluate factors associated with opioid prescription, and whether or not there was consistency between the presence of pain and prescription. Opioid prescriptions were gathered from the REgistro POLiterapie Societa' Italiana di Medicina Interna (REPOSI) data for the years 2008, 2010 and 2012. 1,380 in-patients, 65+ years old, were enrolled in the first registry run, 1,332 in the second and 1,340 in the third. The prevalence of opioid prescription was calculated at hospital admission and discharge. In the third run of the registry, the degree of pain was assessed by means of a numerical scale. The prevalence of patients prescribed with opioids at admission was 3.8 % in the first run, 3.6 % in the second and 4.1 % in the third, whereas at discharge rates were slightly higher (5.8, 5.3, and 6.6 %). The most frequently prescribed agents were mild opioids such as codeine and

tramadol. The number of total prescribed drugs was positively associated with opioid prescription in the three runs; in the third, dementia and a better functional status were inversely associated with opioid prescription. Finally, as many as 58 % of patients with significant pain at discharge were prescribed no analgesic at all. The conservative attitude of Italian physicians to prescribe opioids in elderly patients changed very little between hospital admission and discharge through a period of 5 years. Reasons for such a low opioid prescription should be sought in physicians' and patients' concerns and prejudices.

Keywords Older persons · Pain · Analgesic opioids

Introduction

Older adults make up a large portion of the population with chronic persistent pain, that often interferes with health status perception, quality of life, cognition and functional abilities of the elderly [1, 2]. Other recurring consequences of chronic pain in seniors are depression, anxiety, malnu-

REPOSI denotes the REgistro POLiterapie SIMI, Società Italiana di Medicina Interna. The participating units and co-authors are listed in the Appendix.

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trition and sleep disorders [3, 4]. In comparison with younger adults, the elderly patient is usually affected by a higher prevalence of cancer-related and non-cancer-related pain [5]. Nevertheless, the likelihood of receiving analgesic medications is negatively related to age [6], so that among people 85 years old or more, one of three receives no treatment for pain control, and in only 10 % of them is an opioid prescribed [6].

Opioids are the most powerful painkillers. Their use is appropriate for the treatment of moderate-to-severe chronic pain (5–10 point pain intensity) with the goal to control this symptom and to improve functions and quality of life [7]. The main challenges of opioid prescription in the elderly are to choose the most appropriate molecule in relation to the patients' clinical conditions, to find the minimum effective dose able to relieve pain, but also to monitor and manage any drug-related adverse events. On the other hand, pain alleviation is even more challenging in the elderly if compounds other than opioids are used, such as non-steroidal anti-inflammatory drugs, owing to their unfavorable side effect profile, mainly the onset of renal failure and thrombosis risk. Indeed, the American Geriatrics Society suggests avoiding the use of these drugs, and prefers opioids in old patients with moderate-to-severe chronic pain [8]. Italy is one of the European countries with the lowest per capita opioid expenditure, [9] but ranks first in Europe for the prescription of non-steroidal anti-inflammatory drugs [10].

With this background, our primary goal was to evaluate the prevalence and type of analgesic and opioid prescriptions at hospital admission and discharge in elderly patients through the use of data from three runs (2008, 2010, 2012) of the REgistro POLiterapie Societa' Italiana di Medicina Interna (REPOSI) registry. Additional aims were the evaluation of factors associated with opioid prescription, and the relationship between presence of pain and analgesic prescription at hospital discharge.

Methods

Data collection

The REPOSI registry is a collaborative and independent joint effort of the Italian Society of Internal Medicine (SIMI, Società Italiana di Medicina Interna), the Mario Negri Institute of Pharmacological Research and the IRCCS Ca' Granda Maggiore Policlinico Hospital Foundation. The design of REPOSI was previously described [11]. Briefly, this registry was designed to create a network of internal medicine and geriatric wards to evaluate several features of elderly patients affected by multiple diseases and prescribed with multiple medications. The

main aims of REPOSI were to describe prevalence of concurrent diseases and multiple treatments in the hospitalized elderly, to correlate clinical characteristics of these patients with type and number of diseases and treatments, to evaluate the main clinical outcomes at hospital discharge and compare drug prescription at admission, discharge and follow-up.

All the patients consecutively recruited were 65 years old or older. Participation was voluntary and an informed consent was signed. The registry enrolled patients consecutively admitted to the participating hospital wards (36 in 2008, 66 in 2010 and 70 in 2012) during a period of 4 weeks, 3 months apart from each other (in February, June, September and December 2008, 2010, and 2012). A standardized web-based case report form was filled-in by the attending physicians, including socio-demographic factors, clinical parameters, diagnoses and medications prescribed at hospital admission and discharge, plus clinical events occurring during hospitalization. Each wave of the REPOSI was slightly different according to the minimum data set. This was decided to improve the quality and increase the quantity of the data. In particular, during the first wave in 2008, data on functional and cognitive status were not collected. All the data collected and recorded were checked by a central monitoring institution (the Mario Negri Institute for Pharmacological Research, Milan) for consistency and accuracy (with contacts of the peripheral clinical centers if needed).

The study was approved by the ethics committee of the IRCCS Ca' Granda Maggiore Policlinico Hospital Foundation, Milan.

Assessment of drug prescriptions

All the drugs taken at the time of hospital admission, and those prescribed at discharge were recorded and encoded according to the Anatomical Therapeutic Chemical (ATC) classification system [12]. In each run of the registry, the physicians filling medication prescriptions were required to report the indication for each prescription (e.g., 'tramadol'='treatment of pain in metastatic cancer'; or 'citalopram'='treatment of depression', etc.). Prevalence of opioids prescribed at admission was calculated on the total number of patients, whereas patients who died or were transferred to another hospital ward during hospitalization were excluded from prevalence calculation at hospital discharge. Polypharmacy was described as the concomitant prescription of five or more drugs [13].

Assessment of disease diagnosis

Diseases examined in this study were collected at hospital discharge on the basis of clinical examination, medical

history and laboratory and instrumental data. The International Classification of Diseases, Ninth Revision (ICD-9) was used to classify the diseases [14].

Assessment of pain intensity

Pain intensity was specifically assessed only in the third run of the registry (2012), because collection of this information was not foreseen in the data set for the first two runs (2008, 2010). Pain intensity was measured by means of 0 (no pain) to 10 point (the worst pain one can imagine) numeric rating scale (NRS). This measure was obtained both at the time of hospital admission and at discharge.

Assessment of cognitive and functional status

The data on the cognitive and functional status were obtained only in the second and third runs of the registry. The short blessed test (SBT) was performed within 2 days of hospital admission. SBT is a 6-item orientation–memory–concentration test validated as a measure of cognitive impairment [15]. The final score varies from 0 to 28; an increasing score indicates worse cognitive status. The Barthel Index, used to assess performance in basic activities of daily living [16], considers 10 basic functions and yields a score of 0–100, a higher score being associated with a greater likelihood of being able to live at home with a good degree of independence following hospital discharge.

Statistical analysis

Socio-demographic and clinical characteristics of the case material, as well as the prevalence of opioid prescription for analgesia were described using univariate analysis (mean or percentage). Logistic regression models were employed to evaluate factors associated with opioid prescription at hospital discharge in the three REPOSI runs. Independent variables were age (years), gender and total number of drugs prescribed in the three runs, plus diagnosis of dementia, severe constipation and functional status as measured with the Barthel Index in the last two runs. All the statistical calculations were performed with the software STATA 12th version (College Station, Texas, US).

Results

1,332 patients aged more than 65 years were enrolled in the 2008, 1,380 in 2010 and 1,340 in 2012. Socio-demographic characteristics of the three samples were similar (Table 1); the mean age was 79.3 years (SD = 7.5) in the first, 78.9 (SD = 7.3) in the second and 79.3 (SD = 7.4) in the third. Males and females were almost equally distributed. The

Table 1 Characteristics of the three REPOSI samples (2008, 2010, 2012)

	Sample 2008 (N = 1,332)	Sample 2010 (N = 1,380)	Sample 2012 (N = 1,340)
Age, years, mean (SD)	79.3 (7.5)	78.9 (7.3)	79.3 (7.4)
65–74 years	356 (26.7)	387 (28.0)	351 (26.4)
75–84 years	606 (45.5)	644 (46.7)	583 (43.8)
≥85 years	370 (27.8)	349 (25.3)	396 (29.8)
Male, number (%)	610 (45.8)	681 (49.3)	657 (49.1)
Education, years, mean (SD)	6.3 (3.7)	7.1 (4.0)	6.4 (4.3)
Length of hospital stay, days, median (range)	9 (6–14)	9 (6–14)	9 (6–14)
Total drugs at admission, mean (SD)	4.9 (2.8)	5.3 (2.8)	5.4 (3.2)
Total drugs at discharge, mean (SD)	6.0 (2.9)	6.3 (2.8)	6.4 (3.1)
Opioids at admission, number (%)	50 (3.8)	49 (3.6)	55 (4.1)
Opioids at discharge, number (%)	67 (5.8)	63 (5.3)	77 (6.6)
Short blessed test, mean (SD)	–	9.9 (8.1)	9.1 (7.8)
Barthel index, mean (SD)	–	76.8 (30.7)	72.6 (32.5)
Dementia diagnosis, number (%)	122 (9.2)	90 (6.5)	116 (8.7)
Severe constipation, number (%)	34 (2.6)	20 (1.4)	9 (0.7)
Discharged, number (%)	1,155 (86.7)	1,178 (87.4)	1,166 (88.6)
Transferred to another hospital ward, number (%)	111 (8.3)	120 (8.9)	108 (8.2)
In-hospital mortality, number (%)	66 (5.0)	50 (3.6)	42 (3.1)

Ten missing values for age in wave 3

Table 2 Prevalence (%) of diseases potentially painful in the three samples of REPOSI

Diseases	Sample 2008	Sample 2010	Sample 2012
Diabetes mellitus	27.0	27.2	29.8
Cerebrovascular disease	26.5	21.6	21.7
Coronary heart disease	25.5	24.1	20.2
Chronic obstructive pulmonary disease	21.7	25.2	24.5
Malignancy	19.7	17.3	15.2
Heart failure	18.6	19.1	16.6
Gastric diseases	17.1	24.9	20.6
Gut diseases	11.1	13.9	13.9
Arthritis	7.5	9.9	11.7

Table 3 Prescriptions of opioids during the three samples of REPOSI (2008, 2010, 2012) at hospital admission and discharge

	Sample 2008		Sample 2010		Sample 2012	
	Admission (N = 1,332)	Discharge (N = 1,155)	Admission (N = 1,380)	Discharge (N = 1,178)	Admission (N = 1,340)	Discharge (N = 1,166)
Codeine	9	18	15	13	7	30
Tramadol	18	30	15	25	17	17
Morphine	5	11	4	0	6	10
Hydromorphone	0	0	3	3	3	1
Oxycodone	4	3	4	8	12	12
Fentanyl	13	12	9	8	9	10
Buprenorphine	2	6	2	4	2	2
Tapentadol	0	0	0	0	3	4

Table 4 Univariate associations with opioid prescription at hospital discharge in the three samples of REPOSI

	Sample 2008		Sample 2010		Sample 2012	
	Opioids		Opioids		Opioids	
	No	Yes	No	Yes	No	Yes
Age, yrs, mean (SD)	79.2 (7.5)	77.7 (8.0)	78.9 (7.4)	78.6 (7.9)	79.3 (7.5)	78.7 (6.9)
Male, number (%)	506 (46.5)	29 (43.3)	540 (48.4)	25 (39.7)	523 (48.1)	40 (51.9)
Total drugs at discharge, mean (SD)	5.9 (2.8)	6.4 (3.3)	6.2 (2.8)	6.9 (3.0)*	6.3 (3.1)	7.1 (2.8)†
SBT, mean (SD)	–	–	9.6 (8.0)	8.4 (8.8)	9.1 (7.8)	8.6 (7.1)
Barthel Index, mean (SD)	–	–	78.4 (29.6)	72.9 (31.6)	74.9 (31.1)	68.1 (32.8)
Dementia diagnosis, number (%)	102 (9.4)	4 (6.0)	84 (7.5)	6 (9.5)	113 (10.4)	3 (3.9)
Severe constipation, number (%)	23 (2.1)	3 (4.5)	19 (1.7)	1 (1.6)	7 (0.6)	2 (2.6)*

* $p = 0.05$ † $p < 0.01$

mean number of prescribed drugs was also similar in the three samples, both at hospital admission and discharge. Median length of hospital stay was the same (9 days, with a range of 6–14). No statistically significant differences were found according to the prevalence of potentially painful diseases in the three registry runs (Table 2). The proportion of patients discharged from hospital was 86.7, 87.4 and 88.6 %, respectively. In-hospital mortality changed from 5.0 % in the first run to 3.1 % in the third (p value for trend = 0.05).

The proportion of patients prescribed with analgesic opioids at hospital admission was 3.8 % in 2008 the first run, 3.6 % in the second and 4.1 % in the third, whereas at hospital discharge the prescription rates were slightly higher (5.8, 5.3 and 6.6 %). The most frequently prescribed opioids were weak opioids such as codeine and tramadol (Table 3). Pertaining to the indications for their prescription, in the 2008 registry run 26 % of patients received these drugs for cancer pain, 48 % for non-cancer pain (e.g., osteoarthritis), whereas in 26 % the indication was not reported. In 2010, 14 % of the patients received opioids for cancer pain, 60 % for non-cancer pain, in 26 % the

indication was not reported. In 2012, 20 % of patients received opioids for cancer pain, 45 % for non-cancer pain and in 35 % prescription indication was missing.

Univariate analysis and logistic regression models were run to identify factors associated with opioid prescription (Table 4). In all the three registry runs, age and gender were not associated with prescription. The total number of all prescribed drugs at discharge (after excluding opioids) was the only factor independently associated with opioid prescription, similarly in the three runs (OR = 1.1; 95 % CI = 1.0–1.2 in 2008; OR = 1.15; 95 % CI = 1.10–1.24 in 2010; OR = 1.13; 95 % CI = 1.10–1.2 in 2012). In the third run, a diagnosis of dementia and a better functional status were inversely related with opioid prescription (data not shown).

Presence of pain at hospital discharge, specifically evaluated only in the 2012 run, indicated that among 1,166 patients 121 (10.4 %) were discharged with pain, 22 of them with cancer pain. Pain intensity measures varied from 1 to 10, with a mean value of 4.0 (SD = 2.1). Only 37 (30.5 %) of patients with pain were prescribed opioids at the time of discharge. Pain intensity measures were

Table 5 Allocation of the 121 painful patients according to analgesic prescription at hospital discharge

Patients (N, %)	Subjects with pain intensity ≥ 4	Analgesic prescription
37 (30.5)	16	Opioids
12 (9.9)	5	Acetaminophen
2 (1.7)	0	NSAIDs
70 (57.9)	29	None

NSAIDS denotes non-steroidal anti-inflammatory drug

available for all these 37 patients: 16 of them (43.2 %) had a score ≥ 4 . Amongst the remaining 84, 12 were prescribed with acetaminophen and two with non-steroidal anti-inflammatory drugs. Thus, 70 of patients with pain (57.8 %) were discharged with no analgesic prescription. Pain intensity was available for 58 of them and 29 (50 %) had a value ≥ 4 (Table 5).

Discussion

It is well established that the prevalence of chronic pain climbs steadily until the seventh decade of life [17], often exceeding 50 % in community-based cohorts of people and up to 80 % in the frame of residential care [18, 19]. In a recent study [20] evaluating cancer pain in 24, 410 patients older than 65 years, 63 % had pain: 20 % mild, 20 % moderate and 23 % severe. In this Canadian study 24 % patients with mild, 45 % with moderate and 67 % with severe pain received opioids [20]. These literature data, that establish the impact of pain in the elderly and make us aware of the need to provide adequate pain relief with opioids, are in striking contrast with our registry findings: in all the three REPOSI runs (spanning a time interval of 5 years), the prevalence of opioid prescription at hospital admission ranged from as little as 3.6 to 4.1 % and increased marginally at discharge from 5.3 to 6.6 %. The most frequently prescribed agents were weak opioids, such as codeine and tramadol. The only factor associated with opioid prescription in all the REPOSI runs was the total number of prescribed drugs. In the third run, a diagnosis of dementia and a better functional status of the patients were inversely correlated with opioids prescription. Finally, at least half of the patients with significant pain at discharge were not prescribed any analgesic.

Data from the Italian Observatory on Medications (OsMed) showed a 17 % average increase in the prescription of opioids and adjuvant analgesics for neuropathic pain from 2004 to 2012, ranging in prevalence from 7.6 to 23.5 % in the general population, albeit with large variations in different regions. In the same time period, major and minor opioid prescription did increase by 12.1

and 46.3 %, respectively [21]. The present data from REPOSI show a much smaller increase of opioid prescription from 2008 to 2012 to hospitalized elderly patients, who were very similar in the three registry runs pertaining to socio-demographic characteristics, age, gender, health status, diseases potentially painful and total number of prescribed drugs. Furthermore, the observed tiny increase of opioid prescription between hospital admission and discharge indicates that there were similarly conservative prescription attitudes among general practitioners (who are usually the prescribers before hospital admission) and internists and geriatricians (who are the final prescribers at the time of hospital discharge). The small prevalence of opioid prescription in this REPOSI sample compared to the general Italian population, the higher prescription rate of weak than strong opioids, as well as the fact that more than 50 % of patients with pain at the time of discharge were not prescribed any analgesic are in line with previous reports on pain undertreatment of the elderly in Italy [6].

In order to facilitate opioid prescription, a ministerial bill permitted, in June 2009, the prescription of these drugs on the basis of a simple no-repeat prescription, using the usual pad of the Italian Health Service. Hence, the first REPOSI run in 2008 took place before the enforcement of this bill, but the next two runs (2010, 2012) took place after the bill. Yet, there was no evidence that this easing bill has changed the pattern of spare prescription of opioids.

There are several possible explanations for this prescription behavior. One is knowledge that opioids may cause a variety of adverse effects that can be particularly problematic in the frail elderly. Whereas physicians working in specialized hospital wards (such as oncology, pain therapy and palliative care, anesthesiology and surgery units) are more user-friendly with opioids, internal medicine and geriatric physicians, as well as general practitioners, may not fully appreciate that understanding, anticipating and managing the side effects of opioids is an important component of their active strategy towards pain management in the elderly [22]. For instance, an accurate personalized modulation of the daily dose may limit adverse reactions. Furthermore, according to the STOPP criteria for prescription appropriateness in the elderly, opioids should be avoided for long-term use in people with dementia unless in severe pain, as well as in those at high risk of falls [23]. Indeed, a diagnosis of dementia and a better functional status were inversely associated with opioid prescription in the last REPOSI run. Finally, older patients themselves may not agree with opioid prescription because of multiple concerns and prejudices (e.g., fear of addiction, constipation, negative social stigma), which may limit their compliance with this prescribed therapy. Consistently with the reasons explained above, a preferential

choice of weak opioids, such as codeine and tramadol, was indeed observed in this study.

Strengths and limitations

A strength of the REPOSI registry is the multicenter prospective observational design that involves internal medicine and geriatric wards throughout Italy, resulting in a sample representative of the hospitalized elderly population in the country; and the inclusion of patients during a period of four different weeks, in order to balance the effect of seasons on acute diseases leading to hospitalization. However, limitations need to be mentioned. Hospital admissions are sometime selective on the basis of ward characteristics, severity of disease, associated medical conditions and admissions policies that may vary from hospital to hospital. Moreover, the assessment of pain intensity was included only in third run of REPOSI, so that this information was obtained only partially.

Conclusions

Opioid prescription did not change over a 5-year period in hospitalized elderly patients in Italy. The Ministry of Health decree, focused on reducing the complexity of prescription, had little influence on the therapeutic decisions of hospital internists. Furthermore, a high degree of inconsistency was found between presence of pain and analgesic prescription at hospital discharge. Reasons for the persistence of a low opioid prescription and pain under treatment in elderly patients should be sought in physicians' and patients' prejudices and concerns that warrant more information and education.

Conflict of interest None.

Appendix: Investigators and co-authors of the REPOSI (REgistro POLiterapie SIMI, Società Italiana di Medicina Interna) Study Group are as follows

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References

1. Reyes-Gibby CC, Aday L, Cleeland C (2002) Impact of pain on self-rated health in the community-dwelling older adults. *Pain* 95:75–82
2. Pahor M, Guralnik JM, Wan JY, Ferrucci L, Penninx BW, Lyles A, Ling S, Fried LP (1999) Lower body osteoarticular pain and dose of analgesic medications in older disabled women: the Women's Health and Aging Study. *Am J Public Health* 89:930–934
3. Lamberg L (1999) Chronic pain linked with poor sleep; exploration of causes and treatment. *JAMA* 281:691–692
4. de Leon-Casasola OA (2013) Opioids for chronic pain: new evidence, new strategies, safe prescribing. *Am J Med* 126(3 Suppl 1):S3–S11
5. Abdulla A, Adams N, Bone M, Elliott AM, Gaffin J, Jones D, Knaggs R, Martin D, Sampson L, Schofield P, British Geriatric Society (2013) Guidance on the management of pain in older people. *Age Ageing* 42(Suppl 1):i1–57
6. Bernabei R, Gambassi G, Lapane K, Landi F, Gatsonis C, Dunlop R, Lipsitz L, Steel K, Mor V (1998) Management of pain in elderly patients with cancer. SAGE study group. Systematic assessment of geriatric drug use via epidemiology. *JAMA* 279:1877–1882
7. Huang AR, Mallet L (2013) Prescribing opioids in older people. *Maturitas* 74:123–129
8. Papaleontiou M, Henderson CR, Turner BJ, Moore AA, Olkhovskaya Y, Amanfo L, Reid MC (2010) Outcomes associated with opioid use in the treatment of chronic non cancer pain in older adults: a systematic review and meta-analysis. *J Am Geriatr Soc* 58:353–369
9. Filippini M, Campanelli MM (2011) Cronaca di una legge che ci difende dal dolore. *La legge* 38/10, la più evoluta d'Europa. Gruppo 24ore
10. Griffin MR (2013) High-dose non-steroidal anti-inflammatories: painful choices. *Lancet* 382:746–748
11. Nobili A, Licata G, Salerno F, Pasina L, Tettamanti M, Franchi C, De Vittorio L, Marengoni A, Corrao S, Iorio A, Marcucci M, Mannucci PM, Investigators SIMI (2011) Polypharmacy, length of hospital stay, and in-hospital mortality among elderly patients in internal medicine wards. The REPOSI study. *Eur J Clin Pharmacol* 67:507–519
12. World Health Organization (1990) Guidelines for ATC Classification. In: World Health Organization. Collaborating Centre for Drug Statistics Methodology, Norway and Nordic Councils on Medicines. Sweden
13. Hajjar ER, Cafiero AC, Hanlon JT (2007) Polypharmacy in elderly patients. *Am J Geriatr Pharmacother* 5:345–351
14. World Health Organization (1987) International classification of diseases, injuries, and causes of death. In: Ninth revision (ICD-9). World Health Organization. Geneva
15. Katzman R, Brown T, Fuld P, Peck A, Schechter R, Schimmel H (1983) Validation of a short orientation-memory-concentration test of cognitive impairment. *Am J Psychiatry* 140:734–739
16. Mahoney FI, Barthel DW (1965) Functional evaluation: THE BARTHEL Index. *Md State Med J* 14:61–65
17. Helme RD, Gibson SJ (2001) Age-related differences in pain perception and report. *Clin Geriatr Med* 17:417–432
18. Jones GT et al (2005) In: Gibson SJ, Weiner DK (eds) Pain in older persons. progress in pain research and management, vol 35. IASP Press, Seattle, pp 3–22
19. Parmelee PA, Smith B, Katz IR (1993) Pain complaints and cognitive status among elderly institution residents. *J Am Geriatr Soc* 41:517–522
20. Barbera L, Seow H, Husain A, Howell D, Atzema C, Sutradhar R, Earle C, Sussman J, Liu Y, Dudgeon D (2012) Opioid prescription after Pain assessment: population-based cohort of elderly patients with cancer. *J Clin Oncol* 30:1095–1099
21. <http://www.agenziafarmaco.gov.it/it/content/luso-dei-farmaci-italia-rapporto-osmed-2012>
22. Martin CM, Forrester CS (2013) Anticipating and managing opioid side effects in the elderly. *Consult Pharm* 28:150–159
23. Gallagher P, Ryan C, Byrne S, Kennedy J, O'Mahony D (2008) STOPP (screening tool of older person's prescriptions) and START (screening tool to alert doctors to right treatment). Consensus validation. *Int J Clin Pharmacol Ther* 46:72–83