Pharmacist comprehensive review of treatment compared with STOPP-START criteria to detect potentially inappropriate prescription in older complex patients

E Delgado-Silveira,¹ M S Albiñana-Pérez,² M Muñoz-García,¹ M García-Mina Freire,³
E M Fernandez-Villalba,⁴ CRONOS Group

¹Department of Pharmacy,
Hospital Universitario Ramón y
Cajal, Madrid, Spain

²Department of Pharmacy,
Complejo hospitalario
Arquitecto Marcide, Ferrol,
Spain

³Residencia La Vaguada
Department of Pharmacy,
Pamplona, Spain

⁴Department of Pharmacy,
Residencia para mayores
dependientes La Cañada,
Paterna, Valencia, Spain

Correspondence to

Dr E Delgado Silveira,
Department of Pharmacy,
Hospital Universitario Ramón
y Cajal, Carretera de Colmenar
Viejo km 9,1, Madrid 28034,
Spain;
eva.delgado@salud.madrid.org

Received 14 July 2016

Revised 24 October 2016

Accepted 2 November 2016

Published Online First

23 November 2016

EAHP Statement 4: Clinical
Pharmacy Services

ABSTRACT

Objectives To compare potentially inappropriate prescribing (PIP) according to the clinical judgement of the pharmacist with PIP according to explicit STOPP-START criteria in institutionalised and hospitalised patients with multiple pathologies. To describe and compare the main pharmacological groups involved and determine the factors associated with the detection of PIP in these patients.

Method A prospective multicentre observational study of institutionalised and hospitalised multipathology patients aged >65 years. A specialised pharmacist used his best clinical judgement to detect PIP based on a comprehensive review of the complete chronic treatment of patients, which is an essential activity in interdisciplinary care. STOPP-START criteria were used as an aid tool to detect PIP. The main variable was the number of PIP incidents detected.

Results Detected PIP incidents were analysed in 338 patients. Clinical judgement detected more PIP incidents (35%) than did STOPP-START criteria. More PIP incidents unrelated to these criteria were detected in institutionalised patients than in hospitalised patients. Clinical judgement mainly detected PIP incidents related to incorrect doses and drug interactions ($p<0.001$); however, STOPP-START criteria mainly detected PIP incidents related to drug duplication and insufficiently treated diagnosis or symptoms ($p=0.001$ and $p<0.001$). In total, 93.8% of the PIP incidents were detected in polypharmacy patients (≥ 5 drugs). Institutionalised and high-level polypharmacy (≥ 10 drugs) patients were at the highest risk of PIP.

Conclusions A large number of PIP incidents were detected in institutionalised and hospitalised patients with multiple pathologies. The inclusion of a pharmacist in the multidisciplinary team facilitated the detection of PIP incidents, particularly in the institutionalised population and patients treated with high-level polypharmacy which were not detected by explicit STOPP-START criteria.

INTRODUCTION

Patients with chronic disease, especially older ones, are the target of a range of integrated care plans focused on pharmacotherapy and medication-associated problems.^{1–5} These patients receive polymedication, which can entail potentially inappropriate prescribing (PIP) and an increased risk of adverse effects, increased morbidity and mortality, and increased healthcare costs.⁶

Such care plans involve continuous monitoring by teams that increasingly include pharmacists. Several studies have found a decrease in negative outcomes associated with medication when a pharmacist is present.^{7–8}

With the opening of pharmacy services in nursing homes (NHs), pharmacists have had to specialise in all areas related to the use of drugs in patients with complex chronic disease.⁹ The interventional activity of these pharmaceutical specialists is beginning to be more common in hospitals.

The explicit Beers,¹⁰ Priscus¹¹ and STOPP-START criteria have been shown to be good tools for detecting PIP and improving prescription quality in elderly people in all care settings.^{12–15}

International and national studies have found different PIP prevalence using the STOPP-START criteria, but the different methodologies used means that their usefulness cannot be compared in relation to the care setting.^{16–18} A systematic review of the Cochrane Library of 12 studies on interventions to reduce PIP incidents in elderly patients found that there was a decrease. Two of these studies used STOPP criteria and one used START criteria. However, the results were less clear regarding the effect of this decrease on the patients' state of health and clinical benefit.¹⁹

These varied results raise several questions. It is indisputable that the systematic application of explicit criteria inevitably requires subsequent reflection supplemented by clinical judgement. Furthermore, the healthcare objectives differ in the two settings studied.

Thus, we established the following objectives:

- To compare PIP according to the clinical judgement of the pharmacist with PIP according to explicit STOPP-START criteria in institutionalised and hospitalised patients with multiple pathologies.
- To describe and compare the main pharmacological groups involved in each approach (STOPP-START criteria; pharmacist's clinical judgement).
- To determine the possible factors related to the two approaches in their different capacity to detect PIP in institutionalised and hospitalised patients.

MATERIALS AND METHODS

In 2013, CRONOS (the working group of the Spanish Society of Hospital Pharmacy) conducted a

CrossMark

To cite: Delgado-Silveira E, Albiñana-Pérez MS, Muñoz-García M, et al. *Eur J Hosp Pharm* 2018;**25**:16–20.

prospective interventional multicentre study on multipathology patients >65 years old admitted to acute hospitals (18 centres) or institutionalised in NHs (eight centres) in Spain. The aim was to analyse the impact of pharmaceutical intervention by the care team on drug-related problems and negative outcomes associated with medication (according to the Granada Consensus²⁰). The sampling selection, inclusion/exclusion criteria and sample size were predefined²¹ as follows.

In hospitals, participants were selected by consecutively sampling a list of daily admissions; in NHs, participants were consecutively enrolled on admission.

Exclusion criteria were: patients >65 years old with unknown chronic pharmacological treatment on arrival at the hospital or centre; readmission during the study period; patients who had undergone intervention by the pharmacist on an aspect of their pharmacotherapy; and patients in palliative care.

In the first 24–48 hours after admission, the pharmacist in charge obtained a list of chronic medication and other essential variables from each of these patients, and reviewed all the available documentation by centre (clinical record, admission report, report from primary care or NH, list or medication bag provided by the patient, etc). The patient and/or the caregiver were interviewed whenever needed.

The detected PIP incidents were analysed during the comprehensive review of the complete chronic treatment of the patients included in the initial study. This review was conducted by the specialist pharmacist as an essential activity in the interdisciplinary care of these patients. In addition to his clinical judgement, the pharmacist used STOPP-START criteria 2008 as an aid tool to detect PIP.²² After taking the medical history, the pharmacist identified PIP based on the patients' clinical data, systematic procedures, and the pharmacist's own knowledge, attitudes, skills and experience. The PIP incidents detected by clinical judgement were compared with those detected by STOPP-START criteria, by group of patients and by type of health centre (hospital or NH). The pharmacological groups most commonly involved in PIP and their polypharmacy were analysed as possible factors in PIP. Finally, the factors related to the capacity of the STOPP-START criteria to detect PIP in institutionalised and hospitalised patients were identified.

A prescription was considered to be potentially inappropriate in the following cases: when the risk of an adverse event was greater than the clinical benefit, especially when safer or more efficient alternative therapies were available; when drugs were duplicated or those of the same class were also used; when drugs were used at a greater frequency or for longer than indicated; when there was a high risk of drug–drug or drug–disease interactions; when beneficial drugs were not used; and when the prescribing doctor made a poor selection of medication or dose. **Box 1** shows the classification²⁰ of the detected PIP incidents.

The main variable was the number of PIP incidents detected during the comprehensive review of the complete chronic treatment. The origin of the PIP was classified either by STOPP-START criteria or by the pharmacist's clinical judgement. The secondary independent variables were: demographic (age, sex), type of health centre, clinical variables, multipathology classification,²³ Charlson index²⁴ in the first 24–48 hours, number of active principles (chronic treatment), description of the active principle, and ATC classification.²⁵ Each patient was classified as non-polypharmacy (fewer than five active principles), polypharmacy (between five and nine) and high-level polypharmacy (10 or more) according to the number of active principles in the chronic treatment.

Box 1 Classification of cases of potentially inappropriate prescribing (PIP)*

Contraindication
Diagnosis/insufficiently treated symptom
Inappropriate dose
Drug duplication
Inappropriate duration
Interaction
Low-therapeutic-use drug
Inefficient drug
Non-indicated drug
Other health problems that affected treatment
Inappropriate pattern
Likelihood of adverse effects

*Classification adapted from that used by the Research Group on Pharmaceutical Care.²⁰

Statistical analysis

A descriptive analysis of the demographic variables and participant data was conducted; qualitative variables are expressed as percentages and quantitative variables as means or medians.

A bivariate analysis of the institutionalised and hospitalised patients was conducted. Depending on the frequencies observed, qualitative variables were analysed using the χ^2 test or Fisher exact test. Quantitative variables were analysed using the non-parametric Mann-Whitney U test because none of the variables of the institutionalised patient group had a normal distribution.

A backward binary logistic regression adjusted to the likelihood ratio was conducted to evaluate the independent factors associated with PIP not detected by STOPP-START criteria. The entry and exit criteria of the model were 0.5 and 0.10, respectively. The goodness-of-fit was evaluated using the Hosmer-Lemeshow parameter. The OR was expressed with its corresponding 95% CI.

All tests were conducted using a p value of <0.05 as a cut-off for statistical significance. All analyses were conducted using the IBM SPSS Statistics V19.0 software package.

Patient informed consent was obtained orally and in writing according to the study protocol of the hospital Ethics Committee for Clinical Research.

RESULTS

Treatments administered to 338 patients were reviewed; 287 patients were from 18 acute care hospitals and 51 from 8 NHs. **Table 1** shows the general characteristics of the patients, and **table 2** shows the PIP distribution. In total, 35% of the PIP incidents (381/1089) were detected by the pharmacist's clinical judgement and 65% (708/1089) by STOPP-START criteria. The pharmacist detected 67.9% (110/162) of PIP incidents in institutionalised patients compared with 29.2% (271/927) in hospitalised patients ($p<0.001$). In contrast, the STOPP-START criteria detected 70.8% (656/927) of PIP incidents in hospitalised patients compared with 32.1% in institutionalised patients ($p<0.001$).

Regarding the detection methods, clinical judgement mainly detected PIP incidents related to inadequate doses, interactions, non-indicated drugs, other problems affecting treatment ($p<0.001$), and low-therapeutic-use drugs ($p=0.0403$).

Table 1 General characteristics of patients

Characteristic	Total, N=338	Hospitalised, N=287 (84.9%)	Institutionalised, N=51 (15.1%)	p Value
Sex (women), n (%)	184 (54.4%)	153 (53.3%)	31 (60.8%)	0.323
Age, median (IQR)	84.6 (10)	85 (19)	84 (10)	0.991
Charlson index adjusted to age, median (IQR)	7 (3)	7 (3)	7 (8)	0.568
Chronic pathologies, median (IQR)	3 (1)	3 (1)	3 (1)	0.270
Drugs, median (IQR)	9 (4)	9 (4)	9 (5)	0.808

Table 2 Cases of potentially inappropriate prescribing (PIP) detected by clinical judgement of the pharmacist and by STOPP-START criteria in hospitalised and institutionalised patients

PIP	Total	Clinical judgement		STOPP-START		p Value
		N	Per cent	N	Per cent	
Hospitalised	927	271	29.2	656	70.8	p<0.001
Institutionalised	162	110	67.9	52	32.1	
Total	1089	381	35.0	708	65.0	

However, STOPP-START criteria mainly detected PIP incidents related to drug duplication and insufficiently treated diagnosis or symptoms ($p=0.001$ and $p<0.001$) (table 3).

Regarding the care setting, in hospitalised patients, the pharmacist mainly detected PIP incidents related to inadequate dose (80.9% vs 19.1%, $p=0.009$), contraindication (91.6% vs 8.3%, $p=0.022$) and non-indicated medication (53.1% vs 46.9% $p=0.003$) and, in institutionalised patients, the pharmacist mainly detected those related to insufficient duration of treatment (80.0% vs 20.0% $p=0.026$). The drugs most commonly involved in PIP incidents belonged to group C 'cardiovascular system' (367 PIP incidents; 33.7%). This group was involved in most of the PIP incidents detected by STOPP-START criteria (72.5% vs 27.5%, $p<0.001$) and was also the second most common group involved in PIP incidents detected by clinical judgement. Group N was the group most commonly involved in PIP incidents detected by clinical judgement (53.7% vs 46.3%, $p<0.001$).

Regarding polypharmacy as a risk factor, 93.8% (1021) of PIP incidents were detected in patients receiving five or more drugs. The pharmacist's clinical judgement was the most effective approach in detecting PIP incidents in high-level polypharmacy (≥ 10 drugs) ($p<0.001$) (table 4).

Finally, two types of factor related to PIP incidents detected by the pharmacist's clinical judgement were observed (table 5): those related to the type of patient and those related to the treatment. Regarding the type of patient, living in an institution and receiving high-level polypharmacy entailed a higher risk of PIP unrelated to STOPP-START criteria. Regarding treatment, PIP incidents involving digitalis glycosides and other N02B analgesics (salicylic acid, paracetamol, pyrazolones and combinations with codeine) were less likely to be detected by STOPP-START criteria.

DISCUSSION

The number of PIP incidents detected reflects the complexity of the therapeutic management of older people and patients with multiple chronic conditions in hospital settings and NHs.

Table 3 Types of potentially inappropriate prescribing (PIP) detected by clinical judgement of the pharmacist and by STOPP-START criteria in hospitalised and institutionalised patients

Classification of PIP	Total	Clinical judgement		STOPP-START	p Value
		N	Per cent		
Contraindication	55	24 (43.6)		31 (56.4)	0.167
Non-appropriate dose	138	105 (76.1)		33 (23.9)	<0.001
Diagnosis/insufficiently treated symptom	410	25 (6.1)		385 (93.9)	<0.001
Duplication	51	2 (3.9)		49 (96.1)	<0.001
Inappropriate duration	19	5 (31.2)		14 (68.8)	0.428
Interaction	77	70 (90.9)		7 (9.1)	<0.001
Low-therapeutic-use drug	3	3 (100)		0	0.0403
Inefficient drug	10	5 (50)		5 (50)	0.332
Non-indicated drug	77	49 (56.3)		28 (43.7)	<0.001
Other health problems that affect treatment	16	13 (81.3)		3 (18.7)	<0.001
Inappropriate pattern	26	8 (30.8)		18 (69.2)	0.648
Likelihood of adverse effects	201	68 (33.8)		133 (66.2)	0.704
Unknown	6	4 (66.7)		2 (33.3)	0.103

Values are n (%).

Frequent care transitions and polypharmacy place these patients at a higher risk of inappropriate treatment.²⁶

The prevalence of PIP detected by STOPP-START criteria in institutionalised patients was lower than reported in other publications, in which PIP prevalence ranged between 48% and 79% for STOPP criteria and 29% and 74% for START criteria.^{27 28} However, the prevalence was similar to that found by Galván-Banqueri *et al*⁶ in their study on multipathology patients, in which STOPP-START criteria, despite their usefulness, overlooked 75% of pharmaceutical interventions.

In the present study, the lower detection rate by explicit criteria in institutionalised patients may be related to the use of criteria from a hospital care setting,⁸ which could not address the different needs of institutionalised patients, in whom the objective is not always to achieve healing, but to improve quality of life.²⁹ These criteria have recently been updated to increase the number of recommendations.¹³ It would be of interest to assess whether the new version, compared with clinical judgement, would have increased the number of PIP incidents detected in our institutionalised population.

PIP incidents detected by clinical judgement were mainly related to interactions, inappropriate doses and inappropriate drugs. This finding is similar to that found in a study conducted in 10 Swiss NHs, in which the problems detected by pharmacist review of treatment and subsequent assessment were also mainly related to potential interactions (32.16%), inappropriate doses (17.39%) and insufficient duration of treatment (16.24%).³⁰

Table 4 Distribution of cases of potentially inappropriate prescribing (PIP) according to number of drugs

Classification according to number of drugs	Clinical judgement	STOPP-START	P Value	P Value
Not polypharmacy (<5)	19 (5.0)	49 (6.9)	0.208	0.0012
Polypharmacy (≥5–≤9)	128 (33.6)	306 (43.2)	0.002	
High-level polypharmacy (≥10)	234 (61.4)	353 (49.9)	<0.001	
Total	381	708		

Values are n (%).

Table 5 Regression model of independent factors associated with potentially inappropriate prescribing (PIP) that does not fulfil STOPP-START criteria

Factor	OR	95% CI		p Value
		Low	high	
High-level polypharmacy	1.57	1.15	2.13	<0.004
Institutionalised	4.61	3.03	7.02	<0.001
Antithrombotic agents	0.15	0.08	0.25	<0.001
Digitalis glycosides and other stimulants	6.83	1.48	31.52	0.014
β-Blockers	0.49	0.25	0.96	0.039
ACE inhibitors	0.20	0.10	0.39	<0.001
Cholesterol and triglyceride reducers	0.13	0.07	0.27	<0.001
Other analgesics	6.52	1.41	30.17	0.016

The STOPP-START criteria mainly detected problems related to cardiovascular drugs, whereas clinical judgement mainly detected those related to nervous system drugs. The inadequate use of antipsychotics and antidepressants, especially in institutionalised patients, has been previously described.^{27 28 31} These drugs entail a high risk of sedation and are associated with confusion, cognitive impairment, impaired balance, and falls.³² This aspect suggests that there is a clear opportunity to improve pharmaceutical intervention, given that positive experiences have been reported in reducing their prescription.³³

In the regression model, two groups of risk factors associated with PIP incidents were identified by clinical judgement compared with those detected by STOPP-START criteria. One group was related to treatment with 'digitalis glycosides' and 'other analgesics', and the other group was related to the type of patient (institutionalised and polypharmacy).

Pharmacokinetic monitoring of digoxin may increase its efficiency and, above all, limit its adverse effects, which are strongly associated with supratherapeutic concentrations.³⁴ Thus, validation of its indication and pharmacokinetic monitoring are opportunities to take action within pharmaceutical clinical judgement.

Institutionalisation is a factor associated with inappropriate prescribing. On admission of patients to an NH, a comprehensive care approach is needed while bearing in mind their functional and cognitive situation, life expectancy or prognosis, social situation, preferences, beliefs, and so on. In this way, problems are prioritised and the aim of therapy shifts from the curative and preventive to the symptomatic and palliative.

Both hospitalised and institutionalised patients were characterised by polypharmacy. There was a higher prevalence of PIP incidents in polypharmacy patients (53.9% PIP in patients

receiving more than 10 drugs and 39.9% PIP in patients receiving 5–9 drugs). San José *et al*^{35 36} found that polypharmacy was the most important factor related to inappropriate prescribing in hospitalised patients aged >85 years.

Polypharmacy has consequences at the clinical level on quality of life and independence, and has been independently associated with higher mortality in elderly patients.³⁷ The importance of follow-up in these patients is reflected in the fact that polypharmacy is an indicator of prescription quality in different national health systems.^{38 39}

The results show that the comprehensive treatment review by the pharmacist was more effective in detecting PIP incidents than STOPP-START criteria in extreme polypharmacy patients. It is difficult to solve the problem of PIP only by the use of explicit methods that comprise a set of closed criteria. Although useful, they are insufficient, particularly in this group of patients in whom more interconnected strategies are required to address this problem.⁴⁰

In line with the results of our study, different experiences have shown how pharmacist intervention in this patient profile can improve correct treatment in hospitalised as well as institutionalised patients. The best results are obtained by the integration of the pharmacist into the interdisciplinary group and the use of tools (computerised or lists) that help in PIP detection.^{41–43}

The main limitation of our study is the difference in sample size of institutionalised and hospitalised patients, which could distort the results. Two other limitations are related to the application of STOPP-START criteria: the availability of certain clinical information needed for their correct assessment in NHs; and the different degree of experience or knowledge regarding the management of these criteria by the care team, given that 90.6% of the hospitalised patients were attended by specialist physicians with more training in multipathology (geriatrics, internal medicine) compared with 13.7% in institutionalised patients ($p < 0.001$).²¹

In conclusion, a significant number of PIP incidents were found in elderly patients with multiple chronic diseases regardless of whether they were hospitalised or institutionalised. The inclusion of a pharmacist in the interdisciplinary team led to the

What this paper adds

What is already known on this subject

- Polypharmacy is common in elderly patients admitted to hospitals or care homes.
- Polypharmacy is associated with an increased risk of inappropriate treatment and potentially inappropriate prescribing (PIP).
- Explicit criteria decrease the degree of inappropriate treatment and improve prescription quality.

What this study adds

- The clinical judgement of a pharmacist is a necessary addition to explicit criteria, which may not detect all PIP.
- Explicit criteria are less effective in institutionalised patients, polypharmacy patients, and those receiving nervous system drugs.
- In hospitalised patients, PIP is mainly associated with cardiovascular drugs, whereas in institutionalised patients, PIP is mainly associated with antipsychotics, antidepressants, and proton pump inhibitors. In these cases, explicit criteria fail to detect the majority of PIP incidents.

detection of PIP incidents that were not detected by the explicit STOPP-START criteria, especially in the case of PIP associated with nervous system drugs and in institutionalised and high-level polymedicated patients. These complex patients need more comprehensive follow-up.

Twitter Follow Eva Delgado at @eva_del_sil

Funding This study was financed by research grants, educational projects, and healthcare working groups of the Spanish Society of Hospital Pharmacy in 2012–2013.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- Plan Estratégico de la Sociedad Española de Farmacia Hospitalaria sobre Atención Farmacéutica al Paciente Crónico. SEFH. 2012. (20 October 2016). http://www.sefh.es/sefhpdfs/plan_estrategico_sefh_af_paciente_cronico2012.pdf
- Estrategia para el abordaje de la cronicidad en el Sistema Nacional de Salud. Ministerio de Sanidad, Servicios sociales e igualdad. 2012. (20 October 2016) http://www.msssi.gob.es/organizacion/sns/planCalidadSNS/pdf/ESTRATEGIA_ABORDAJE_CRONICIDAD.pdf
- Chronic diseases and health promotion. WHO. (20 October 2016). <http://www.who.int/chp/en/>
- Long Term Conditions. The Scottish Government. (20 October 2016) <http://www.gov.scot/Topics/Health/Services/Long-Term-Conditions>
- U.S. Department of Health and Human Services. Multiple Chronic Conditions. A Strategic Framework: Optimum Health and Quality of Life for Individuals with Multiple Chronic Conditions. Washington DC. December 2010. (20 October 2016). http://www.hhs.gov/ash/initiatives/mcc/mcc_framework.pdf
- Galván-Banqueri M, González-Méndez AI, Alfaro-Lara E, et al. Evaluation of the appropriateness of pharmacotherapy in patients with high comorbidity. *Aten Primaria* 2013;45:235–43.
- Gillespie U, Alsaad A, Henrohn D, et al. A comprehensive pharmacist intervention to reduce morbidity in patients 80 years or older. *Arch Intern Med* 2009;169:894–900.
- Delgado-Silveira E, Álvarez-Díaz A, Pérez-Menéndez-Conde C, et al. Results of integrating pharmaceutical care in an Acute Geriatric Unit. *Rev Esp Geriatr Gerontol* 2012;47:49–54.
- Prestación farmacéutica especializada en centros sociosanitarios: Análisis de situación y propuesta CRONOS-SEFH. (17 June 2015). http://www.sefh.es/sefhpdfs/dossier_CRONOS_2013.pdf
- The American Geriatrics Society 2012 Beers Criteria Update Expert Panel. American geriatrics society updated beers criteria for potentially inappropriate medication use in older adults. *J Am Geriatr Soc* 2012;60:616–31.
- Holt S, Schmiedl S, Thürmann PA. Potentially inappropriate medications in the elderly: the Priscus list. *Deutsches Ärzteblatt International* 2010;107:543–51.
- Gallagher P, O'Mahoney D. STOPP (Screening Tool of Older Person's potentially inappropriate Prescriptions): application to acutely ill elderly patients and comparison with Beers' criteria. *Age Ageing* 2008;37:673–9.
- Delgado Silveira E, Montero Errasquin B, Muñoz García M, et al. Improving drug prescribing in the elderly: a new edition of STOPP/START criteria. *Rev Esp Geriatr Gerontol* 2015;50:89–96.
- Hill-Taylor B, Sketris I, Hayden J, et al. Application of the STOPP-START criteria: a systematic review of the prevalence of potentially inappropriate prescribing in older adults, and evidence of clinical, humanistic and economic impact. *J Clin Pharm Ther* 2013;38:360–72.
- Naveiro-Rilo JC, Díez-Juárez D, Flores-Zurutuza ML, et al. Intervention in elderly patients with multiple morbidities and multiple medications: results of the prescription and the quality of life. *Rev Calid Asist* 2014;29:256–62.
- Iniesta C, Urbieta E, Gascón JJ, et al. Causes and factors associated with inappropriate prescribing in elderly patients detected to hospital admission. Application of STOPP-START criteria. *Eur J Clin Pharmacol* 2012;14:100–7.
- Gómez-Lobón A, Periañez Parraga L, Galán Ramos N, et al. Systematic detection of inappropriate prescription using the STOPP/START criteria. *Farm Hosp* 2012;36:305–7.
- García-Gollarte F, Baleriola-Júvez J, Ferrero-López I, et al. An educational intervention on drug use in nursing homes improves health outcomes resource utilization and reduces inappropriate drug prescription. *J Am Med Dir Assoc* 2014;15:885–91.
- Patterson SM, Cadogan CA, Kerse N, et al. Interventions to improve the appropriate use of polypharmacy for older people. *Cochrane Database Syst Rev* 2014;10:CD008165.
- Research Group on Pharmaceutical Care. University of Granada. Pharmacology Research Group. University of Granada. Foundation Pharmaceutical Care Spain. Spanish Society of Community Pharmacy. Third Consensus of Granada on Drug Related Problems (DRP) and Negative Outcomes associated with Medication (NOM). *Ars Pharm* 2007;48:5–17.
- Delgado-Silveira E, Fernández-Villalba EM, García-Mina Freire M, et al. The impact of pharmacy intervention on the treatment of elderly multi-pathological patients. *Farm Hosp* 2015;39:192–202.
- Delgado-Silveira E, Muñoz-García M, Montero-Errasquin B, et al. Inappropriate prescribing of drugs in older people attending primary care health centres: detection using STOPP-START criteria. *Rev Esp Geriatr Gerontol* 2009;44:273–9.
- Ramírez-Duque N, Ollero-Baturone M, Bernabeu-Wittel M, et al. Clinical, functional, mental and sociofamiliar features in pluripathological patients. One-year prospective study in Primary Health Care. *Rev Clin Esp* 2008;208:4–11.
- Charlson M, Pompei P, Ales KL, et al. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chron Dis* 1987;40:373–83.
- ATC Drugs Classification System. (10 August 2015). <http://www.aemps.gob.es/industria/etiquetado/conduccion/listadosPrincipios/home.htm>
- Santos-Ramos B, Otero-López MJ, Galván-Banqueri M, et al. Health care models for patients with multiple chronic conditions and the role of the hospital pharmacy/the hospital pharmacist. *Farm Hosp* 2012;36:506–17.
- Conejos MD, Sánchez M, Delgado E, et al. Potentially inappropriate drug prescription in older subjects across healthcare settings. *Eur Geriatr Med* 2010;1:9–14.
- García-Gollarte F, Baleriola-Júvez J, Ferrero-López I, et al. Inappropriate drug prescription at nursing home admission. *J Am Med Dir Assoc* 2012;13:83.e9–15.
- Cruz-Jentoft AJ, Boland B, Rexach L. Drug therapy optimization at the end of life. *Drugs Aging* 2012;29:511–21.
- Brulhart MI, Wermeille JP. Multidisciplinary medication review: evaluations of a pharmaceutical care model for nursing homes. *In J Clin Pharm* 2011;33:549–57.
- Molist Bruneta N, Sevilla-Sánchez D, Amblàs Novellasa J, et al. Optimizing drug therapy in patients with advanced dementia: a patient-centered approach. *Eur Geriatr Med* 2014;5:66–71.
- Freeland KN, Thompson AN, Zhao Y, et al. Medication use and associated risk of falling in a geriatric outpatient population. *Ann Pharmacother* 2012;46:1188–92.
- Declercq T, Petrovic M, Azemai M, et al. Withdrawal versus continuation of chronic antipsychotic drugs for behavioural and psychological symptoms in older people with dementia (Review) Copyright © 2013 The Cochrane Collaboration.
- Adams KF Jr, Ghali JK, Herbert Patterson J, et al. A perspective on re-evaluating digoxin's role in the current management of patients with chronic systolic heart failure: targeting serum concentration to reduce hospitalization and improve safety profile. *Eur J Heart Fail* 2014;16:483–93.
- San-José A, Agustí A, Vidal X, et al. Potentially Inappropriate Prescription in Older Patients in Spain (PIPOPS) Investigators' project. Inappropriate prescribing to the oldest old patients admitted to hospital: prevalence, most frequently used medicines, and associated factors. *BMC Geriatrics* 2015;15:42.
- San-José A, Agustí A, Vidal X, et al. Potentially Inappropriate Prescription in Older Patients in Spain (PIPOPS) Investigators' Project. Inappropriate prescribing to older patients admitted to hospital: a comparison of different tools of misprescribing and underprescribing. *Eur J Intern Med* 2014;25:710–16.
- Gavilán-Moral E, Villafaina-Barroso A, Jiménez-de Gracia L, et al. Polypharmacy in frail elderly patients: is deprescribing the answer? *Rev Esp Geriatr Gerontol* 2012;47:162–7.
- Fastbom J, Johnell K. National indicators for quality of drug therapy in older persons: the Swedish experience from the first 10 years. *Drugs Aging* 2015;32:189–99.
- Onder G, Bonassi S, Abbatecola AM, et al. High prevalence of poor quality drug prescribing in older individuals: a nationwide report from the Italian Medicines Agency (AIFA). *J Gerontol A Biol Sci Med Sci* 2014;69:430–7.
- Gavilán A, Villafaina E. Pacientes polimedificados frágiles, un reto para el sistema sanitario. Polymedicated frail patients, a challenge for the health system *Inf Ter Sist Nac Salud* 2011;35:114–23.
- O'Sullivan D, O'Mahony D, O'Connor MN, et al. The impact of a structured pharmacist intervention on the appropriateness of prescribing in older hospitalized patients. *Drugs Aging* 2014;31:471–81.
- Gheewala PA, Peterson GM, Curtain CM, et al. Impact of the pharmacist medication review services on drug-related problems and potentially inappropriate prescribing of renally cleared medications in residents of aged care facilities. *Drugs Aging* 2014;31:825–35.
- Raimbault-Chupin M, Spiesser-Robelet L, Guir V, et al. Drug related problems and pharmacist interventions in a geriatric unit employing electronic prescribing. *Int J Clin Pharm* 2013;35:847–53.