Frailty and polypharmacy in elderly patients are associated with a high readmission risk

Elizabeth Rosted[1], Martin Schultz[2] & Suzanne Sanders[3]

ABSTRACT

INTRODUCTION: Many acutely ill elderly people are frail and suffer from polypharmacy. They often present with nonspecific symptoms at hospital admission and are therefore often under-triaged and insufficiently treated resulting in adverse health outcomes. This study aimed to investigate the prevalence of polypharmacy and frailty and to identify if frailty and polypharmacy may predict adverse health outcomes in elderly patients who are acutely admitted to hospital.

METHODS: The study was a descriptive cohort study including patients ≥ 65 years acutely admitted to hospital during a 14-day period, n = 250. The included patients were assessed for frailty, and the total number of health problems requiring treatment, geriatric problems and medication were registered.

RESULTS: Frail patients suffering from polypharmacy had significantly more health problems, 13-fold longer hospital stays, they were more often discharged to nursing homes and had a five times greater risk of readmission than patients without frailty and polypharmacy. Polypharmacy was present in 62% and hyper-polypharmacy in 20% of the patients, and frailty was present in 85% of the patients with polypharmacy and in 40% of those without polypharmacy.

CONCLUSION: Compared with non-frail patients without polypharmacy, frail elderly patients with polypharmacy belong to a high-risk group and should receive an immediate geriatric assessment and treatment including long-term planning by the Mobile Geriatric Team.

FUNDING: none.

TRIAL REGISTRATION: The study was approved and registered with the Danish Data Protection Agency under the Capital Region of Denmark's joint notification of health research (j. no.: 2007-58-0015, AMH-2013-003, I-Suite no: 02495).

The prevalence of diseases like hypertension, heart disease, stroke, diabetes, osteoporosis and dementia is high in the elderly population and multi-morbidity is present in up to 98% [1]. As many diseases require treatment with medication, elderly people are likely to suffer from polypharmacy. In Denmark, 60% of the resident population of > 75 year olds use > 3 and 33% use > 5 medications [2]. The use of several different medications and age-related changes in pharmacokinetics and pharmacodynamics often result in adverse drug events, drug interactions and increased morbidity [3].

The term polypharmacy is used ambiguously. In some studies, elderly people's use of ≥ 3 different medications on a daily basis is defined as polypharmacy [4], whereas other studies define polypharmacy as long-term use of ≥ 2 medications [5]. The results from a study by Gnjidic et al, including 1,705 older men, support the definition of polypharmacy as the use of ≥ 5 medications on a daily basis. Thus, an association was found between the use of 6.5 medications and frailty, 5.5 and disability and mortality, and the use of 4.5 medications and falls. They also found that, when the number of medication increases by one the risk of being frail increases by 27% (odds ratio (OR) = 1.27; 95% confidence interval (CI): 1.20-1.34) and the risk of early death increases by 15% (OR = 1.15; 95% CI: 1.11-1.20) [6]. Falls have also been associated with use of medications, and Neutel et al found a six times greater risk of falls for individuals with hyper-polypharmacy [7].

Reviewing the patients' medication is often seen as a key element in reducing inappropriate prescribing and thus in reducing adverse health outcomes, but a recent Cochrane review was unable to establish significant evidence on the effect of medication reviews for hospitalised old people. This may be because of an unclear definition of the high-risk patients who were comprised by the review [8]. One way of defining high-risk patients is by using the concept of frailty described as a condition of diminished tolerance of stress associated with a high prevalence of adverse health outcomes including both physical and cognitive decline, falls, institutionalisation and mortality [9]. In an earlier study, we found that two-thirds of acutely admitted elderly patients were frail [10].

In frail elderly people, further changes in their responses to medication will occur, and an even greater risk of adverse drug events may be observed [11]. Thus, it seems that both polypharmacy and frailty are factors that should be taken into consideration when elderly patients are assessed in the emergency department (ED) or the acute medical unit (AMU).

The primary aim of the present study was to identify if frailty and polypharmacy could predict long hospital stay, institutionalisation, readmission and death in pa-

ORIGINAL ARTICLE

1) Medical Department, Amager and Hvidovre Hospital, Amager
2) Department of Internal Medicine and Geriatrics, Herlev Hospital
3) Medical Department, Amager and Hvidovre Hospital, Amager, Denmark

Dan Med J 2016;63(9):A5274

tients aged > 65 years who were admitted to the ED or AMU. The secondary aim was to describe the prevalence of polypharmacy and hyper-polypharmacy specifically in patients suffering from the following geriatric problems: cognitive impairment, depression, delirium, malnutrition, pain and falls.

METHODS

This was a descriptive cohort study. During a 14-day period in January 2013, all patients admitted to the ED/AMU of Amager Hospital, Denmark, aged ≥ 65 years were included, regardless of diagnosis. Excluded were patients who were admitted from nursing homes due to a high Identification of Seniors at Risk (ISAR) score, as we expected that their inclusion might have biased the results.

We used the ISAR screening tool to identify frail elderly patients [12]. ISAR consists of six questions to predict functional decline and other adverse outcomes after an ED stay. The answers were Yes/No and scores ranged from zero to six points; at a score of ≥ 2 patients were considered frail and at risk of readmission and/or loss of function.

The Mobile Geriatric Team ISAR screened all included patients admitted to the ED/AMU.

Data on patient characteristics were extracted from the medical records and included age, sex, number of medications at discharge, length of stay, discharge to nursing home or rehabilitation (nursing home), readmission and mortality. From the medical records, the senior geriatrician assessed the patients' geriatric problems defined as cognitive impairment, depression, delirium, malnutrition, pain and falls, and the total number of health problems that needed treatment such as acute infections, dehydration, electrolyte balance, acute exacerbation of chronic obstructive pulmonary disease and continued treatment of chronic diseases like diabetes, heart disease and osteoporosis. Because of the patients' multi-morbidity, the total number of health problems was used rather than the primary discharge diagnoses. At the time of assessment, the ISAR score was blinded to the senior geriatrician.

Polypharmacy was defined as a prescribed regular daily intake of five or more medications. As earlier studies have found that daily use of multivitamins, vitamin D and calcium preparations increased the risk of falling [7], these supplements were included. Temporarily prescribed medications such as antibiotics were not included. Hyper-polypharmacy was defined as a prescribed regular daily intake of ten or more medications.

Statistical analyses

Patient characteristics are presented as means with standard deviation (SD) and as proportions.

Differences in patients with polypharmacy versus those without were assessed using chi-squared for categorical variables and the t-test for comparison of means. With the independent variables of interest being frailty and polypharmacy, the dependent variables were days in hospital, health problems, readmission, admission to nursing home and death. Adjusted results were calculated using backward stepwise logistic regression concerning the potential covariates age, sex and symptoms of depression, delirium, pain, fall and nutrition. Multivariate comparisons were made using logistic or linear regression. A p-value < 0.05 was considered significant. All statistical procedures were performed using SPSS for Windows, version 14.0 (SPSS Inc., Chicago, IL, USA).

Trial registration: The study was approved and registered with the Danish Data Protection Agency under the Capital Region of Denmark's joint notification of health research (j. no.: 2007-58-0015, AMH-2013-003, I-Suite no: 02495).

RESULTS

During the inclusion period, 250 patients aged ≥ 65 years were admitted to the ED/AMU. Information on medication at discharge was available for 219 patients of whom 189 were ISAR screened. We found no difference in sex, age or mean number of health problems in patients with information on medication at discharge compared with those without such information. The mean number of medications was six (SD: ± 4.13). Polypharmacy was present in 135 (62%) among whom the mean number of medication was 8.6 (SD: ± 3.34); and hyper-polypharmacy was found in 43 (20%) among whom the mean number of medications was 12.5 (SD: ± 2.88). Fifteen (7%) patients were discharged without any prescribed medications and 12 (6%) were treated with a single medication only. The distribution of medications at different ISAR scores is shown in **Table 1**. Of the 189 ISAR-screened patients, 127 (67%) were found to be frail

TABLE 1

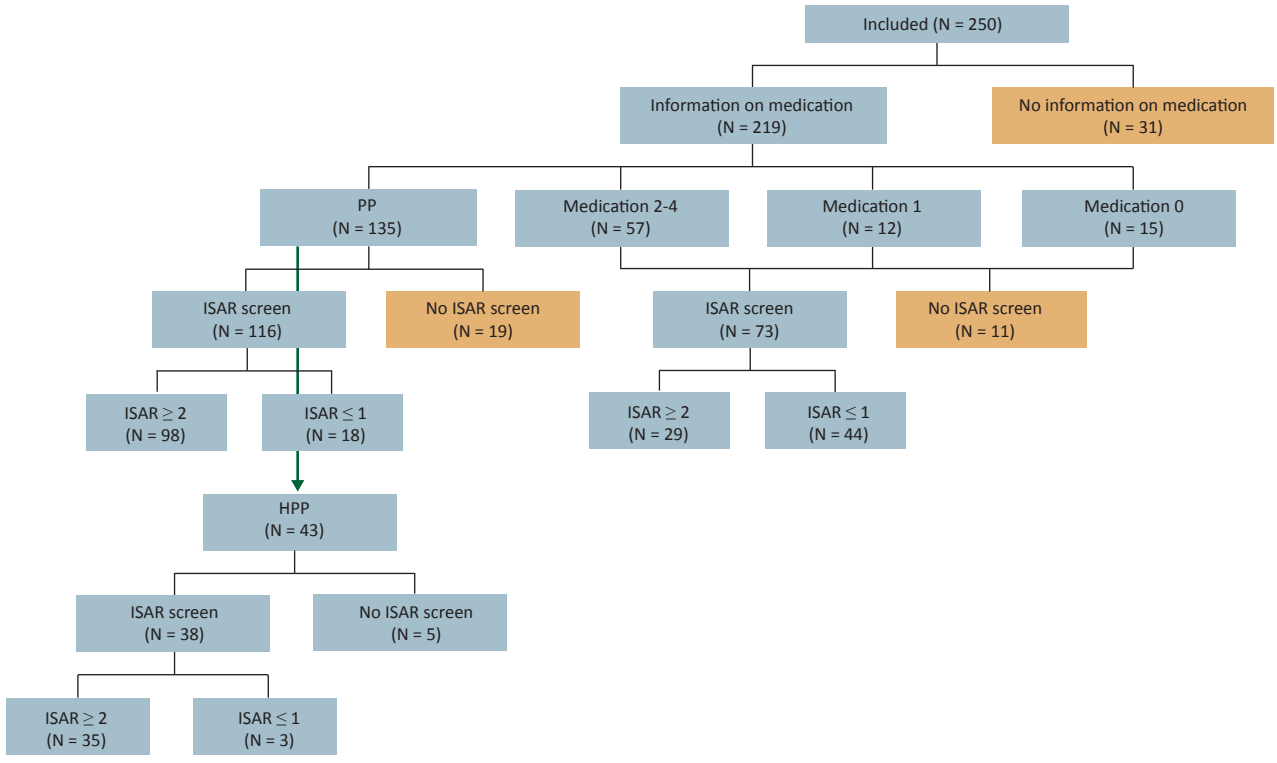
Distribution of medications on ISAR score (N = 219).

ISAR score	n	Mean (95% CI)	± SD	Min.	Max.
0	24	1.21 (0.71-1.71)	± 1.18	0	4
1	38	4.95 (3.99-5.90)	± 2.91	0	12
2	42	5.74 (4.80-6.67)	± 3.01	0	13
3	43	8.12 (6.84-9.39)	± 4.14	0	17
4	26	8.38 (6.87-9.90)	± 3.75	4	17
5	12	8.33 (6.26-10.40)	± 3.26	3	15
6	4	14.50 (2.56-26.44)	± 7.51	8	24

CI = confidence interval; ISAR = Identification of Seniors at Risk; SD = standard deviation.

FIGURE 1

Flow chart of 250 patients analysed with regard to medication and frailty.



HPP = hyper-polypharmacy; ISAR = Identification of Seniors at Risk; PP = polypharmacy

(**Figure 1**). Among these patients, 96 (51%) suffered from pain, 66 (35%) from falls, 43 (23%) from depression, 31 (16%) from malnutrition and cognitive impairment and ten (5%) from delirium (**Table 2**).

We found an increased risk of polypharmacy for women versus men (68% versus 53%) with an OR of 1.96 (95% CI: 1.13-3.41), p = 0.02. Patients with polypharmacy were significantly older than patients without (78 versus 75 years, p = 0.01) and significantly more frail patients had polypharmacy (p = 0.00).

Patients who were both frail and had polypharmacy also had significantly more health problems than patients without these two factors, 5.9 versus 2.7 p = 0.00. They also had a significantly longer stay in hospital, more discharges to nursing homes and a higher readmission rate at 30 and at 90 days (Table 2). Compared with non-frail patients with no polypharmacy, frail patients with polypharmacy were five times more likely to be readmitted at 30 days and almost eight times more likely to be admitted at 90 days. Adjusting for confounders made no difference (**Table 3**). Pain was the only confounder with a significant effect on readmission (p = 0.03). In patients who were either frail or who received polypharmacy, no difference in risk of readmission was found.

With respect to geriatric problems, we found that a significantly larger part of the patients who were both frail and had polypharmacy suffered from depression (p = 0.00), malnutrition (p = 0.02) and falls (p = 0.04) (Table 2).

DISCUSSION

In Emergency Medicine, most of the patients present with a complaint. If the symptom or complaint is specific, e.g. chest pain, the staff in the ED/AMU will enrol the patient into a well-defined management protocol. If, on the other hand, the patient arrives with nonspecific symptoms, they may be more likely not to receive immediate attention. In a recent study by Djärv et al, it was found that patients presenting with only “decreased general condition” received a low triage priority and had a threefold increased risk of in-hospital death [13]. As many elderly patients present to the ED/AMU with nonspecific symptoms, it is thus important to identify those who are at risk to ensure that they undergo geriatric assessment and receive help to prevent early death.

TABLE 2

Differences in health problems, length of stay, discharge destination, readmission and death relative to polypharmacy and frailty (N = 189).

	Non-PP + non-frail (N = 44)	Non-PP + frail (N = 29)	PP + non-frail (N = 18)	PP + frail (N = 98)	p-value
Length of stay, days, mean (± SD)	0.5 (± 1.37)	5.4 (± 6.62)	1.3 (± 2.85)	6.3 (± 7.82)	0.00
Discharged to nursing home, n (%)	0 (0)	5 (17)	1 (6)	17 (17)	0.02
Readmission within 30 days, n (%) (N = 187)[a]	4 (9)	5 (18)	3 (17)	32 (32)	0.01
Readmission within 90 days, n (%) (N = 182)[b]	5 (11)	7 (24)	5 (28)	47 (50)	0.00
Dead within 30 days, n (%)	0 (0)	1 (3)	0 (0)	1 (1)	0.52
Dead within 90 days, n (%)	0 (0)	4 (14)	0 (0)	3 (3)	0.11
Health problems, n, mean (± SD)	2.7 (± 1.98)	4.9 (± 2.19)	4.4 (± 1.81)	5.9 (± 2.63)	0.00
Geriatric problems					
Depression, n (%) (N = 43)	2 (5)	8 (18)	2 (5)	31 (72)	0.00
Cognitive impairment, n (%) (N = 31)	3 (10)	6 (19)	1 (3)	21 (68)	0.08
Malnutrition, n (%) (N = 31)	3 (10)	8 (26)	0 (0)	20 (64)	0.02
Pain, n (%) (N = 96)	22 (23)	12 (13)	7 (7)	55 (57)	0.37
Fall, n (%) (N = 66)	11 (17)	15 (23)	3 (4)	37 (56)	0.04
Delirium, n (%) (N = 10)	4 (40)	2 (20)	0	4 (40)	0.44

PP = polypharmacy; SD = standard deviation.
a) As 2 patients either died or were not discharged within 30 days.
b) As 7 patients either died or were not discharged within 90 days.

TABLE 3

Risk of readmission within 30 and 90 days in patients relative to polypharmacy and frailty[a] (N = 189).

	Non PP + frail (N = 29)		PP + non frail (N = 18)		PP + frail (N = 98)	
	OR (CI 95%)	p-value	OR (CI 95%)	p-value	OR (CI 95%)	p-value
Unadjusted model						
Readmission 30 days[c]	2.17 (0.53-8.92)	0.28	2.00 (0.40-10.01)	0.40	4.92 (1.62-14.96)	0.01
Readmission 90 days[d]	2.87 (0.81-10.25)	0.10	3.00 (0.75-12.04)	0.12	7.80 (2.82-21.52)	0.00
Adjusted model[b]						
Readmission 30 days[c]	2.27 (0.51-10.08)	0.28	1.67 (0.32-8.59)	0.54	5.04 (1.51-16.81)	0.01
Readmission 90 days[d]	2.79 (0.67-11.56)	0.17	2.79 (0.67-11.56)	0.16	7.41 (2.49-22.07)	0.00

CI = confidence interval; OR = odds ratio; PP = polypharmacy.
a) Non-frail patients not suffering from PP were chosen as reference group with OR = 1.
b) Patient outcomes were adjusted for sex, age, depression, delirium, malnutrition, fall and pain.
c) N = 187 as 2 patients either died or were not discharged within 30 days.
d) N = 182 as 7 patients either died or were not discharged within 90 days.

In our study we found that suffering from frailty and having polypharmacy significantly predicted length of stay, institutionalisation and readmission. Thus, to identify the elderly patients who must be offered geriatric assessment, it makes sense to supplement the triage with screening for frailty and the number of medications. As sex, age, depression, delirium, pain, fall and malnutrition alone may predict an adverse outcome, we conducted confounding analyses for those dimensions. When including the confounders, we still found that frailty and polypharmacy significantly predicted readmission. No significance was found concerning death, probably because of the small number of included patients. From our results, we also see that the frail elderly patients with polypharmacy have six health problems on average. This underpins the fact that they are complex patients who require an immediate multidimensional and interdisciplinary effort such as a comprehensive geriatric assessment, which may increase the patients' likelihood of remaining alive and staying in their own homes after an emergency admission to hospital [14].

For three of the geriatric problems (depression, falls and malnutrition), we found a significantly higher prevalence of both frailty and polypharmacy. This indicates that patients suffering from those problems are at particularly risk of suffering an adverse health outcome, why these patients require special attention in the ED/AMU and should be offered comprehensive geriatric assessment.

The intervention directed towards polypharmacy should include a continuing plan for future reduction of medication and maintenance of the changes in medica-

tion of the patient and it should involve the patient's general practitioner (GP). This has been found to be challenging as studies have shown that only 64% of medication changes were maintained and only 42% of the newly prescribed medicines were implemented by primary care [15, 16]. Therefore, an important focus of the intervention plan must be information and acceptance from the patient and family as well as involvement of the GP. Furthermore, the information must include a precise explanation stating which medications are changed or discontinued and why. A well-proven guidance that may be used to inform decisions to prescribe new or review existing medication is the STOPP/START criteria [17]. When using the STOPP/START criteria, a 9% reduction in adverse drug events and a three-day reduction in the length of stay were found, provided the criteria were applied within the first 72 hours of admission [18]. In patients with polypharmacy, it is crucial to consider the benefits against the potential harm for each medication, especially for preventive medication in patients with a diminished remaining life expectancy. Attention should focus not only on the number of medications, but also on the type of medications as it is known that very commonly used medications such as paracetamol and calcium preparations have side effects including an increased risk of falls in patients ≥ 65 years [19].

The limitations to our study include the relatively small number of patients in the assessed cohort due to practical limitations and the time available to us. Probably, as a result of this, we found no significant association between frailty, polypharmacy and mortality. In addition, it would have been preferable if the study had been longitudinal. On the other hand, a strength of the study is the small number of excluded patients and the new knowledge produced concerning the significance of combining frailty and polypharmacy in predicting readmission of the patients within a short time after their discharge from hospital.

The findings of the present study suggest that initial triage in the ED/AMU must be supplemented with assessment of both polypharmacy and frailty to ensure that frail patients are admitted. Thus, we suggest an immediate comprehensive geriatric assessment carried out by the Mobile Geriatric Team of patients suffering from both frailty and polypharmacy.

Today's ED/AMU treatment seems to be aimed primarily at the acute problems, and an early date of discharge in itself often becomes the most important goal of the intervention. When frailty screening at admission is followed by assessment by the Mobile Geriatric Team, an early intervention is possible, including the preparation of a solid long-term plan for medication alterations that includes continued contact with the patients, their families and primary care to ensure the maintenance and any necessary changes to the plan.

Combining the Identification of Seniors at Risk instrument with observations on polypharmacy in the emergency department/acute medical unit predicts a longer hospitalisation, greater risk of being discharged to institutions and readmission.

The high rates of readmissions tells us very clearly that our plans for intervention at discharge from hospital fail for every other patient, and future studies are warranted to ascertain the possible effect of the described geriatric assessment and intervention in the ED/AMU followed by long-term intervention in cooperation with primary care.

CONCLUSION

In this study we found a high prevalence of polypharmacy in patients suffering from geriatric problems and established that by using the ISAR instrument and combining it with observations on polypharmacy in the ED/AMU we can predict a longer hospitalisation, greater risk of being discharged to institutions and readmission within 30 and 90 days. We therefore suggest that the triage process in the ED/AMU is supplemented with frailty and polypharmacy screening.

Patients afflicted with both conditions should then be immediately assessed by the Mobile Geriatric Team who should draw up an intervention plan addressing the patient's most pressing acute needs. The assessment should also include a robust long-term plan that should be accepted by both the patient and the family and which should involve primary care and include follow-up by the Mobile Geriatric Team to ensure that any needed alterations and maintenance of the plan were in place. The monitoring by the Mobile Geriatric Team should remain in place for more than 90 days to prevent readmission of the patient.

CORRESPONDENCE: *Elizabeth Rosted.* E-mail: eros@regionsjaelland.dk
ACCEPTED: 21 June 2016

CONFLICTS OF INTEREST: Disclosure forms provided by the authors are available with the full text of this article at www.danmedj.dk

LITERATURE

1. Fortin M, Stewart M, Poitras ME et al. A systematic review of prevalence studies on multimorbidity: toward a more uniform methodology. Ann Fam Med 2012;10:142-51.
2. Lægehåndbogen. Polyfarmaci blandt ældre. The Danish Regions and the five regions, Online medical encyclopaedia being a part of the National Danish eHealth Portal: sundhed.dk, 2014. www.sundhed.dk/sundhedsfaglig/laegehaandbogen/geriatri/tilstande-og-sygdomme/behandling/polyfarmaci-hos-aeldre/ (29 Sep 2014).
3. Gnjidic D, Hilmera SN. Use of potentially inappropriate medications in the care of frail older people. Aging Health 2010;6:505-716.
4. Frazier SC. Health outcomes and polypharmacy in elderly individuals: an integrated literature review. J Gerontol Nurs 2005;31:4-11.
5. Jensen GL, Friedmann JM, Coleman CD et al. Screening for hospitalization and nutritional risks among community-dwelling older persons. AM J Clin Nutr 2001;74:201-5.
6. Gnjidic D, Hilmera SN, Blyth FM et al. Polypharmacy cutoff and outcomes: five or more medicines were used to identify community-dwelling older men at risk of different adverse outcomes. J Clin Epidemiol 2012;65:989-95.
7. Neutel CI, Perry S, Maxwell C. Medication use and risk of falls. Pharmacoepidemiol Drug Saf 2002;11:97-104.
8. Christensen M, Lundh A. Medication review in hospitalised patients to reduce morbidity and mortality. Cochrane Database Syst Rev 2013;2: CD008986.
9. Walston J, Hadley EC, Ferrucci L et al. Research agenda for frailty in older adults: Toward a better understanding of physiology and etiology: Summary from the American Geriatrics Society/National Institute on Aging Research Conference on Frailty in Older Adults. J Am Geriatr Soc 2006; 54:991-1001.
10. Rosted E, Schultz M, Dynesen H et al. The Identification of Seniors at Risk screening tool is useful for predicting acute readmissions. Dan Med J 2014;61(5):A4828.
11. Drljevic-Nielsen A, Laursen T. Polypharmacy to the elderly prevails. Ugeskr Læger 2015;177:V08140461.
12. McCusker J, Bellavance F, Cardin S et al. Detection of older people at increased risk of adverse health outcomes after an emergency visit: the ISAR screening tool. J Am Geriatr Soc 1999;47:1229-37.
13. Djärv T, Castrén M, Mårtenson L et al. Decreased general condition in the emergency department: high in-hospital mortality and a broad range of discharge diagnoses. Eur J Emerg Med 2015;22;4:241-6.
14. Ellis G, Whitehead MA, Robinson D et al. Comprehensive geriatric assessment for older adults admitted to hospital: meta-analysis of randomised controlled trials. BMJ 2011;343:d6553.
15. Larsen MD, Rosholm JU, Hallas J. The influence of comprehensive geriatric assessment on drug therapy in elderly patients. Eur J Clin Pharmacol 2014;70:233-9.
16. Williams ME, Pulliam CC, Hunter R et al. The short-term effect of interdisciplinary medication review on function and cost in ambulatory elderly people. J Am Geriatr Soc 2004;52:93-8.
17. O'Mahony D, O'Sullivan D, Byrne S et al. STOPP/START criteria for potentially inappropriate prescribing in older people: version 2. Age Ageing 2015;44:213-8.
18. Ziere G1, Dieleman JP, Hofman A et al. Polypharmacy and falls in the middle age and elderly population. Br J Clin Pharmacol 2006;61:218-23.
19. Gnjidic D, Hilmer SN, Blyth FM et al. High-risk prescribing and incidence of frailty among older community-dwelling men. Clin Pharmacol Ther 2012;91:521-8.