INTRODUCTION

Cardiovascular diseases are the main cause of drug prescription and death in western countries. In the therapeutic arsenal, loop diuretics and particularly furosemide, are the most frequently used, especially for heart failure (HF). Its main indications concern oedematous complications of renal, liver and mostly HF. Indeed, diuretics are still the only efficient therapy for fluid retention. However, though acute HF is a universally accepted indication of furosemide, its use is not recommended in the absence of congestive signs, because it induces iatrogenic effects, especially in elderly people. Indeed, the chronic use of furosemide appears to be associated with increased long-term mortality in elderly people population, and is associated with worsening renal function, electrolyte disorders, urinary urgency and incontinence, myocardial fibrosis, ototoxicity, osteoporosis and fractures, orthostatic hypotension and falls.

Summary

Objective: Little is known about furosemide prescription modalities in elderly people. We describe furosemide prescription in ambulatory elderly patients.

Methods: All patients aged over 80 years, affiliated to Mutualité Sociale Agricole de Bourgogne, a French regional health insurance plan, with a medical prescription delivered in March 2015, were retrospectively included.

Results: Among 15 141 patients with a median age of 86 years, comprising 61.3% of women, 3937 patients (26%) had a prescription for furosemide. Severe heart failure was the most common chronic comorbidity (27.7%). Furosemide was considered a long-term therapy for almost all patients (98.7% with prescriptions for 3 months or more). Recommended indications for long-term furosemide therapy included severe heart failure (50.9%), chronic nephropathy (3%) and cirrhosis (0.1%). The furosemide prescription rate increased with age (81-85: 20.4%, 86-90: 28.5%, 91-95: 35.6%, >95: 42.7%, P<.001), and the increase was associated with a decrease in recommended heart failure therapeutics (beta-blockers, angiotensin-conversion-enzyme-inhibitors or angiotensin-receptor-blockers). Prescribers were mostly general practitioners (81.3%). Plasma electrolytes were controlled in less than a half of the patients with furosemide.

Conclusions: In this large study, long-course furosemide was prescribed in a quarter of ambulatory patients. Half of those taking furosemide suffered from severe heart failure. Age was associated with a linear increase in furosemide use and a decrease in recommended heart failure therapeutic prescriptions. A large part of these prescriptions do not seem to be in accordance with recommendations.
In the European Society of Cardiology (ESC) guidelines for the management of HF, furosemide is indicated to relieve the symptoms and signs of congestions, in association with a beta-blocker and an angiotensin conversion enzyme inhibitor (ACEI) or an angiotensin receptor blocker (ARB) if the ACEI is not tolerated. To date, this is the only therapeutic strategy able to modify the course of systolic HF and to decrease mortality. However, previous large-scale surveys in both primary and secondary care have shown that a majority of older patients do not receive these recommended agents, whereas furosemide was prescribed in more than 80% of patients, and age was an independent factor of suboptimal prescription. Other loop diuretics are only marginally prescribed in France. Despite the very high furosemide prescription rate, few data to date concern this very old ambulatory population. Yet, this population is specific in terms of prescription practices, the frequency of comorbidities and tolerance. There is a need to confront “real-life” large population data with recommendations to improve pharmacological care in this growing, frail, elderly population.

The aim of this study was thus to describe furosemide prescription modalities, indications and concordance with the recommendations in a large population of ambulatory very elderly patients.

2 | METHOD

2.1 | Study design

This observational retrospective study was conducted from the 1st to the 31st of March, 2015, based on existing databases of a French regional health insurance plan (Mutualité Sociale Agricole de Bourgogne, MSA).

The study was conducted in accordance with the Declaration of Helsinki and National standards. The Ethics Committee of our institution was consulted; however, because this was an observational study with no modification in the management of participants, its approval was not necessary.

2.2 | Population

The population consisted of all MSA-affiliated patients, aged over 80, living in Burgundy, who had been given a medical prescription (MP) during the study period. Two groups were constituted: a group of patients with a prescription for furosemide (FG) and a group of patients without furosemide (noFG).

2.3 | Collected Data

2.3.1 | Data concerning all patients

For each enrolled subject, the demographic characteristics, including gender and age, were collected. Registered chronic diseases (RCD), according to the 10th edition of the International Statistical Classification of Diseases and related Health Problems, for which medical expenses are reimbursed by the French national health insurance agency, in accordance with French law, were recorded. Among these, potential indications for furosemide, according to the summary of product characteristics (SPCs) and to the European recommendations were identified. Cardiovascular co-prescriptions, ie, beta-blockers, ACEI, ARB, calcium channel blockers, nitrate derivatives and other diuretics, were collected.

2.3.2 | Data concerning patients with furosemide

For FG, the following data were also collected: Duration of furosemide prescription, speciality of the prescriber, plasma electrolyte tests carried out during the inclusion period or the two preceding months (January to March 2015).

2.4 | Statistical analysis

Categorical variables were described as numbers and percentages while quantitative variables were described as means and standard deviations in cases of normal distribution or medians and interquartile ranges (IQR) otherwise.

The descriptive analysis was used to describe the two groups (FG and noFG). These two groups were compared regarding age ranges, mean age, gender, existence of one or more RCD, frequency of most common RCD, number of drugs per MP, cardiovascular co-prescriptions (ie, beta-blockers, ACEI, ARB, calcium channel blockers, nitrate derivatives, aldactone and thiazide diuretics, antiplatelet agents and anticoagulants, statins).

In bivariate analysis, data were compared using the chi-square test for categorical variables and the analysis of variance for quantitative variables. Statistical significance was defined for $P<.05$.

3 | RESULTS

Altogether, 15 141 patients aged over 80 years were included. Among these, 3937 (26%) had received furosemide (FG) and 11 204 (74%)
had not received furosemide (noFG). Table 1 reports the characteristics of the two groups.

### 3.1 Characteristics of the two groups

Compared with noFG patients, FG patients were older (median age [IQR]: 87 [84-90] vs 86 [83-89] years, \( P < .001 \)), more frequently male (43.5% vs 37%, \( P < .001 \)) and more frequently had one or more RCD (83.7% vs 62.9%, \( P < .001 \)).

### 3.2 Furosemide indications

Among potential furosemide indications, severe HF was the most frequent RCD in both groups, but more frequent in FG (50.9%) than in noFG patients (19.5%, \( P < .001 \)). Chronic nephropathy was more frequent in patients in FG than in noFG patients (3.0 vs 0.7, \( P < .001 \)). Active chronic liver disease or cirrhosis represented less than 1% of patients in both groups (0.1 vs 0.2, \( P = .4 \)).

### 3.3 Other chronic diseases

Other RCD associated with furosemide prescription included severe arterial hypertension, coronary disease, diabetes, peripheral artery disease with ischemic manifestations, Alzheimer disease and other dementias (\( P < .001 \) for all), severe chronic respiratory failure (\( P = .001 \)) and disabling stroke (\( P = .009 \)). Neoplasia or hematologic malignancy, severe rheumatoid polyarthritis and Parkinson disease were not significantly associated with furosemide prescription. Psychosis and mental retardation were less frequent in the FG than in the noFG (\( P = .03 \)).

### 3.4 Furosemide prescription rates according to age and gender

As shown in Figure 1, the percentage of patients with furosemide increased with increasing age range (81-85: 20.4%, 86-90: 28.5%, 91-95: 35.6%, >95: 42.7%, \( P < .001 \)). Furosemide prescription was less frequent in women (24%) than in men (29.2%, \( P < .001 \)).

### 3.5 Cardiovascular co-prescriptions

The mean number of co-prescriptions was 6.8±3 in the FG and 4.7±2.6 in the noFG (\( P < .001 \)). Table 2 reports cardiovascular co-prescriptions in the FG and noFG. Concerning HF therapy, beta-blockers and ACEI were more frequently prescribed in the FG than in the noFG (41.1% vs 25.5% for beta-blockers and 28.8% vs 17.6% for ACEI, respectively, \( P < .001 \) for both), but the frequency of ARB prescription was similar in both groups (21.9% vs 21.5%, \( P = .4 \)).

| TABLE 1 | Demographic data and registered chronic diseases (RCD): comparison between the furosemide and no furosemide group |
|---------|----------------------------------------------------------------------------------------------------------------|
|         | Group | FG (N=3937) | noFG (N=11204) | \( P \)-value |
| Median age (years) | FG | 87 | 85 | <.0001 |
| Women | FG | 2226 (56.5) | 7057 (63.0) | <.0001 |
| No RCD | FG | 642 (16.3) | 4155 (37.1) | <.0001 |
| RCD | FG | 1058 (26.9) | 1791 (16) | <.0001 |
| Severe heart failure | FG | 991 (25.2) | 1585 (14.1) | <.0001 |
| Coronary disease | FG | 808 (20.5) | 1681 (15) | <.0001 |
| Diabetes | FG | 733 (18.6) | 2146 (19.1) | 0.46 |
| Neoplasia or Hematologic malignancy | FG | 329 (8.4) | 729 (6.5) | <.0001 |
| Peripheral artery disease with ischemic manifestations | FG | 265 (6.7) | 270 (2.4) | .001 |
| Disabling Stroke | FG | 229 (5.8) | 533 (4.8) | .009 |
| Alzheimer disease and other dementia | FG | 205 (5.2) | 892 (8) | <.0001 |
| Psychosis and mental retardation | FG | 123 (3.1) | 437 (3.9) | 0.03 |
| Parkinson disease | FG | 81 (2.1) | 242 (2.2) | 0.7 |
| Severe rheumatoid arthritis | FG | 58 (1.5) | 163 (1.4) | 0.9 |
| Other | FG | 62 (1.6) | 216 (1.9) | 0.2 |

FG, group of patients with furosemide; noFG, group of patients without furosemide; N, number; RCD, Registered Chronic Disease. *RCD that were not potential indications for furosemide and that affected less than 1% of patients are not shown. Unless specified, data are expressed as numbers (%).
As shown in Figure 1, the percentage of patients with beta-blockers on the one hand and ACEI or ARB on the other hand decreased with increasing age range (for beta-blockers, 81-85: 29.7%, 86-90: 30%; 91-95: 26.9%; >95: 18.7%; for ACEI/ARB, 81-85: 43.8%, 86-90: 42.7%, 91-95: 36.5%, >95: 34.5%; P <.001 for both).

Concerning other cardiovascular therapies, statins, antiplatelet agents, anticoagulants, nitrate derivatives (P <.001 for all) and calcium channel blockers (P = .007) prescriptions were associated with furosemide prescription, whereas the prescription of other diuretics (aldactone, thiazide diuretics) correlated inversely with furosemide prescription (P <.001).

### 3.6 Modality of furosemide prescriptions

As shown in Table 3, furosemide was prescribed for less than 3 months in 52 patients (1.3%), between 3 and 12 months in 408 patients (10.3%), and for more than 12 months in 3477 patients (88.4%).
TABLE 3  Furosemide prescription modalities

| Parameter                      | N (%)         |
|--------------------------------|---------------|
| Prescription duration (months) |               |
| <3                            | 52 (1.3)      |
| 3–6                           | 124 (3.1)     |
| 6–12                          | 284 (7.2)     |
| 12–24                         | 703 (17.9)    |
| >24                           | 2774 (70.5)   |
| Prescriber speciality          |               |
| General Medicine               | 3202 (81.3)   |
| Cardiology                     | 143 (3.6)     |
| Pneumology                     | 6 (0.1)       |
| Nephrology                     | 5 (0.1)       |
| Other                          | 30 (0.8)      |
| Not identified                 | 551 (14)      |
| Electrolyte panel over 3 months|               |
| None                           | 2027 (51.5)   |
| One                            | 1820 (46.2)   |
| Two or more                    | 90 (2.3)      |
| Total                          | 3937          |

Data are expressed as numbers (%).

Furosemide prescribers were mostly general practitioners (for 81.3% of patients) followed by cardiologists (3.6%). The prescriber speciality was not identified in 14% of cases.

Among the 3937 patients of the FG, a plasma electrolyte test was done in 46.2% of cases during the study month or the 2 months preceding the study (January to March 2015). Two electrolyte tests or more were done in 90 patients (2.3%). Among the patients with a new furosemide prescription (prescription duration <3 months), 26 (50%) had an electrolyte test vs 1884 (48.5%) among patients with a long furosemide prescription (≥3 months).

4 | DISCUSSION

To our knowledge, this study on furosemide prescriptions in an ambulatory elderly population is unique for both its size and the very advanced age of the patients.

The first main result is the chronic use of furosemide in a quarter of our study population, among whom half had no recommended indication according to their RCD and recent recommendations.4,18–20 These results are consistent with previous studies, which showed the same rate of furosemide prescription in western geriatric series.2,21–23 Second, most of these patients had severe cardiovascular comorbidities, including severe HF in about a half of the patients with a furosemide prescription. Third, furosemide prescription increased with age; it concerned 20.4% of patients aged 81–85 and reached 42.7% for patients aged over 95. This confirms previous results.2,21,22 Fourth, this age-related overuse of furosemide was associated with the abandon of medications that improve the long-term prognosis of HF (beta-blockers, ACEI, ARB).21,24

In our study, only 41% of patients with furosemide received a beta-blocker and 29% an ACEI. However, these therapeutics are systematically recommended in chronic HF.4 Only half of the patients with furosemide were given one or both of these drugs. Thus, our results confirm previous studies highlighting inappropriate pharmacologic care of chronic HF in elderly people,23 with an overuse of diuretics and an underuse of recommended long-term protective therapies. The outcome of suboptimal management could be not only increased mortality but also repeated hospitalisations, increased dependency and institutionalization.8

The duration of furosemide prescription suggests that it is considered a long-term treatment in ambulatory elderly patients. However, a carefully guided intermittent diuretic treatment modality, rather than chronic continuous prescription, may be preferable for these patients.2,8 In such a strategy, furosemide should be stopped as soon as the congestive signs disappear, while preventive treatments should continue (beta-blockers, ACEI, ARB).6

An explanation for this non-compliance with current clinical guidelines in the therapeutic management of HF in elderly people may be their inappropriateness, as there are no specific recommendations for the therapeutic management of HF in frail elderly patients,25 and medical management of older patients is frequently based on the extrapolation of evidence obtained in younger patients.5 The present findings in a population of frail elderly individuals may reflect difficult applications of the recommendations to these patients. Indeed, the recommendations do not take into account the specificities of the very old, particularly the frequency of comorbidities and co-medications, or the predominance of preserved systolic function HF, for which drug classes that improve outcomes in systolic HF have not demonstrated a similar benefit.26 The challenge ahead is to establish age-specific clinical evidence so as to improve the pharmacotherapy of chronic HF in elderly patients in everyday practice.

One reason for inappropriate pharmacologic care among older patients with chronic HF may be that practitioners are reluctant to add long-term protecting therapies and to supress diuretics after the acute phase of HF in frail patients whose condition is clinically stabilized, and by so doing to expose them to the potential adverse effects of new treatments. Nevertheless, a former study showed that diuretic therapy could safely be withdrawn for a large proportion of very old geriatric patients, regardless of the initial indications,5 thus protecting them from the above-mentioned furosemide complications and adverse effects. In addition, congestive signs, especially lower-limb oedema, are particularly frequent among older patients, but are not specific to HF.27 It is not always easy to affirm their cardiac origin in ambulatory medicine, because of the limited access to confirmatory diagnostic tools (eg, echocardiography). This leads to palliative pharmacologic care, limited to symptom reduction.

Another interesting result of this study is the lack of biological control of furosemide tolerance. Indeed, in the FG, a plasma electrolyte test was done in less than half of the patients during the month of the study or the 2 months preceding the study. Only a half of the
new prescriptions (ie, initiated less than 3 months earlier) were associated with an electrolyte control. Gérardin-Marais et al already reported no biological monitoring for 22.8% of patients during 1 year of diuretic treatment in an ambulatory cohort of subjects aged 75 or more. Surprisingly, SPCs do not specify how often a plasma electrolyte control should be monitored, but the monitoring of plasma sodium and potassium, and renal function is consensually required. 30 as electrolyte disturbances are frequent during furosemide treatment. 8 Indeed, furosemide induces hypokalemia (up to 8%), especially in elderly people 16 which can cause not only cardiac arrhythmia and sudden death, but also muscle weakness. Hyponatremia (up to 17%) may contribute to confusion, thus exacerbating age-related cognitive disorders. 8

The mean number of drugs in this study (6.8) is similar to that in another study conducted in 2012 in the same cohort, 29 but is less than that in other geriatric studies. 30 However, this is an ambulatory population and the polypharmacy rate is expected to be lower than in hospitalized patients or nursing home residents. 31 Furthermore, as this study concerns patients older than 80, the lower polypharmacy rate can be explained by the very advanced age. Indeed, a decline in polypharmacy in people older than 85 has been described, and might be explained by doctors’ fears of age-related side effects, 32 or by the abandon of preventive medications with age, as suggested in our study. Thus, the potentially inappropriate use of furosemide appears to be particularly frequent, even in a population relatively sheltered from polypharmacy.

Some limitations of our study need to be acknowledged. The first is its retrospective design, which meant it was impossible to assess the impact of furosemide on the quality of life, morbidity, or mortality of the studied population. Second, to estimate the frequency of comorbidities, we studied the RCD, and the medical history may have been underestimated because of non-declaration. However, as it is necessary to declare RCD to obtain the complete reimbursement of healthcare expenditure in France, we believe that our results reflect the real frequency of severe comorbidities, and these rates are in agreement with the literature. 1 Third, we did not know the specific indication for which furosemide was prescribed. An unknown proportion of prescriptions could have been made outside the approved indications, in particular as an antihypertensive agent or for venous insufficiency. Furthermore, some potential indications, including hypertension with a glomerular filtration rate <30 mL/min 33 and rare situations of ambulatory management of hyperkalemia 34 and hypercalcemia 35 by increased urinary excretion, have not been taken into account either.

Finally, our results reflect the prescribing attitudes of physicians in Burgundy, and these may differ from those in other countries. However, available evidence suggests that France is by no means different from other western countries with regard to cardiovascular treatment. 3

5 | CONCLUSION

This study of a representative very old population highlights the high frequency of furosemide prescription, especially among frailer older patients with cardiovascular comorbidities. Severe HF was the main indication. Chronic furosemide use increased steadily with increasing age while therapeutics to improve the long-term prognosis (beta-blockers, ACEI, ARB) were simultaneously abandoned. Specific data concerning the therapeutic management of HF among older patients, which is a growing public health issue, are urgently needed.

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DISCLOSURE

None.

REFERENCES

1. Go AS, Mozaffarian D, Roger VL, et al. Heart disease and stroke statistics–2013 update: a report from the American Heart Association. Circulation. 2013;127:e6-e245.
2. van Kraaij DJ, Jansen RW, Bruijns E, Gribnau FW, Hoeftagels WH. Diuretic usage and withdrawal patterns in a Dutch geriatric patient population. J Am Geriatr Soc. 1997;45:918-922.
3. Komajda M, Follath F, Swedberg K, et al. The EuroHeart Failure Survey programme—a survey on the quality of care among patients with heart failure in Europe. Part 2: treatment. Eur Heart J. 2003;24:464-474.
4. McMurray JJV, Adamopoulos S, Anker SD, et al. ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012: the Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC. Eur Heart J. 2012;33:1787-1847.
5. Cheng JWM, Nayar M. A review of heart failure management in the elderly population. Am J Geriatr Pharmacother. 2009;7:233-249.
6. Dini FL, Ghio S, Klersy C, et al. Effects on survival of loop diuretic dosing in ambulatory patients with chronic heart failure using a propensity score analysis. Int J Clin Pract. 2013;67:656-664.
7. Ahmed A, Husain A, Love TE, et al. Heart failure, chronic diuretic use, and increase in mortality and hospitalization: an observational study using propensity score methods. Eur Heart J. 2006;27:1431-1439.
8. Wehling M. Morbus diureticus in the elderly: epidemic overuse of a widely applied group of drugs. J Am Med Dir Assoc. 2013;14:437-442.
9. Baglin A, Boulard JC, Hanslik T, Prinseau J. Metabolic adverse reactions to diuretics. Clinical relevance to elderly patients. Drug Saf. 1995;12:161-167.
10. Zuccalà G, Pedone C, Cocchi A, et al. Older age and in-hospital development of hypokalemia from loop diuretics: results from a multicenter survey. GIFA Investigators. Multicenter Italian Pharmacoepidemiologic Study Group. J Gerontol A Biol Sci Med Sci. 2000;55:M232-M238.
11. Ekundayo OJ. The association between overactive bladder and diuretic use in the elderly. Curr Urol Rep. 2009;10:434-440.
12. Lópéz B, Querejeta R, González A, Sánchez E, Larmán M, Díez J. Effects of loop diuretics on myocardial fibrosis and collagen type I turnover in chronic heart failure. J Am Coll Cardiol. 2004;43:2028-2035.
13. Rybak LP. Ototoxicity of loop diuretics. Otolaryngol Clin North Am. 1993;26:829-844.
14. Xiao F, Qu X, Zhai Z, et al. Association between loop diuretic use and fracture risk. Osteoporos Int J. 2015;26:775-784.
15. Rejmark L, Vestergaard P, Heickendorff L, Andreasen F, Moselidde L. Loop diuretics increase bone turnover and decrease BMD in osteopenic postmenopausal women: results from a randomized controlled study with bumetanide. J Bone Miner Res. 2006;21:163-170.
16. Poon IO, Braun U. High prevalence of orthostatic hypotension and its correlation with potentially causative medications among elderly veterans. J Clin Pharm Ther. 2005;30:173-178.
17. Cleland JGF, Cohen-Solal A, Aguilar JC, et al. Management of heart failure in primary care (the IMPROVEMENT of Heart Failure Programme): an international survey. Lancet. 2002;360:1631-1639.
18. European Association for the Study of the Liver. EASL clinical practice guidelines on the management of ascites, spontaneous bacterial peritonitis, and hepatorenal syndrome in cirrhosis. J Hepatol. 2010;53:397-417.
19. Mancia G, Fagard R, Narkiewicz K, et al. 2013 ESH/ESC Guidelines for the management of arterial hypertension: the Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). J Hypertens. 2013;31:1281-1357.
20. Go AS, Bauman MA, Coleman King SM, et al. An effective approach to high blood pressure control: a science advisory from the American Heart Association, the American College of Cardiology, and the Centers for Disease Control and Prevention. J Am Coll Cardiol. 2014;63:1230-1238.
21. Wastesson JW, Parker MG, Fastbom J, Thorslund M, Johnell K. Drug use in centenarians compared with nonagenarians and octogenarians in Sweden: a nationwide register-based study. Age Ageing. 2012;41:218-224.
22. Onder G, Gambassi G, Landi F, et al. Trends in antihypertensive drugs in the elderly: the decline of thiazides. J Hum Hypertens. 2001;15:291-297.
23. Litaker JR, Chou JY. Patterns of pharmacologic treatment of congestive heart failure in elderly nursing home residents and related issues: a review of the literature. Clin Ther. 2003;25:1918-1935.
24. Bungard TJ, McAlister FA, Johnson JA, Tsuyuki RT. Underutilization of ACE inhibitors in patients with congestive heart failure. Drugs. 2001;61:2021-2033.
25. Wehling M. Guideline-driven polypharmacy in elderly, multimorbid patients is basically flawed: there are almost no guidelines for these patients. J Am Geriatr Soc. 2011;59:376-377.
26. Senni M, Paulus WJ, Gavazzi A, et al. New strategies for heart failure with preserved ejection fraction: the importance of targeted therapies for heart failure phenotypes. Eur Heart J. 2014;35:2797-2815.
27. Damy T, Kallvikbacka-Bennett A, Zhang J, et al. Does the physical examination still have a role in patients with suspected heart failure? Eur J Heart Fail. 2011;13:1340-1348.
28. Gérardin-Marais M, Victorri-Veyrac C, Allain-Veyrac G, et al. Diuretic drug therapy monitoring in the elderly: a cohort study. Eur J Clin Pharmacol. 2008;64:433-437.
29. Manckoundia P, Lorenzini M, Disson-Dautriche A, et al. Assessment of the use of hypolipidemic agents (HAs), mainly statins, in elderly subjects aged 80 years and more in Burgundy: analysis of 13,211 patients. Arch Gerontol Geriatr. 2012;55:101-105.
30. Sánchez-Fidalgo S, Guzmán-Ramos MI, Galván-Banqueri M, Bernabéu-Wittel M, Santos-Ramos B. Prevalence of drug interactions in elderly patients with multimorbidity in primary care. Int J Clin Pharm. 2017;39:343-353.
31. Cojutti P, Arnoldo L, Cattani G, Brusaferro S, Pea F. Polytherapy and the risk of potentially inappropriate prescriptions (PIPs) among elderly and very elderly patients in three different settings (hospital, community, long-term care facilities) of the Friuli Venezia Giulia region, Italy: are the very elderly at higher risk of PIPs? Pharmacoepidemiol Drug Saf. 2016;25:1070-1078.
32. Nobili A, Licata G, Salerno F, et al. Polypharmacy, length of hospital stay, and in-hospital mortality among elderly patients in internal medicine wards. The REPOSI study. Eur J Clin Pharmacol. 2011;67:507-519.
33. Chapter 2: lifestyle and pharmacological treatments for lowering blood pressure in CKD ND patients. Kidney Int Suppl. 2012;2:347-356.
34. Sterns RH, Grief M, Bernstein PL. Treatment of hyperkalemia: something old, something new. Kidney Int. 2016;89:546-554.
35. LeGrand SB, Leskuski D, Zama I. Narrative review: furosemide for hypercalcemia: an unproven yet common practice. Ann Intern Med. 2008;149:259-263.

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