Patient Preference and Adherence

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ORIGINAL RESEARCH

Identification of drug-related problems of elderly patients discharged from hospital

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Background: Drug-related problems (DRP) following hospital discharge are common among elderly patients using multiple drugs for the treatment of chronic diseases. The aim of this study was to investigate the occurrence of DRP in these patients using a specific tool for the identification of DRP by community pharmacists.

Methods: An observational study involving 340 patients aged over 60 years using at least five prescription drugs and discharged from hospital. The occurrence of DRP was assessed by means of an identification tool specifically developed for use by community pharmacists, including a semistructured patient interview and a checklist of common DRP.

Results: In total, 992 potential DRP were observed in the 340 patients (mean 2.9 ± 1.7). No drug prescribed but clear indication, an unnecessarily long duration of treatment, dose too low, and incorrect drug selection were the DRP most commonly observed. Ten percent of DRP occurring in 71 patients were drug–drug interactions. The number of DRP was related to the number of drugs prescribed. Frequently occurring DRP found using the patient interview were fear of side effects and no or insufficient knowledge of drug use. Medication of patients discharged from the pulmonary department and of those with type 2 diabetes was particularly associated with occurrence of DRP.

Conclusion: Following hospital discharge, DRP occur frequently among elderly patients using five or more drugs for the treatment of chronic disease. The number of DRP increased with the number of drugs used. An important task for community pharmacists is to identify, resolve, and prevent the occurrence of DRP among this patient group. Since DRP are associated with an increased risk of hospital readmissions, morbidity, and mortality, it is very important to develop intervention strategies to resolve and prevent DRP.

Keywords: drug-related problems, elderly, discharge from hospital, community pharmacy

Introduction

The global population is aging. In 1950, there were 205 million people aged 60 years and older and this number is expected to increase to nearly 2 billion in 2050.[1] Particularly for the treatment of chronic diseases, elderly patients were found to use about three times more drugs than younger patients.[2] They are therefore at a higher risk of experiencing drug-related problems (DRP).[3–6] DRP described in the literature include contraindications, drug–drug interactions, adverse drug reactions, prescription errors, and noncompliance with drug use.[2,7–10] With respect to older patients with comorbidities and using multiple drugs, DRP are associated with an increased risk of hospital readmissions, morbidity, and mortality.[11,12] Discharge of patients from the hospital setting to home care is another important risk factor for DRP.[13]

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Lack of continuity of care and discontinuity of medication following inadequate transfer of information between hospital and primary care, especially in the event of changes in the drug regimen, were found to be major underlying causes.[14–16]

Several explicit criteria have been developed to identify DRP among older patients with chronic diseases.[17–20] Explicit criteria, occasionally combined with other measures, are also used as tools to conduct medication reviews.[21] After their introduction in the US in 1991, the Beers' criteria listing drugs inappropriate for elderly patients and adapted sets in various countries, have been revised and refined.[18,19,22] STOPP (Screening Tool of Older Person's Prescriptions)/START (Screening Tool to Alert doctors to Right Treatment) criteria have addressed several shortcomings of the Beers' criteria, including detection of undertreatment, inclusion of drugs not available outside the US, and lack of physiologic categorization.[18,19,23] However, these tools appear less useful in identifying DRP among older patients, since medical status and clinical parameters are not taken into account. Moreover, these evaluations do not consider patients' experience of their treatment.[24–27] With the aim to facilitate the identification of DRP among these patients, we have developed a tool consisting of a checklist of commonly occurring DRP and a semistructured patient interview to support the performance of a medication review (Mast et al, unpublished data, 2013).

Few studies have assessed the frequency and specific nature of DRP among older patients with multiple drug use discharged from hospital. Probably due to differences in setting, patient characteristics, and measures addressing possible DRP, the results of these studies are also inconsistent.[28,29] In order to develop effective interventions to identify and address these DRP, it is very important to get more insight into the specific nature of DRP in this specific patient group and determinants of their occurrence. The aim of the present study was to investigate the nature and frequency of prescriber-related and patient-experienced DRP among older patients using multiple chronic drugs on discharge from hospital. The effect of determinants on the occurrence of these DRP was also studied.

Materials and methods

Setting and participants

This observational study was conducted with patients discharged from academic and nonacademic hospitals in the Amsterdam area. In total, eight hospitals were involved, of which two were academic and six were nonacademic. Twenty-three community pharmacists serving patients in the region participated. The present observational study, analyzing baseline data, was part of a randomized controlled study of the effect of medication review by community pharmacists on the occurrence of DRP among elderly patients discharged from hospital. The design of this trial, as approved by the ethical committee of the VU University Medical Center in 2007, has been described previously.[30]

Patients aged 60 years or older, using five or more chronic drugs, and discharged from hospital in the period from 2008 to 2010, were asked to participate by their community pharmacist. Patients using five of more chronic drugs were selected because polypharmacy is generally defined as five or more chronic drugs. Each community pharmacy aimed to include 15–20 patients. Patients discharged from psychiatric or oncology departments were excluded, because less common DRP were expected in these patient groups. Those discharged to a nursing home and those not able to understand the Dutch language were also excluded. Patients willing to participate were sent an information leaflet after which pharmacy technicians invited them to visit the pharmacy within 2 weeks. If necessary or requested, patients were also visited at home. Patients were asked for written informed consent.

Assessment of drug-related problems

DRP are events or circumstances involving drug therapy that actually or potentially interfere with desired health outcomes (definition by Pharmaceutical Care Network Europe [PCNE] 2006).[31] We assessed DRP by means of a structured medication review. To support the structured medication review, we developed a tool including a checklist of commonly occurring DRP and a semistructured patient interview. The tool was developed because existing tools, including the Beers' list, STOPP/START criteria, and Australian list do not include the patients' perspective and were not specifically developed for the detection of common DRP as part of a structured medication review.[22,24,29,32] Development and validation of the tool have been described elsewhere (Mast et al, unpublished data, 2013). A summary of the possible DRP that could be identified with the checklist is shown in Supplement 1.

Medication records kept in the electronic pharmacy administration and information systems of the participating pharmacies (PAIS) listing all drugs prescribed and dispensed during the 6 months preceding the date of discharge were printed. In addition, general practitioners were contacted for information about the chronic diseases of each patient.

PAIS were also used for identification of possible drug–drug interactions.[33] The semistructured patient interview was used to identify DRP experienced by patients, like ineffectiveness of treatment, side effects, and fear of side effects.

Using the checklist medication records, hospital discharge prescriptions, interview data, and other relevant information (eg, PAIS signals) were reviewed by two experienced clinical pharmacologists. DRP were categorized according to a number of key items using the PCNE classification scheme (Table 1).[30] Each clinical pharmacologist independently conducted a structured medication review for each patient, after which the results were compared and differences reconciled.

Statistical analysis

The baseline characteristics of all patients were analyzed. The occurrence of DRP (based on the final result of the structured medication review) was calculated by dividing the total number of (potential) DRP by the number of patients. Linear regression analysis was performed using DRP as a dependent variable and the following independent variables: age, sex, number of medication used by a patient, discharge from different hospital departments, and chronic disease. The effect of number of drugs taken by the patient on the number of DRP was adjusted for age and sex. The number of drugs taken by the patient had a significant effect on the occurrence of DRP. Therefore, discharge and chronic diseases were adjusted for age, sex, and number of drugs. The nonstandardized B and 95% confidence intervals are presented. The nonstandardized B regression coefficient indicates the change in number of DRP with a one unit change in the independent variables (age, sex, number of drugs taken, hospital departments, and chronic disease). The different departments were analyzed using dummy variables and cardiology as a reference group because most patients were discharged from this department during the study. The statistical analysis was performed using Statistical Package for the Social Sciences version 15 software (SPSS Inc, Chicago, IL, USA).

Table 1 Categories of drug-related problems

Use checked with	Drug-related problems: key items
Review	Incorrect drug choice
	No drugs prescribed but clear indication
	Dose too low
	No clear indication of drug use
	Contraindication
	Unnecessarily long duration of treatment
	Double medication
	Dose too high
	No drugs administered
Pharmacy administration and information system	Drug–drug interaction
Interview with patient	Ineffectiveness
	Side effects of drug use
	No knowledge of drugs used
	Not satisfied with medication
	Fear of side effects

Results

Of 489 patients discharged from the participating hospitals, 340 (69.5%) were willing to participate in the study. Of the 149 nonresponders, 121 felt too sick and 32 considered participation to be too time-consuming. Age and the percentage of females among responders and nonresponders were similar. Nonresponders were slightly older than responders, but the difference was not significant. The mean age and percentage of females among responders and nonresponders was 75.4 ± 8.7 and 78.1 ± 9.0 years and 54% and 48%, respectively. The majority of patients were discharged from cardiology, followed by internal medicine, pulmonary, surgery, and the coronary care unit department (Table 2). Most patients suffered from a chronic disease, such as heart failure, hypertension, angina pectoris, diabetes type 2, or atrial fibrillation.

Drug-related problems

Table 3 lists the DRP identified by the structured medication review process. A total of 992 (potential) DRP were observed in the data of the 340 patients who participated (mean 2.9 ± 1.7). For nearly all patients (95.9%), at least one existing or potential DRP was detected. Two or more DRP were identified in 78% of patients. The number of DRP was significantly associated with the number of drugs per patient ($P < 0.001$). The most common DRP identified using the checklist included no drugs prescribed but clear indication, unnecessarily long duration of treatment, too low dose of drug, and incorrect drug selection. Ten percent of DRP associated with medication in 71 patients were drug–drug interactions.

Frequently occurring DRP identified by patient interview were fear of side effects and no knowledge of drug use. Table 4 shows the influence of different factors on the number of DRP corrected for age and sex. For patients discharged from the department of pulmonary diseases, significantly more DRP were found, as well as for patients suffering from type 2 diabetes. Adjustment for age, sex, and number of drugs taken did not alter this ranking.

Table 2 Patient characteristics (n = 340)

Determinants	n, %	Median (range of DRP)
Sex, female	183 (53.8)	
Age, years (median and range)		76 (60–95)
<76		3 (0–8)
>76		3 (0–9)
Number of drugs prescribed per patient (median and range)		8.0 (5–24)
<8		3 (0–7)
>8		3 (0–9)
Hospital departments		
Cardiology	155 (45.6)	3 (0–7)
Internal medicine	72 (21.2)	3 (0–7)
Pulmonary	31 (9.1)	4 (0–9)
Surgery	19 (5.6)	3 (0–7)
Coronary care unit	15 (5.3)	2.5 (0–8)
Others	45 (13.2)	2.9
Chronic diseases*		
Heart failure	138 (40.6)	3 (0–7)
Hypertension	130 (38.2)	3 (0–7)
Angina pectoris	90 (26.5)	3 (0–7)
Type 2 diabetes	73 (21.5)	3 (0–8)
Atrial fibrillation	67 (19.7)	3 (0–8)
Others	528 (155.5)	3.1

Note: *Patients could have more than one chronic disease.
Abbreviation: DRP, drug-related problems.

Table 3 Nature and frequency of drug-related problems among elderly discharged from hospital

	Frequency	%	Patients* n = 340
Pharmacy computer system			
Interactions	97	9.8	71
Review			
Incorrect drug choice	81	8.2	74
No drugs prescribed but clear indication	160	16.1	139
Dose too low	48	4.8	46
No clear indication for drug use	12	1.3	11
Contraindication	3	0.3	3
Unnecessarily long duration of treatment	106	10.7	89
Double medication	14	1.4	14
Dose too high	3	0.3	3
No drugs administered	1	0.1	1
Interview			
Ineffectiveness	19	1.9	19
Side effects of drug use	174	17.5	174
No knowledge of drugs used	145	14.6	145
Not satisfied with medication	68	6.9	68
Fear of side effects	61	6.1	61
Total DRP	992	100	

Note: *Each patient could have more than one DRP and is counted more than once.
Abbreviation: DRP, drug-related problems.

Table 4 Effects of number of drugs used, departments, and chronic disease on number of drug-related problems

Variables	B	95% CI
Age	–0.13	
Gender	0.167	
Number of drugs**	0.104	
Department		
Internal versus cardiology	0.167	–0.290 to 0.623
Pulmonary versus cardiology	0.848	0.215 to 1.481*
CCU versus cardiology	0.139	–0.666 to 0.944
Surgery versus cardiology	0.306	–0.472 to 1.058
Others versus cardiology	0.096	–0.447 to 0.640
Chronic disease***		
Heart failure	–0.46	–0.412 to 0.319
Hypertension	–0.185	–0.550 to 0.179
Angina pectoris	0.175	–0.226 to 0.577
Type 2 diabetes	0.725	0.299 to 1.150*
Atrial fibrillation	0.237	–0.211 to 0.684

Notes: *$P < 0.05$; **corrected for age and sex; ***corrected for age, sex, and number of drugs; F test for equality of five departments yields: F 5.332 = 1.41; $P = 0.221$.
Abbreviations: CI, confidence interval; CCU, coronary care unit; B, Beta.

Discussion

This study shows that DRP occur frequently among elderly patients discharged from hospital and using several drugs to treat chronic diseases. The number of DRP was also significantly associated with the number of drugs prescribed. Moreover, patients with type 2 diabetes had significantly more DRP than patients with other diseases. Patients discharged from the department of pulmonary diseases also had more DRP than those discharged from other departments. Prescriber-related DRP most commonly detected by conducting the structured medication review were no drug prescribed but clear indication, unnecessarily long duration of treatment, incorrect drug choice, dose of drug used being too low, and drug–drug interactions. Side effects and lack of knowledge about the drugs were the most common DRP identified by patient interview.

Several studies have also found a high prevalence of DRP among patients discharged from hospital.[8,13,29,34] In this respect, changes in the drug regimen during hospital admission and the high number of drugs used are contributing factors.

Polypharmacy is a major risk factor in experiencing DRP. As expected, the number of DRP per patient increased with an increase in the number of drugs used.[35,36] In line with the results of previous studies,[9,29,37] patients with type 2 diabetes appeared to have more DRP than patients with other chronic diseases. International guidelines recommend that patients with type 2 diabetes

should be treated with a cholesterol-lowering drug.[38] The frequent absence of these drugs in the medication of these patients strongly contributed to the prominent presence of the DRP "no drug but clear indication" among patients in this specific group.

We also found that patients discharged from the pulmonary department had more DRP. Stuurman-Bieze et al have already observed that patients using pulmonary drugs have a high number of DRP, and suggested that this was due to a lack of knowledge about their medication and its use, including insufficient skills to use an inhaler properly.[39]

In line with the literature, the proportion of drug–drug interactions in our study was approximately 0.3 per patient. The number of drug–drug interactions reported varies from 0.05 per patient to 1.4 in the studies of Paulino et al and Vinks et al, respectively,[2,8] which may be explained by differences in the study set-up and population. Paulino et al did not use the medication history of patients, which limited their capacity to detect interactions.[2]

In the present study, about 50% of the DRP were prescriber-related. In older patients discharged from a cardiology department, more than half of DRP were prescriber-related.[2,40] More than half of the patients were reported to have experienced at least one side effect. This percentage is considerably higher than that found in other studies of elderly patients discharged from hospital.[8,34,41,42] The difference can be explained by the number of drugs used by each patient. The present study included only patients using five or more drugs, whereas in other studies any number of drugs could be used. The high prevalence of side effects also corroborates the results of Creswell et al, who showed that the number of drugs used by older patients was a risk factor for occurrence of side effects.[43]

Not knowing the purpose and use of at least one of their medicines and fear of side effects were also DRP frequently reported by patients. The former DRP was also reported in other studies,[8,40] and the latter DRP was reported by no less than 20% of patients. A similar percentage was found in the only study in which this patient-related DRP was also observed.[35] Both these DRP are important factors contributing to nonadherence with drug treatment. These issues therefore should be specifically addressed when patients are counseled on their medication.[44,45]

The strength of the present study was the large number of patients who participated and the high response rate. However, a substantial number of patients did not participate because of the severity of their illness or the idea that participating would be time-consuming. This may have introduced a selection bias because occurrence of DRP is likely to be high in this group of patients, and the number of DRP identified might have been underestimated.

In addition to the study aim, the present study also further validated the method used to identify DRP. The tool used to evaluate DRP was initially developed on the basis of an extensive literature search and a face validity procedure with experts (Mast et al, unpublished data, 2013). Research assistants interviewed patients. Although they may have had varying capacity to identify DRP, a structured interview was used to minimize these differences.

Certain DRP identified using the checklist as part of the structured medication review, might not be actual DRP because of a decision by the prescriber to deviate from existing standards, taking into account the individual characteristics of the patients. We therefore did not classify DRP as actual problems, but as potential problems.

Discharge of elderly patients from hospital using five or more drugs for treatment of chronic disease is associated with DRP. As confirmed by the results of the present study, the number of DRP increases with the number of drugs prescribed. Particularly in the patient group included in the present study, occurrence of DRP may result in increased risk of hospital readmission, morbidity, mortality, and health care costs. An important task for community pharmacists is therefore to identify, resolve, and prevent the occurrence of DRP in this group of patients which, in the coming years, is expected to grow considerably in size. Using comprehensive tools to identify DRP, it is very important to develop intervention strategies to achieve this goal.

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Disclosure

The authors report no conflicts of interest.

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Supplementary material

Supplement 1 Summary of checklist for potential DRP in elderly patients with a chronic disease used for this study

	DRP related to medication	
General medication-related problems	• Double medication • Indication ended but medication was continued • Unknown indication • Relevant drug interactions or contraindications identified by pharmacy/GP/electronic information system • Medication record suggesting nonadherence	
Patient-related problems Frailty Patient perspective (interview)	• Drugs associated with higher risk of fall incidents (eg, benzodiazepines, antidepressants, antipsychotics, anticholinergics, and cardiovascular medication) • Use of medication with a higher risk of decline of cognition (antipsychotics and anticholinergics) • Treatment indication unknown to patient • Absence of awareness about how to use the medication • Dissatisfaction with the medication • No trust in drug treatment or doubt about effectiveness of the medication • Adverse drug event(s) • Fear for adverse drug events	
Medical problem	**DRP related to medication**	**DRP related to medical status**
Hypertension	• High dosage use of NSAID • Beta-blocker combined with NSAID • More than three different antihypertensive drugs in combination with NSAID • Use of prazosin, doxazosin, or methyldopa (no proven effect on cardiovascular clinical outcomes)	• Systolic blood pressure ≥140 mmHg • No regular assessment of creatinine or potassium blood levels in combination with renal dysfunction that use diuretics, ACE inhibitors, or angiotensin II antagonists • Hypertension as a result of renal insufficiency treated with antihypertensive medication
Angina pectoris	• No use of acetylsalicylic acid or other antiplatelet drug • Acetylsalicylic acid combined with NSAID or SSRI without stomach protector • Clopidogrel combined with omeprazole or esomeprazole • Sildenafil combined with nitrates • Overuse of nitroglycerine sprays • Use of short-acting nifedipine capsules	• Heart rate ≤50–60 beats per minute in rest
Cardiovascular disease (myocardial infarction, angina pectoris, stroke, transient ischemic attack, aorta aneurysm, peripheral arterial disease)	• Statin not prescribed or dosage too low (<40 mg simvastatin equivalent) • No use of acetylsalicyclic acid or other antiplatelet drug	• LDL >2.5 mmol/L
Atrial fibrillation	• Beta-blocker combined with verapamil/diltiazem • Digoxin used with combination of amiodarone with either verapamil or diltiazem without reduction of digoxin dosage • No use of coumarin although indication on the basis of CHADS criteria and absence of a contraindication (frequent falls, low adherence) • Use of digoxin and/or verapamil and/or beta-blocker in combination with sotalol, amiodarone, or a class I antiarrhythmic drug	• No monitoring of digoxin or potassium blood levels • Heart rate 70–90 per minute at rest or >120 per minute during exercise
Systolic heart failure	• No use of diuretic • No use of RAS inhibitor • Tickling cough during use of ACE inhibitor	• NYHA classification of heart failure is not applied • No renal function assessment in previous year

(*Continued*)

Supplement 1 (*Continued*)

Medical problem	DRP related to medication	DRP related to medical status
	• Use of verapamil • Diltiazem or verapamil without concomitant use of digoxin • Chronic use of NSAID • NSAID combined with high dosage loop diuretics or thiazides • Creatinine clearance <30 mL per minute and thiazide diuretic is used without concomitant loop diuretic • No beta-blocker • No spironolactone although NYHA class II or III heart failure and reasonable renal function • Combination of ACE inhibitor and an AT1 antagonist • Use of diuretic for static edema without diagnosis of heart failure • Ankle edema due to calcium channel blocker without diagnosis of heart failure • Reconsider indication for thiazides if there is a diagnosis of gout	
Anticoagulant use (use related to heart disease or stroke prevention)	• INR < 2.5 target is not reached • Absence of gastric protective medication in patients ≥70 years of age • Combination of coumarin with acetylsalicylic acid or other antiplatelet drug without indication • Combination of coumarin with acetylsalicylic acid or other antiplatelet drug without gastric protection	• INR target incorrectly set at value <2 or >3
Arthritis or other rheumatic disease	• NSAID in combination with renal failure • Acetylsalicylic acid in combination with NSAID without gastric protection • Use of NSAID without stomach protection in patients ≥65 years of age • Use of NSAID whereas alternative like paracetamol is possible	
Type 2 diabetes mellitus	• Frequent occurrence of hypoglycemic episodes and use of glibenclamide • Pioglitazone use in combination with loop diuretic • Hypoglycemic medication combined with nonselective beta-blockers (except sotalol) • Statin dosage too low (<40 mg simvastatin equivalent) • Concomitant use of medication that potentially disturbs blood glucose levels, eg, high-dose thiazides or corticosteroids • Calcium channel blocker is sole antihypertensive medication	• Fasting glucose level in venous plasma 4.5–8 mmol/L • Frequent occurrence of hypoglycemic episodes • HbA_{1c} >58 mmol/L (7.5%) • Systolic blood pressure >140 mmHg in absence of antihypertensive drug • LDL >2.5 mmol/L or total cholesterol >4.5 mmol/L in absence of statin • (Micro) albuminuria in absence of treatment with ACE inhibitor or AT1 antagonist • Ankle edema in combination with pioglitazone • Metformin dosage not adapted because of renal insufficiency • Microvascular complications without antihypertensive medication • Renal function, HbA_{1c}, blood pressure, and urinary microalbuminuria is not assessed periodically (minimum once/year)
Asthma/COPD	• Daily dose of beta-sympathomimetic is higher than maximum dose • Daily dose of inhalation corticosteroid is higher than maximum dose	• Severity of disease not classified • Fluctuating clinical status • Frequent episodes of oral corticosteroids use (possible sign of compliance problem)

(*Continued*)

Supplement 1 (*Continued*)

Medical problem	DRP related to medication	DRP related to medical status
	• Severe asthma combined with beta-blocker tablets or beta blocker eye drops • Dosage of long-acting beta-2 antagonist or inhalation corticosteroid "if needed, if necessary or on demand"	
Osteoporosis	• No use of vitamin D while indicated • No use of calcium while indicated • Use of bisphosphonates or denosumab without supplementation of calcium and vitamin D • No use of bisphosphonates or previous use for a period of 5 years • Chronic use of high-dose (≥7.5 mg prednisolone equivalent) without concomitant use of a bisphosphonate or denosumab • Use of etidronate • Bisphosphonates not taken in a fasting state • Simultaneous use of a bisphosphonate and a drug containing Ca, Al, Mg, Fe, or Zn • Severe decrease of renal function (GFR <30 mL per minute) and no use of vitamin D • Vitamin D metabolites in primary care setting • Dosage antidepressant is incorrect	
Depression	• Duration of treatment with SSRI <4 weeks • Use of SSRI longer than 6 months after first episode of depression • Tricyclic antidepressant as first choice in presence of cardiovascular risk factors or cardiovascular disease • Tricyclic antidepressant use and a history of glaucoma, orthostatic hypotension, or bladder retention • Use of SSRI and history of hyponatremia	• Continued treatment for depression without indication • Withdrawal symptoms due to abrupt cessation • Absent monitoring of sodium blood level during concomitant use of SSRI and diuretic medication
Sleep disorder	• Benzodiazepine prescribed other than temazepam or zolpidem • Chronic use of hypnotic medication • Benzodiazepine dosage is too high • Use of benzodiazepines with history of falls • Chronic use of benzodiazepines without indication for sedation or anxiolysis	
Other psychiatric problems	• Unnecessary or ineffective use of anticholinergic medication • No periodic evaluation of antipsychotic drug use • Concomitant use of NSAID with lithium • Use of haloperidol in patients with recent myocardial infarction or heart failure, or history of ventricular arrhythmias	• Use of lithium without monitoring of lithium blood level, renal function, mineral (calcium, magnesium), thyroid function • Use of clozapine without monitoring of white blood count
Parkinson's disease	• Use of other antipsychotics than clozapine and quetiapine	• Consider whether symptoms could be related to the use of neuroleptics, SSRI, or metoclopramide
Stomach pain or esophageal reflux		• Indication for acid inhibition no longer present but treatment continued
Constipation	• Codeine prescribed for pain or coughing complaints	• Unnecessary and/or prolonged use of laxatives
Pain	• Use of opioids without use of laxatives	

Abbreviations: ACE, angiotensin-converting enzyme inhibitor; AT1, angiotensin II type 1 receptor; CHADS, congestive heart failure/hypertension/age/diabetes mellitus/stroke; COPD, chronic obstructive pulmonary disease; DRP, drug-related problems; INR, International Normalized Ratio; LDL, low-density lipoprotein; NYHA, New York Heart Association; SSRI, selective serotonin reuptake inhibitors; NSAID, nonsteroidal anti-inflammatory drugs; HbA_{1c}, glycosylated hemoglobin; GFR, glomerular filtration rate; GP, general practitioner; RAS, renin angiotensin system.