BJCP British Journal of Clinical Pharmacology

DOI:10.1111/j.1365-2125.2009.03531.x

Potentially inappropriate prescribing in an Irish elderly population in primary care

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Keywords
elderly patients, primary care, screening tools

Received
23 January 2009

Accepted
14 August 2009

WHAT IS ALREADY KNOWN ABOUT THIS SUBJECT

- Potentially inappropriate prescribing in older people is a well-documented problem and has been associated with adverse drug reactions and hospitalization.
- Beers' criteria, Screening Tool of Older Persons' potentially inappropriate Prescriptions (STOPP) and Screening Tool to Alert doctors to Right Treatment (START) are screening tools that have been formulated to help physicians and pharmacists identify potentially inappropriate prescribing and potential prescribing omissions.
- The prevalence of potentially inappropriate prescribing and prescribing omissions in the elderly population presenting to hospital with acute illness is high according to STOPP and START criteria.

WHAT THIS STUDY ADDS

- Potential errors of prescribing and of omission of medicines are prevalent among medically stable older people in primary care.
- Screening tools should be incorporated into the everyday practice of primary care doctors and community pharmacists as a means of preventing potential errors of prescribing commission and prescribing omission in older people.

AIMS

Screening tools have been formulated to identify potentially inappropriate prescribing (IP) in older people. Beers' criteria are the most widely used but have disadvantages when used in Europe. New IP screening tools called Screening Tool of Older Person's Prescriptions (STOPP) and Screening Tool to Alert doctors to Right Treatment (START) have been developed to identify potential IP and potential prescribing omissions (PPOs). The aim was to measure the prevalence rates of potential IP and PPOs in primary care using Beers' criteria, STOPP and START.

METHODS

Case records of 1329 patients ≥65 years old from three general practices in one region of southern Ireland were studied. The mean age ± SD of the patients was 74.9 ± 6.4 years, 60.9% were female. Patients' current diagnoses and prescription medicines were reviewed and the Beers' criteria, STOPP and START tools applied.

RESULTS

The total number of medicines prescribed was 6684; median number of medicines per patient was five (range 1–19). Overall, Beers' criteria identified 286 potentially inappropriate prescriptions in 18.3% (243) of patients, whilst the corresponding IP rate identified by STOPP was 21.4% (284), in respect of 346 potentially inappropriate prescriptions. A total of 333 PPOs were identified in 22.7% (302) of patients using the START tool.

CONCLUSION

Potentially inappropriate drug prescribing and errors of drug omission are highly prevalent among older people living in the community. Prevention strategies should involve primary care doctors and community pharmacists.

Introduction

Screening tools to detect potentially inappropriate medicines (PIMs) and potential prescribing omissions (PPOs) have been described previously. The Assessing Care of Vulnerable Elders tool is a set of indicators to measure the quality of care provided to elderly patients and includes a medication review tool [1]. Other tools including The Improving Prescribing in the Elderly Tool [2], The Medication Appropriate Index [3], Beers' criteria [4], and Screening Tool of Older Person's Prescriptions (STOPP) and Screening Tool to Alert doctors to Right Treatment (START) [5] have also been developed to identify PIMs and PPOs in older people. A recent review by Laroche *et al.* examining the strengths and weakness of inappropriate prescribing (IP) screening tools endorses the use of STOPP and START and highlights important deficiencies of Beers' criteria in the European context [6].

Beers' criteria are the most widely cited older person IP criteria in the literature and are designed to quantify potential IP in older people in primary care, secondary care and nursing homes. They consist of two explicit lists, i.e. those medicines that should be avoided independent of diagnosis (ID), and those medicines that should be avoided considering diagnosis (CD) with each potential IP incident described as 'high severity' and 'low severity'. Beers' criteria were originally formulated in 1991 [7], updated in 1997 [8] and recently revised in 2003 [4]. Using Beers' criteria in primary care, IP rates of 9.8–38.5% have been reported in various European countries [9–14], while IP rates of 21.3–28.8% have been reported in the USA [15–17]. Beers' criteria have a number of serious deficiencies in relation to European prescribing patterns. Principally, they contain several medicines that are either not prescribed or not available in most European countries and highlight drugs not considered potentially inappropriate in older people in most European countries, e.g. doxazosin [18]. In addition, Beers' criteria do not identify PPOs, they lack organization and are cumbersome to use in day-to-day practice. The need for an organized, up-to-date, generalizable set of criteria that considers PPOs has recently been highlighted [19].

STOPP and START were formulated and validated to address the perceived deficiencies of Beers' criteria [5]. STOPP, which is based on physiological systems, contains a list of 65 explicit rules for avoidance of certain drugs/drug classes. START is also system based and lists 22 common instances of PPOs in patients with particular medical conditions. A recent study of elderly hospitalized patients in Ireland, using the 2003 Beers' criteria to determine the prevalence of potential IP, reported that 34% of patients had at least one PIM on admission [20]. A follow-up study using the STOPP criteria found at least one PIM among the regular prescriptions of 35% of acutely hospitalized elderly patients [21]. A PPO rate of 57.9% was identified using the START criteria in a similar hospitalized elderly population [22]. Elderly patients admitted to hospital are generally sicker and frailer than elderly patients reviewed in primary care, and the prevalence rates for IP and PPOs among elderly patients obtained in these Irish hospital studies do not reflect the Irish population as a whole. The present study therefore aimed to determine: (i) the rate of potential IP in primary care using Beers' criteria (Appendices 1,2) and STOPP (Appendix 3); (ii) the rate of PPOs using the START tool (Appendix 4); (iii) the relationship between age and number of prescription drugs and IP; and (iv) the specific areas of prescribing that contribute most to IP and PPOs.

Methods

Three large general practices agreed to participate in this study: two urban and one rural, in County Cork in the Munster region of Ireland. All patients were ≥65 years old and were prescribed at least one daily medicine. Patients were excluded if they were nursing home residents or terminally ill, as either of these groups would be more likely to have higher rates of IP [23] and therefore not be representative of independently living community-based elderly patients, the group of particular interest in this study.

Alphabetical lists were compiled from each surgery's electronic database of all patients aged ≥65 years. We focused on patients who had received prescription medicines within the previous 3 months and excluded those who had died since electronic registration (>3 months prior to commencing the study), those not prescribed any regular medicines and those who had not attended the practice in the previous 6 months. Each list was therefore analysed to determine the number of actual patients in each practice aged ≥65 years who had been prescribed at least one regular medicine in the previous 6 months. Patients were then recruited prospectively from the active alphabetical list.

Data collection took place over an 18-month period, between January 2007 and July 2008. Patient data, including medical histories, current diagnoses, current medications and biochemical data, were recorded from a combination of electronic and paper-based records. Data collection was conducted by a research pharmacist (C.R.), supported by an academic consultant physician in Geriatric Medicine, three senior academic pharmacists and the general practitioners in the practices involved. The primary researcher referred to this team of senior academic and clinical staff in the event of uncertainty regarding precise diagnosis, interpretation of clinical and laboratory data and application of the screening tools. Each patient was given a unique identifying number in each surgery to ensure confidentiality and to prevent duplication of data collection.

Patients' lists of diagnoses and medical histories were examined and the Charlson Co-morbidity Index (CCI) was calculated and recorded for each patient. The CCI is a

weighted index that takes into account the number and seriousness of comorbid diseases in determining patients' health status [24]. It has been used in various studies to predict patients' long-term outcomes [25] and mortality [26]. It lists 17 clinical conditions that are ranked on a score of 1–6 in terms of the seriousness of comorbid disease. In this study, we used it as a tool to quantify the chronic illness status of the patients and determine the association between the degree of comorbid illness and potential IP.

All patients then had 2003 Beers' criteria, STOPP and START applied to their clinical datasheets. The severity of the potential IP incidents identified by Beers' criteria was determined, based on Beers' criteria classification. All recorded disease states and medical conditions were coded to facilitate data analysis. Disease codes were assigned so that each disease was given a unique number from 1 to 262 and was then grouped according to the principal physiological system affected. We decided not to use the International Classification of Diseases 10 as the diagnoses documented were sometimes insufficiently detailed to meet the classification requirements. Each medicine was assigned a seven-digit code in accordance with the Anatomical Therapeutic Chemical (ATC) Classification System (11th edn, 2008) formulated by the World Health Organization Collaborating Centre for Drug Statistics Methodology [27].

The ATC classification system divides medicines into different groups according to the organ or system affected by their prime mode of action and/or their therapeutic and chemical characteristics, and allows for more efficient and manageable analysis. All data were collated using Microsoft Excel® 2003 and subsequently transferred to SPSS Version 15.0 (SPSS Inc., Chicago, IL, USA) for statistical analysis.

To determine the statistical relationship between the number of medicines prescribed, age, gender, CCI and the occurrence of potential IP, one-tailed biviariate correlations (using Spearman's ρ correlation coefficient) for nonparametric data were calculated. The Wilcoxon signed rank test for nonparametric data was performed to compare the rates of identification of IP using Beers' criteria and STOPP. A probability value of <0.05 was considered significant. Approval for the study was granted by the local research ethics committee.

Results

Demographics

A total of 1329 patients were recruited into the study. The mean age (± SD) of the patients was 74.9 ± 6.4 years, 60.9% were female. The total number of medicines prescribed was 6684, with a range of 1–19 per patient and a median of five per patient (interquartile range 3–7). The average CCI value for the whole population was 0.67, indicating relative wellness rather than chronic illness (Table 1). As expected, the median number of medicines prescribed increased gradually per age category and decreased for those ≥85 years old (Figure 1).

Table 1

Patient demographics

Demographics	Total (n = 1329)
Male	520 (39.1%)
Female	809 (60.9%)
Age, mean (years ± SD)	74.9 (± 6.4)
Age range (years)	65–97
Number of drugs prescribed	6,684
Median drug prescriptions per patient (IQR)	5 (3–7)
Range of drug prescriptions per patient	1–19
Mean CCI* (± SD)	0.67 (± 0.93)

*CCI, Charlson Comorbidity Index score.

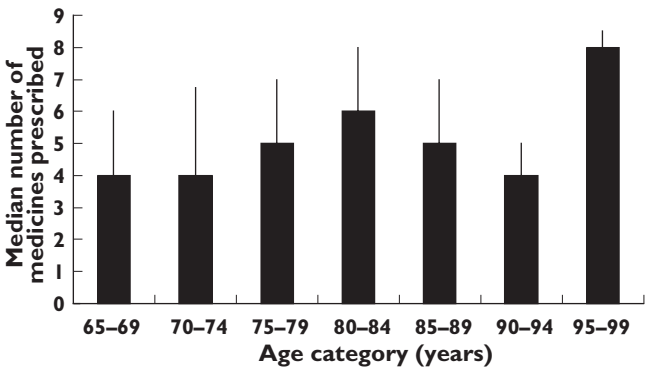

Figure 1

The median number of medicines prescribed per age category (IQR)

Beers' criteria

The application of Beers' criteria to all patient profiles identified 286 PIMs prescribed to a total of 243 (18.3%) patients, with slightly more of the male population taking one or more PIMs (17.9%) than the female population (16.1%). Two hundred and ten (15.8%) patients had one PIM prescribed, and 26 (2.5%) had more than one PIM prescribed (Table 2). Only 19 of the 68 Beers' criteria (27.9%) were used to identify these PIMs (Table 3). One hundred and seventy-seven (61.8%) of the potential IPs identified were of 'high severity'. Those of 'low severity' included: ferrous sulphate at doses >325 mg daily, doxazosin, clonidine and the use of calcium channel blockers or tricyclic antidepressants in patients with chronic constipation.

The prescribing of benzodiazepines accounted for 68 (31.9%) of the PIMs identified by Beers' ID criteria. Doxazosin was prescribed on 86 occasions, accounting for 40.6% of PIMs identified by Beers' ID criteria. None of the patients who were prescribed doxazosin received it as first-line therapy. The adjusted potential IP rate, excluding dox-

Table 2

Number of patients with potentially inappropriate prescriptions identified by Beers' criteria and STOPP

Number of potentially inappropriate prescriptions	Beers' criteria Total (%) (*n* = 1329)	STOPP Total (%) (*n* = 1329)
1	210 (15.8)	232 (17.46)
2	26 (2.0)	42 (3.16)
3	4 (0.3)	10 (0.75)
4	3 (0.2)	
Total	243 (18.28)	284 (21.37)
Male (*n* = 520)	93 (17.88)	102 (19.6)
Female (*n* = 809)	130 (16.07)	182 (22.5)
Total potential inappropriate prescriptions	286	346

STOPP, Screening Tool of Older Persons' potentially inappropriate Prescriptions.

Table 3

Potentially inappropriate prescriptions identified using Beers' criteria Independent of Diagnosis (ID) and Considering Diagnosis (CD)

Medication	Total
ID	
Oxybutynin *(unless XL)*	7
Flurazepam	15
Amitriptyline	11
Short-acting benzodiazepines: (doses >)	
Lorazepam 3 mg	2
Temazepam 15 mg	8
Triazolam 0.25 mg	3
***Long-acting benzodiazepines*:**	
Chlordiazepoxide	4
Diazepam	36
Methyldopa	1
Chlorpheniramine	1
Hydroxyzine	1
Ferrous sulphate >325 mg day^{-1}	13
Long-term long half-life NSAIDs:	
Naproxen	6
Amiodarone	9
Nitrofurantoin	6
Doxazosin	86
Short-acting nifedipine	2
Clonidine	1
Total ID	212
CD	
***Heart failure:* high sodium content medicines**	1
Peptic ulcer disease: NSAIDs	2
Depression	
Long-term benzodiazepine	55
Sympatholytic agents	–
Chronic obstructive pulmonary disease	
Long-acting benzodiazepines	4
β-blocker: propranolol	3
Constipation	
Calcium channel blockers	7
Tricyclic antidepressant	2
Total CD	74
Total (ID and CD)	286

NSAIDs, nonsteroidal anti-inflammatory drugs.

azosin, was 12.6%. A total of 74 PIMs were identified using Beers' CD, the highest proportion being benzodiazepines in patients with concurrent depression. This instance accounted for 74.3% of the PIMs identified by Beers' CD.

STOPP criteria

The STOPP criteria identified a total of 346 PIMs prescribed for 284 (21.4%) patients, with slightly more of the female population taking one or more PIM (22.5%) than the male population (19.6%). Two hundred and thirty-two (17.5%) patients had one PIM and 52 (3.9%) had more than one PIM prescribed (Table 2). Of the 65 criteria in STOPP, 28 (43.1%) were used to identify potential IP. The highest prevalence of potential IP (102) was in relation to the gastrointestinal system [in particular, proton pump inhibitors (PPIs)], followed by drugs whose primary effect is on the central nervous system, musculoskeletal system and cardiovascular system. Prescribing of duplicate drug classes accounted for a total of 29 PIMs, the endocrine system accounted for six and only one inappropriate prescription was identified for the respiratory system.

Three hundred and forty-six (79.1%) instances were attributed to the six groups of medicines: PPIs, benzodiazepines, nonsteroidal anti-inflammatory drugs (NSAIDs), β-blockers, tricyclic antidepressants and calcium channel blockers (Table 4).

The potential IP associated with NSAIDs occurred in patients who had moderate to severe hypertension, their long-term use for osteoarthritis, and in patients with a history of peptic ulcer disease, gout, heart failure and chronic renal failure. The potential IP relating to β-blockers occurred in patients with concurrent chronic obstructive pulmonary disease and for diabetic patients reporting frequent hypoglycaemic attacks. Potential IP relating to tricyclic antidepressants was noted in patients with constipation, glaucoma and urinary retention and in patients receiving concurrent opiates or calcium channel blockers.

A significant correlation was found between the number of medicines prescribed and the occurrence of IP when calculated using Beers' criteria ($r_s = 0.270$, $P < 0.01$) and STOPP ($r_s = 0.356$, $P < 0.01$) using Spearman's ρ correlation test. There was also a positive correlation between age and the occurrence of IP using Beers' criteria ($r_s = 0.068$, $P < 0.01$) and STOPP ($r_s = 0.071$, $P < 0.01$). Similarly, there was a significant correlation between increasing CCI score and potential IP identified by STOPP ($r_s = 0.210$, $P < 0.01$).

The number of PIMs identified was significantly lower using Beers' criteria than STOPP (Wilcoxon signed ranks test $Z = -2.769$; $P < 0.01$).

START criteria

START identified a total of 333 PPOs in 302 (22.7%) patients (Table 5). The incidence of PPOs was significantly higher in women (27.8%) than in men (14.8%) ($P < 0.001$). The mean age (± SD) of those identified with a PPO was 74.5 ± 6.2

Table 4

Potential inappropriate medicines identified by STOPP

Criteria	Total
Cardiovascular System	
Digoxin >125 μg day^{-1}	2
Loop diuretic first line for hypertension	1
Cardioselective β-blocker and COPD	22
β-Blocker and verapamil	4
Calcium channel blockers and constipation	9
Thiazide diuretic and gout	6
Aspirin and warfarin without H_2 antagonist/PPI	4
Aspirin and history of PUD without H_2 antagonist/PPI	3
Aspirin >150 mg daily	4
Aspirin – not indicated	3
Central nervous system	
TCA and glaucoma	1
TCAs and constipation	6
TCAs and opiate or calcium blockers	5
TCA and urinary retention	1
LT/LA benzodiazepine and with LA metabolites	69
>1 week first-generation antihistamines	2
Respiratory system	
Oral steroids instead of inhaled steroids for COPD	1
Gastrointestinal system	
PPI for PUD at full therapeutic dosage for >8 weeks	102
Musculoskeletal system	
NSAID and history of PUD	9
NSAID and hypertension	39
Long-term continuous NSAID for OA	14
NSAID and HF	1
NSAID with chronic renal failure	1
Long-term NSAID/colchicine for gout – no contraindication to allopurinol	2
Endocrine system	
β-Blocker and frequent hypoglycaemic attacks	3
Glibenclamide/chlorpropamide and NIDDM	3
Duplicate class	29
Total potential inappropriate prescriptions	346

STOPP, Screening Tool of Older Persons' potentially inappropriate Prescriptions; COPD, chronic obstructive pulmonary disease; HF, heart failure; LA, long acting; LT, long term; NIDDM, non-insulin-dependant diabetes mellitus; NSAID, nonsteroidal anti-inflammatory drug; OA, osteoarthritis; PPI, proton pump inhibitor; PUD, peptic ulcer disease; TCA, tricyclic antidepressant.

Table 5

The number of patients identified with a potential prescribing omission (PPO) by START

Number of PPOs	Total (%) (n = 1329)
1	274 (20.62)
2	25 (1.88)
3	3 (0.23)
Total patients	302 (22.72)
Male	77 (14.81)
Female	225 (27.81)
Total PPOs	333

START, Screening Tool to Alert doctors to Right Treatment.

Table 6

Details of potential prescribing omissions (PPOs) identified by the START tool

Criteria	Total
Cardiovascular system	185
Warfarin and AF	1
Aspirin	132
Antihypertensives	1
Statin	42
ACE inhibitor and CHF	4
β-Blocker	2
ACE inhibitor and acute MI	3
Respiratory system	14
β_2 agonist for COPD	14
Musculoskeletal system	79
DMARD and RA	1
Bisphosphonate	19
Ca^{2+} and Vitamin D_3 supplement	59
Endocrine system	55
Metformin	12
ACE inhibitor	4
Aspirin	20
Statin	19
Total PPOs	333

START, Screening Tool to Alert doctors to Right Treatment; AF, atrial fibrillation; ACE, angiotensin converting enzyme; CHF, chronic heart failure; MI, myocardial infarction; COPD, chronic obstructive pulmonary disease; DMARD, disease-modifying antirheumatic drug; RA, rheumatoid arthritis.

years, while the mean age (± SD) of those without a PPO was 75.1 ± 6.5 years (difference not significant).

Fifteen of the 22 criteria (68.2%) in START identified the PPOs in this study. The cardiovascular system accounted for most of the PPOs. Aspirin was the commonest cardiovascular PPO identified. Omissions of calcium and vitamin D supplements were the commonest PPO for the musculoskeletal system. Statins were often omitted from both a cardiovascular and an endocrine perspective. No PPOs were identified under the central nervous system or the gastrointestinal system criteria (Table 6). The relationship between the number of medicines prescribed and prescribing omissions was not significant ($r_s = 0.016$, $P = 0.28$).

Discussion

This study indicates that the rate of potential IP in primary care in south-west Ireland is substantial, i.e. 21.4% using STOPP criteria and 18.3% using Beers' criteria. This is the first study using STOPP criteria in primary care, and therefore there are no other studies with which to compare the current STOPP data. The potential IP rate using Beers' criteria lies within the range referred to earlier, 9.8–38.5%, identified in European studies. The reason for the relatively high rate of IP in Polish primary care (28.2%) is unclear; however, over-the-counter medicines accounted for 5.5% of the potential IP identified [10]. A high proportion of the

potential IP identified in a Portuguese primary care study, using the Beers' ID tool only, was attributable to ticlopidine (14.9%) [13], a medicine not licensed for use in Ireland. A large number of general practices ($n = 131$) were involved in the study conducted in the UK, which reported a potential IP rate of 24.8% [14]. However, the rate of potential IP is less in other European centres (9.8% in Turkey and 12.5% in Finland) [9, 11] compared with centres in the USA (21.3%, 23.5%, 28.8%). The reasons for the variation in IP rates are not clear from the literature. Differences in drug availability, prescribing practices and pharmacist routine review of prescriptions are possibilities.

The finding of approximately one-fifth of patients in the present study receiving one or more PIM is an important message for Irish primary care prescribers. We stress that both STOPP and Beers' criteria are designed to identify prescription medicines that are potentially inappropriate for older patients. Nevertheless, prescribing of inappropriate drugs is associated with a significant increase in adverse drug events (ADEs) and iatrogenic morbidity [28, 29]. Although STOPP and Beers' criteria contain comparable numbers of potential IP avoidance rules, in this study 43% of the STOPP potential IP rules were breached compared with 28% of Beers' criteria rules. This, and the recent finding that STOPP showed significantly superior detection of ADEs causing hospitalization *vs.* Beers' criteria [21], suggests that STOPP may be a more relevant potential IP detection tool in primary care in Ireland than Beers' criteria, as many of Beers' criteria are redundant in the Irish setting [30]. Similarly, in a recent Dutch study it was noted that only 24 of the 78 drugs in Beers' list were available in the Netherlands [12]. Conversely, a number of the medicines in the most recent iteration of Beers' independent of diagnosis criteria are not contraindicated in older people according to the latest edition of the British National Formulary [31], e.g. oxybutinin, amitriptyline, nitrofurantoin, naproxen. Also, doxazosin is commonly prescribed in Ireland for hypertension and is not considered inappropriate when prescribed in combination with other antihypertensives or in cases where other antihypertensive drug classes are contraindicated. Similarly, dipyridamole appears in Beers' criteria. According to recent UK guidelines for secondary stroke prevention, dipyridamole is recommended for secondary prevention of stroke in combination with low-dose aspirin [32] (the combination was shown to be superior to aspirin monotherapy in the ESPS-2 trial) [33]. Accordingly, dipyridamole is widely prescribed for stroke prevention throughout Europe.

Nearly 80% of the potential IP detected by STOPP in this study involved five categories of medicines, i.e. PPIs, long-acting benzodiazepines, NSAIDs, nonselective β-blockers and tricyclic antidepressants. It may be argued that long-term, high-dose PPI treatment in older people is relatively harmless in terms of ADEs and this may be true in practice. However, continuation of high-dose PPI treatment without clear indication is expensive and almost always unnecessary. Furthermore, the surge in PPI prescribing in recent years is a cause of major budgetary concern. In Ireland, annual expenditure on PPIs increased from approximately €8 million in 1995 to €64 million in 2002, accounting for >10% of the total expenditure on drugs funded by the Irish government in 2002 [34]. In the current climate of major fiscal pressure on health resources, the overuse of PPIs becomes more relevant in terms of overall drug expenditure by governments globally. Inappropriate prescription of long-acting benzodiazepines in older patients has been highlighted repeatedly in the literature over the last 25 years, in particular given the link with falls and fracture risk and the difficulties with successful withdrawal [35–37]. Despite this, long-acting benzodiazepines continue to be initiated and repeatedly prescribed for older patients in primary and secondary care in Ireland and other countries [10, 12–14]. These realities suggest that long-acting benzodiazepines should not be initiated in older patients, given their high propensity for psychological and physical dependency.

A serious weakness of IP detection tools to date has been the exclusion of prescribing omissions of clinically indicated drugs. The START list of potential errors of prescribing omission has been formulated specifically for use in tandem with STOPP [5] to give a more complete assessment of potential IP in older people. In the present study, 22.7% of patients had one or more clinically indicated medicines omitted from their regular prescriptions without valid reasons. Seventy-five percent of the START rules applied to patients with PPOs, indicating the high degree of relevance of the START rules. The majority of these omissions involved low-dose aspirin, calcium and vitamin D supplements, statins, angiotensin converting enzyme inhibitors and metformin. The evidence for clear-cut benefit from these drugs in secondary prevention of major morbidity and mortality is well established. These drugs are also generally well tolerated in older people. The reasons for omission of indicated medicines in the present study are unclear. Advanced old age did not influence prescribing omission in this study, i.e. there was no significant difference between patients aged 65–74 years compared with patients aged ≥85 years. The reasons for avoidance of indicated medicines in older patients are unclear from the existing literature. Lack of conviction on the part of some physicians as regards efficacy may be a significant reason for nonprescription of indicated statins in some over-80s patients [38]. A desire to avoid major polypharmacy and complexity of treatment regime as well as predictable poor compliance in certain patients may be relevant also. In our study, there was no significant relationship between the number of medicines (indicating degree of polypharmacy) and occurrence of PPOs, i.e. the fact of taking a large number of prescription medicines did not dissuade prescribers from adding more medicines, when clearly indicated. In contrast, Kuijpers *et al.* found that polypharmacy was related to under-prescribing. The difference is

probably due to the relatively healthy population in the present study [39].

The practical applicability of STOPP and START in daily general practice and community pharmacy is not yet established. The STOPP and START tools may be applicable in the completion of Medication Use Reviews (MURs), which are being increasingly requested within the National Health Service at the present time [40, 41]. Although pharmacist-led MURs have not yet been shown to improve patient clinical outcomes [42], they have demonstrated a potential economic saving [43] and a reduction in prescribing [44], with the majority of recommendations being accepted and implemented by general practitioners [45, 46]. Pharmacists could incorporate the STOPP and START tools into their everyday practice, although the lack of complete patient clinical data may limit the full application of the criteria. STOPP and START could also be adapted to existing prescribing systems in primary care as a means of preventing IP in older people at the point of drug initiation. STOPP and START were easy to use and were time efficient. On average, STOPP criteria were fully deployed within 3 min, START criteria within 1 min. However, there is a short but significant learning curve with STOPP and START criteria until one is fully familiar with them.

There were some limitations to the present study. The comparatively reduced sample size in a restricted geographical area of Ireland limits the generalizability of the findings. The potential IP rate from STOPP criteria may be a conservative estimate, since over-the-counter medicines were not included in the analysis. General practitioners were not given the opportunity to state their reasons for prescribing the identified potential errors of commission or omission due to time constraints. Incomplete documentation of serious falls in patients' case notes may have led to a lower rate of reporting of potential IP in relation to iatrogenically increased falls risk. The clinical and financial benefits from routine application of STOPP and START rules to older people's prescriptions are as yet unknown. Therefore, STOPP and START currently have limited applicability in routine practice. Sufficiently large prospective randomized controlled trials are needed to determine if rigorous application of STOPP and START rules has tangible benefits in terms of reduction of ADEs (e.g. falls), cost, hospitalization and mortality. These questions are currently being studied within our research group.

In conclusion, this study of older people's regular prescriptions in primary care has identified potential errors of prescribing commission and omission in significant proportions of patients. We contend that the majority of these instances are avoidable. Prevention of IP in late life is important for avoidance of predictable ADEs and polypharmacy, as well limiting costs of medication. Presentation of the STOPP/START criteria as a prescribing assistant in a user-friendly electronic automated format to primary care physicians will be necessary for the effective use of the STOPP/START criteria in day-to-day clinical practice. Our research group is currently developing electronic versions of the STOPP/START criteria for this purpose.

Competing interests

None declared.

We wish to thank the primary care physicians who gave us access to their patients' medical records for the purpose of this study. Without their cooperation, this work could not have been completed.

Appendix 1

Beers' criteria considering diagnosis

Considering diagnosis Diagnosis	Drug
Heart failure	Disopyramide and high sodium content drugs
Hypertension	Phenylpropanolamine hydrochloride, pseudoephedrine, diet pills and amphetamines
Gastric of duodenal ulcers	NSAIDs and aspirin
Seizures or epilepsy	Clozapine, chlorpromazine, thioridazine and thiothixene
Blood clotting disorders or receiving anticoagulant therapy	Aspirin, NSAIDs, dipyridamole, ticlodipine and clopidogrel
Bladder outflow obstruction	Anticholinergics and antihistamines, GI antispasmodic drugs, muscle relaxants, oxybutynin, flavoxate, anticholinergics, antidepressants, decongestants and tolteridine
Stress incontinence	α-Blockers, anticholinergics, tricyclic antidepressants (imipramine hydrochloride, doxepin hydrochloride and amitriptyline hydrochloride) and long-acting benzodiazepines
Arrhythmias	Tricyclic antidepressants (imipramine hydrochloride, doxepin hydrochloride and amitriptyline hydrochloride)
Insomnia	Decongestants, theophylline, methylphenidate, MAOIs and amphetamines
Parkinson disease	Metoclopramide, conventional antipsychotics and tacrine
Cognitive impairment	Barbiturates, anticholinergics, antispasmodics, muscle relaxants and CNS stimulants: dextroamphetamine, methylphenidate, methamphetamine and pemolin
Depression	Long-term benzodiazepine use. Sympatholytic agents: methyldopa, reserpine and guanethidine
Anorexia and malnutrition	CNS stimulants: dextroamphetamine, methylphenidate, methamphetamine, pemolin and fluoxetine
Syncope or falls	Short to intermediate acting benzodiazepine and tricyclic antidepressants (imipramine hydrochloride, doxepin hydrochloride and amitriptyline hydrochloride)
SIADH/hyponatraemia	SSRIs: fluoxetine, citalopram, fluvoxamine, paroxetine and sertraline
Seizure disorder	Bupropion
Obesity	Olanzapine
COPD	Long-acting benzodiazepines: chlordiazepoxide, chlordiazepoxide-amitriptyline, clidinium-chlordiazepoxide, diazepam, quazepam, halazepam and chlorazepate. β-Blockers: propranolol
Constipation	Calcium channel blockers, anticholinergics, tricyclic antidepressants (imipramine hydrochloride, doxepin hydrochloride and amitriptyline hydrochloride)

CNS, central nervous system; COPD, chronic obstructive pulmonary disease; SIADH, syndrome of inappropriate ADH (antidiuretic hormone); GI, gastrointestinal; MAOI, monoamine oxidase inhibitor; NSAIDs, nonsteroidal anti-inflammatory drugs; SSRI, selective serotonin reuptake inhibitor.

Appendix 2

Beers' criteria independent of diagnosis

Drug	Drug
Propoxyphene and combination products	Diphenhydramine
Indomethacin	Ergot mesyloids and cyclandelate
Pentazocine	Ferrous sulphate >325 mg
Trimethobenzamide	All barbiturates (except Phenobarbital) except when used to control seizures
Muscle relaxants and antispasmodics: methocarbamol, carisprodol, oxybutynin, chloroxazone, metaxalone and cyclobenzaprine (except extended release oxybutynin)	Meperidine
Flurazepam	Ticlopidine
Amitriptyline, chlordiazepoxide-amitriptyline and perphenazine-amitriptyline	Ketorolac
Doxepin	Amphetamines and anorexic agents
Mepobramate	Long-term use of full dosage, longer half-life, non-COX-selective NSAIDs: naproxen, oxaprozin and piroxicam
Doses of short-acting benzodiazepines: doses greater than lorazepam 3 mg; oxazepam 60 mg; alprazolam 2 mg; temazepam 15 mg; triazolam 0.25 mg	Daily fluoxetine
Long-acting benzodiazepines	Long-term use of stimulant laxatives: bisacodyl, cascara sagrada and neoloid except in the presence of opiate analgesic use
Chlordiazepoxide, chlordiazepoxide-amitriptyline, clidinium-chlordiazepoxide, diazepam, quazepam, halazepam and chlorazepate	Amiodarone
Disopyramide	Orphenadrine
Digoxin (should not exceed 0.125 mg daily, except when treating atrial arrhythmias)	Guanethidine
Short-acting dipyridamole. Do not consider the long-acting dipyridamole except in patients with artificial heart valves	Guanadrel
Methyldopa and methyldopa-hydrochlorothiazide	Cyclandelate
Reserpine at doses >0.25 mg	Isoxsurpine
Chlorpropramide	Nitrofurantoin
Gastrointestinal antispasmodic drugs: dicyclomide, hyoscyamine, propantheline, belladonna alkoloids and clinidium-chlordiazepoxide	Doxazocin
Anticholinergics and anthistamines: chlorpheniramine, diphenhydramine, hydroxyzine, cyproheptadine, promethazine, tripelennamine and dexchlorpheniramine	Methyltestosterone
Thioridazine	Mesoridazine
Short-acting nifedipine	Clonidine
Mineral oil	Cimetidine
Ethacrynic acid	Dessicated thyroid
Amphetamines (excluding methylphenidate hydrochloride and anorexics)	Oestrogens only (oral)

COX, cyclooxygenase; NSAIDs, nonsteroidal anti-inflammatory drugs.

Appendix 3

STOPP: Screening Tool of Older People's potentially inappropriate Prescriptions.

The following drug prescriptions are potentially inappropriate in persons aged ≥65 years.

A Cardiovascular system

1 Digoxin at a long-term dose >125 µg day^{-1} with impaired renal function*.
2 Loop diuretic for dependent ankle oedema only, i.e. no clinical signs of heart failure.
3 Loop diuretic as first-line monotherapy for hypertension.
4 Thiazide diuretic with a history of gout.
5 Noncardioselective β-blocker with chronic obstructive pulmonary disease (COPD).
6 β-Blocker in combination with verapamil.
7 Use of diltiazem or verapamil with New York Heart Association Class III or IV heart failure.
8 Calcium channel blockers with chronic constipation.
9 Use of aspirin and warfarin in combination without histamine H_2 receptor antagonist (except cimetidine because of interaction with warfarin) or proton pump inhibitor (PPI).
10 Dipyridamole as monotherapy for cardiovascular secondary prevention.
11 Aspirin with a past history of peptic ulcer disease without histamine H_2 receptor antagonist or PPI.
12 Aspirin at dose >150 mg day^{-1}.
13 Aspirin with no history of coronary, cerebral or peripheral vascular symptoms or occlusive event.
14 Aspirin to treat dizziness not clearly attributable to cerebrovascular disease.
15 Warfarin for first, uncomplicated deep venous thrombosis for >6 months' duration.
16 Warfarin for first uncomplicated pulmonary embolus for >12 months' duration.
17 Aspirin, clopidogrel, dipyridamole or warfarin with concurrent bleeding disorder.

*Serum creatinine >150 µmol l^{-1}, or estimated glomerular filtration rate (GFR) <50 ml min^{-1}.

B Central nervous system and psychotropic drugs

1 Tricyclic antidepressants (TCAs) with dementia.
2 TCAs with glaucoma.
3 TCAs with cardiac conductive abnormalities.
4 TCAs with constipation.
5 TCAs with an opiate or calcium channel blocker.
6 TCAs with prostatism or prior history of urinary retention.
7 Long-term (i.e. >1 month), long-acting benzodiazepines, e.g. chlordiazepoxide, flurazepam, nitrazepam, chlorazepate and benzodiazepines with long-acting metabolites, e.g. diazepam.
8 Long-term (i.e. >1 month) neuroleptics as long-term hypnotics.
9 Long-term neuroleptics (>1 month) in those with parkinsonism.
10 Phenothiazines in patients with epilepsy.
11 Anticholinergics to treat extrapyramidal side-effects of neuroleptic medications.
12 Selective serotonin re-uptake inhibitors (SSRIs) with a history of clinically significant hyponatraemia.
13 Prolonged use (>1 week) of first-generation antihistamines, i.e. diphenydramine, chlorpheniramine, cyclizine, promethazine.

C Gastrointestinal system

1 Diphenoxylate, loperamide or codeine phosphate for treatment of diarrhoea of unknown cause.
2 Diphenoxylate, loperamide or codeine phosphate for treatment of severe infective gastroenteritis, i.e. bloody diarrhoea, high fever or severe systemic toxicity.
3 Prochlorperazine (Stemetil) or metoclopramide with parkinsonism.
4 PPI for peptic ulcer disease at full therapeutic dosage for >8 weeks.
5 Anticholinergic antispasmodic drugs with chronic constipation.

D Respiratory system

1 Theophylline as monotherapy for COPD.
2 Systemic corticosteroids instead of inhaled corticosteroids for maintenance therapy in moderate–severe COPD.
3 Nebulized ipratropium with glaucoma.

E Musculoskeletal system

1 Nonsteroidal anti-inflammatory drug (NSAID) with history of peptic ulcer disease or gastrointestinal bleeding, unless with concurrent histamine H_2 receptor antagonist, PPI or misoprostol.
2 NSAID with moderate–severe hypertension.
3 NSAID with heart failure.
4 Long-term use of NSAID (>3 months) for symptom relief of mild osteoarthritis.
5 Warfarin and NSAID together.
6 NSAID with chronic renal failure*.
7 Long-term corticosteroids (>3 months) as monotherapy for rheumatoid arthritis or osteoarthritis.
8 Long-term NSAID or colchicine for chronic treatment of gout where there is no contraindication to allopurinol.

*Serum creatinine >150 µmol l^{-1}, or estimated GFR 20–50 ml min^{-1}.

F Urogenital system

1 Bladder antimuscarinic drugs with dementia.
2 Antimuscarinic drugs with chronic glaucoma.
3 Antimuscarinic drugs with chronic constipation.
4 Antimuscarinic drugs with chronic prostatism.

5 α-Blockers in men with frequent incontinence, i.e. one or more episodes of incontinence daily.
6 α-Blockers with long-term urinary catheter *in situ*, i.e. >2 months.

G Endocrine system
1 Glibenclamide or chlorpropamide with Type 2 diabetes mellitus.
2 β-Blockers in those with diabetes mellitus and frequent hypoglycaemic episodes, i.e. ≥1 episode per month.
3 Oestrogens with a history of breast cancer or venous thromboembolism.
4 Oestrogens without progestogen in patients with intact uterus.

H Drugs that adversely affect fallers
1 Benzodiazepines.
2 Neuroleptic drugs.
3 First-generation antihistamines.
4 Vasodilator drugs with persistent postural hypotension, i.e. recurrent >20 mmHg drop in systolic blood pressure.
5 Long-term opiates in those with recurrent falls.

I Analgesic drugs
1 Use of long-term powerful opiates, e.g. morphine or fentanyl as first-line therapy for mild–moderate pain.
2 Regular opiates for >2 weeks in those with chronic constipation without concurrent use of laxatives.
3 Long-term opiates in those with dementia unless indicted for palliative care or management of moderate–severe chronic pain syndrome.

J Duplicate drug classes
Any duplicate drug class prescription, e.g. two concurrent opiates, NSAIDs, SSRIs, loop diuretics, ACE inhibitors.

Appendix 4

START: Screening Tool to Alert doctors to Right, i.e. appropriate, indicated but often omitted Treatments.

These medications should be considered for people ≥65 years of age with the following conditions, where no contraindication to prescription exists.

A Cardiovascular system
1 Warfarin in the presence of chronic atrial fibrillation (AF).
2 Aspirin in the presence of chronic AF, where warfarin is contraindicated, but not aspirin.
3 Aspirin or clopidogrel with a documented history of atherosclerotic coronary, cerebral or peripheral vascular disease in patients with sinus rhythm.
4 Antihypertensive therapy where systolic blood pressure consistently >160 mmHg.
5 Statin therapy with a documented history of coronary, cerebral or peripheral vascular disease, where the patient's functional status remains independent for activities of daily living and life expectancy is >5 years.
6 Angiotensin converting enzyme (ACE) inhibitor with chronic heart failure.
7 ACE inhibitor following acute myocardial infarction.
8 β-Blocker with chronic stable angina.

B Respiratory system
1. Regular inhaled β_2 agonist or anticholinergic agent for mild to moderate asthma or chronic obstructive pulmonary disease (COPD).
2 Regular inhaled corticosteroid for moderate–severe asthma or COPD, where predicted forced expiratory volume in 1 s <50%.
3 Home continuous oxygen with documented chronic type 1 respiratory failure (pO_2 <8.0 kPa, pCO_2 <6.5 kPa) or type 2 respiratory failure (pO_2 < 8.0 kPa, pCO_2 > 6.5 kPa).

C Central nervous system
1 L-DOPA in idiopathic Parkinson's disease with definite functional impairment and resultant disability.
2 Antidepressant drug in the presence of moderate–severe depressive symptoms lasting at least 3 months.

D Gastrointestinal system
1 Proton pump inhibitor with severe gastro-oesophageal acid reflux disease or peptic stricture requiring dilation.
2 Fibre supplement for chronic, symptomatic diverticular disease with constipation.

E Musculoskeletal system
1 Disease-modifying antirheumatic drug with active moderate–severe rheumatoid disease lasting >12 weeks.
2 Bisphosphonates in patients taking maintenance corticosteroid therapy.
3 Calcium and Vitamin D supplement in patients with known osteoporosis (previous fragility fracture, acquired dorsal kyphosis).

F Endocrine system
1 Metformin with Type 2 diabetes ± metabolic syndrome (in the absence of renal impairment*).
2 ACE inhibitor or angiotensin receptor blocker in diabetes with nephropathy, i.e. overt urinalysis proteinuria or microalbuminuria (>30 mg per 24 h) ± serum biochemical renal impairment*.
3 Antiplatelet therapy in diabetes mellitus with co-existing major cardiovascular risk factors (hypertension, hypercholesterolaemia, smoking history).
4 Statin therapy in diabetes mellitus if coexisting major cardiovascular risk factors present.

*Serum creatinine >150 μmol l^{-1}, or estimated GFR <50 ml min^{-1}.

REFERENCES

1 Shekelle PG, MacLean CH, Morton SC, Wenger NS. Acove quality indicators. Ann Intern Med 2001; 135: 653–67.

2 Naugler CT, Brymer C, Stolee P, Arcese ZA. Development and validation of an Improving Prescribing in the Elderly Tool. Can J Clin Pharmacol 2000; 7: 103–7.

3 Hanlon JT, Schmader KE, Samsa GP, Weinberger M, Uttech KM, Lewis IK, Cohen HJ, Feussner JR. A method for assessing drug therapy appropriateness. J Clin Epidemiol 1992; 45: 1045–51.

4 Fick DM, Cooper JW, Wade WE, Waller JL, Maclean JR, Beers MH. Updating the Beers criteria for potentially inappropriate medication use in older adults: results of a US consensus panel of experts. Arch Intern Med 2003; 163: 2716–24.

5 Gallagher P, Ryan C, Byrne S, Kennedy J, O'Mahony D. STOPP screening tool of older person's prescriptions) and START (screening tool to alert doctors to right treatment). Consensus validation. Int J Clin Pharmacol Ther 2008; 46: 72–83.

6 Laroche M, Charmes J, Bouthier F, Merle L. Inappropriate medications in the elderly. Clin Pharmacol Ther 2009; 85: 94–7.

7 Beers MH, Ouslander JG, Rollingher I, Reuben DB, Brooks J, Beck JC. Explicit criteria for determining inappropriate medication use in nursing home residents. UCLA Division of Geriatric Medicine. Arch Intern Med 1991; 151: 1825–32.

8 Beers MH. Explicit criteria for determining potentially inappropriate medication use by the elderly. An update. Arch Intern Med 1997; 157: 1531–6.

9 Ay P, Akici A, Harmanc H. Drug utilization and potentially inappropriate drug use in elderly residents of a community in Istanbul, Turkey. Int J Clin Pharmacol Ther 2005; 43: 195–202.

10 Rajska-Neumann A, Wieczorowska-Tobis K. Polypharmacy and potential inappropriateness of pharmacological treatment among community-dwelling elderly patients. Arch Gerontol Geriatr 2007; 44: 303–9.

11 Pitkala KH, Strandberg TE, Tilvis RS. Inappropriate drug prescribing in home-dwelling, elderly patients: a population-based survey. Arch Intern Med 2002; 162: 1707–12.

12 van der Hooft CS, Jong GW, Dieleman JP, Verhamme KM, van der Cammen TJ, Stricker BH, Sturkenboom MC. Inappropriate drug prescribing in older adults: the updated 2002 Beers criteria – a population-based cohort study. Br J Clin Pharmacol 2005; 60: 137–44.

13 de Oliveira Martins S, Soares MA, Foppe van Mil JW, Cabrita J. Inappropriate drug use by Portuguese elderly outpatients – effect of the Beers criteria update. Pharm World Sci 2006; 28: 296–301.

14 De Wilde S, Carey IM, Harris T, Richards N, Victor C, Hilton SR, Cook DG. Trends in potentially inappropriate prescribing amongst older UK primary care patients. Pharmacoepidemiol Drug Saf 2007; 16: 658–67.

15 Zhan C, Sangl J, Bierman AS, Miller MR, Friedman B, Wickizer SW, Meyer GS. Potentially inappropriate medication use in the community-dwelling elderly: findings from the 1996 Medical Expenditure Panel Survey. JAMA 2001; 286: 2823–9.

16 Willcox SM, Himmelstein DU, Woolhandler S. Inappropriate drug prescribing for the community-dwelling elderly. JAMA 1994; 272: 292–6.

17 Simon SR, Chan KA, Soumerai SB, Wagner AK, Andrade SE, Feldstein AC, Lafata JE, Davis RL, Gurwitz JH. Potentially inappropriate medication use by elderly persons in U.S. Health Maintenance Organizations 2000–2001. J Am Geriatr Soc 2005; 53: 227–32.

18 National Institute for Health and Clinical Excellence. Management of Hypertension in Adults in Primary Care. London: June 2006. Available at http://www.nice.org.uk/Guidance/CG34 (last accessed 5 August 2009).

19 O'Mahony D, Gallagher PF. Inappropriate prescribing in the older population: need for new criteria. Age Ageing 2008; 37: 138–41.

20 Barry PJ, O'Keeffe N, O'Connor KA, O'Mahony D. Inappropriate prescribing in the elderly: a comparison of the Beers criteria and the improved prescribing in the elderly tool (IPET) in acutely ill elderly hospitalized patients. J Clin Pharm Ther 2006; 31: 617–26.

21 Gallagher P, O'Mahony D. STOPP Screening Tool of Older Persons' potentially inappropriate Prescriptions): application to acutely ill elderly patients and comparison with Beers' criteria. Age Ageing 2008; 37: 673–9.

22 Barry PJ, Gallagher P, Ryan C, O'Mahony D. START screening tool to alert doctors to the right treatment) – an evidence-based screening tool to detect prescribing omissions in elderly patients. Age Ageing 2007; 36: 632–8.

23 Liu GG, Christensen DB. The continuing challenge of inappropriate prescribing in the elderly: an update of the evidence. J Am Pharm Assoc 2002; 42: 847–57.

24 Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987; 40: 373–83.

25 Goldstein LB, Samsa GP, Matchar DB, Horner RD. Charlson Index comorbidity adjustment for ischemic stroke outcome studies. Stroke 2004; 35: 1941–5.

26 Rius C, Perez G, Martinez JM, Bares M, Schiaffino A, Gispert R, Fernandez E. An adaptation of Charlson comorbidity index predicted subsequent mortality in a health survey. J Clin Epidemiol 2004; 57: 403–8.

27 World Health Organisation (WHO) collaborating centre for drug statistics methodology. ATC classification Index with DDDs. 2008.

28 Onder G, Pedone C, Landi F, Cesari M, Della Vedova C, Bernabei R, Gambassi G. Adverse drug reactions as cause

of hospital admissions: results from the Italian Group of Pharmacoepidemiology in the Elderly (GIFA). J Am Geriatr Soc 2002; 50: 1962–8.

29 Winterstein AG, Sauer BC, Hepler CD, Poole C. Preventable drug-related hospital admissions. Ann Pharmacother 2002; 36: 1238–48.

30 Gallagher P, O'Mahony D. Inappropriate prescribing in older people. Rev Clin Gerontol 2008; 12: 65–76.

31 Martin J, ed. British National Formulary, 55th edn. London: BMA/RPSGB, 2008.

32 Intercollegiate Stroke Working Party. National Clinical Guideline for Stroke, 3rd edn. London: Royal College of Physicians Clinical Effectiveness & Evaluation Unit, Royal College of Physicians, 2008; 67–8.

33 Sivenius J, Cunha L, Diener HC, Forbes C, Laakso M, Smets P, Riekkinen P. Second European Stroke Prevention Study: antiplatelet therapy is effective regardless of age. ESPS2 Working Group. Acta Neurol Scand 1999; 99: 54–60.

34 McGowan B, Bennett K, Tilson L, Barry M. Cost effective prescribing of proton pump inhibitors (PPI's) in the GMS scheme. Ir Med J 2005; 98: 78–80.

35 Wang PS, Bohn RL, Glynn RJ, Mogun H, Avorn J. Hazardous benzodiazepine regimens in the elderly: effects of half-life, dosage, and duration on risk of hip fracture. Am J Psychiatry 2001; 158: 892–8.

36 Pimlott NJ, Hux JE, Wilson LM, Kahan M, Li C, Rosser WW. Educating physicians to reduce benzodiazepine use by elderly patients: a randomized controlled trial. CMAJ 2003; 168: 835–9.

37 Parr JM, Kavanagh DJ, Cahill L, Mitchell G, Young RM. Effectiveness of current treatment approaches for benzodiazepine discontinuation: a meta-analysis. Addiction 2009; 104: 13–24.

38 Kvan E, Pettersen KI, Landmark K, Reikvam A. Treatment with statins after acute myocardial infarction in patients > or =80 years: underuse despite general acceptance of drug therapy for secondary prevention. Pharmacoepidemiol Drug Saf 2006; 15: 261–7.

39 Kuijpers MAJ, Van Marum RJ, Egberts ACG, Jansen PAF, the OLDY (Old people Drug & DYsregulations) Study Group. Relationship between polypharmacy and underprescribing. Br J Clin Pharmacol 2008; 65: 130–3.

40 Department of Health. Pharmacy in England – Building on Strengths – Delivering the Future. London: Department of Health, 2008.

41 Department of Health. Medicines and Older People: Implementing Medicines Related Aspects of the National Service Framework for Older People. London: Department of Health, 2001.

42 Holland R, Lenaghan E, Harvey I, Smith R, Shepstone L, Lipp A, Christou M, Evans D, Hand D. Does home based medication review keep older people out of hospital? The HOMER randomised controlled trial. BMJ 2005; 330: 293–7.

43 Zermansky AG, Petty DR, Raynor DK, Lowe CJ, Freemantle N, Vail A. Randomised controlled trial of clinical medication review by a pharmacist of elderly patients receiving repeat prescriptions in general practice. BMJ 2001; 323: 1340–3.

44 Lenaghan E, Holland R, Brooks A. Home-based medication review in a high risk elderly population in primary care – the POLYMED randomised controlled trail. Age Aging 2007; 36: 292–7.

45 Zermansky AG, Alldred DP, Petty DR, Raynor DK, Freemantle N, Eastaugh J, Bowie P. Clinical medication review by a pharmacist of elderly people living in care homes – randomised controlled trial. Age Aging 2006; 35: 586–91.

46 Krska J, Cromarty JA, Arris F, Jamieson D, Hansford D, Duffus PRS, Downie G, Seymour DG. Pharmacist-led medication review in patients over 65: a randomized, controlled trial in primary care. Age Aging 2001; 30: 205–11.