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STOPP (Screening Tool of Older Person's Prescriptions) and START (Screening Tool to Alert doctors to Right Treatment). Consensus validation

P. Gallagher¹, C. Ryan², S. Byrne², J. Kennedy² and D. O'Mahony³

¹Department of Geriatric Medicine, Cork University Hospital, Wilton, Cork, ²School of Pharmacy and ³Department of Medicine, University College Cork, Cork, Ireland

Key words

inappropriate prescribing – older person – screening

Abstract. Objective: Older people experience more concurrent illnesses, are prescribed more medications and suffer more adverse drug events than younger people. Many drugs predispose older people to adverse events such as falls and cognitive impairment, thus increasing morbidity and health resource utilization. At the same time, older people are often denied potentially beneficial, clinically indicated medications without a valid reason. We aimed to validate a new screening tool of older persons' prescriptions incorporating criteria for potentially inappropriate drugs called **STOPP** (Screening Tool of Older Persons' Prescriptions) and criteria for potentially appropriate, indicated drugs called **START** (Screening Tool to Alert doctors to Right, i.e. appropriate, indicated Treatment). Methods: A Delphi consensus technique was used to establish the content validity of STOPP/START. An 18-member expert panel from academic centers in Ireland and the United Kingdom completed two rounds of the Delphi process by mail survey. Inter-rater reliability was assessed by determining the κ -statistic for measure of agreement on 100 data-sets. Results: STOPP is comprised of 65 clinically significant criteria for potentially inappropriate prescribing in older people. Each criterion is accompanied by a concise explanation as to why the prescribing practice is potentially inappropriate. START consists of 22 evidence-based prescribing indicators for commonly encountered diseases in older people. Inter-rater reliability is favorable with a κ -coefficient of 0.75 for STOPP and 0.68 for START. Conclusion: STOPP/START is a valid, reliable and comprehensive screening tool that enables the prescribing physician to appraise an older patient's prescription drugs in the context of his/her concurrent diagnoses.

Introduction

Older people are a heterogeneous group, often with multiple comorbidities for which they are prescribed multiple medications. People who take multiple medications are at greater risk of adverse drug events (ADEs), drug-drug interactions and drug-disease interactions [Goldberg et al. 1996, Juurlink et al. 2003, Kohler et al. 2000]. This risk is heightened in older people because of age-related physiological changes, which often influence their pharmacokinetics and pharmacodynamics [Mangoni and Jackson 2003]. ADEs commonly present with non-specific symptoms such as confusion, lethargy, dizziness and falls with resultant injury such as hip fracture. ADEs are common in community-dwelling older people with a reported prevalence of up to 35% [Hanlon et al. 1997]. Not surprisingly, ADEs lead to increased healthcare utilization and are responsible for up to 30% of hospital admissions of older people [Lazarou et al. 1998, Lindley et al. 1992]. Inappropriate prescribing is a major cause of ADEs in older people [Klarin et al. 2005].

The prescription of drugs where the risk of an adverse event outweighs the clinical benefit is inappropriate, particularly where there is evidence in favor of a safer or more effective alternative therapy for the same condition. Inappropriate prescribing also encompasses the use of medicines at a higher frequency and for longer periods than clinically indicated, the use of medicines with inherently high risks of adverse drug-drug interactions and drug-disease interactions, and importantly, the under-use of beneficial medi-

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Correspondence to
Dr. D. O'Mahony
Department of Medicine,
University College Cork,
Ireland
denis.omahony@
mailp.hse.ie

cines that are clinically indicated, but often not prescribed for older people for no valid reasons [Rochon and Gurwitz 1999]. Such omission of appropriate medicines in older people has received relatively little attention in the literature to date.

Explicit and implicit criteria for inappropriate prescribing in older people have been developed, the most commonly cited being Beers' criteria [Beers 1997, Beers et al. 1991, Fick et al. 2003], the Improved Prescribing in the Elderly Tool (IPET) [Naugler et al. 2000], the Medication Appropriateness Index (MAI) [Hanlon et al. 1992] and the Assessing Care of Vulnerable Elders (ACOVE) under-use criteria [Shekelle et al. 2001]. Epidemiological studies in Europe and North America have used these criteria to determine the prevalence of inappropriate prescribing in older people, with rates ranging from 11 – 65% depending on the population being studied [Fialova et al. 2005, Pitkala et al. 2002, Spinewine et al. 2007, Stuck et al. 1994, van der Hoof et al. 2005, Zhan et al. 2001]. The use of such criteria as a quality of care measure in health services research has been demonstrated [Fialova et al. 2005, Pitkala et al. 2002, Spinewine et al. 2007, Stuck et al. 1994, van der Hoof et al. 2005, Zhan et al. 2001]. However, there are limited data to suggest a tangible clinical benefit to patients from using these criteria in terms of health outcomes and resource utilization [Spinewine et al. 2007]. Furthermore, the suitability of these criteria for day-to-day clinical use is uncertain.

Beers' criteria comprise two comprehensive lists of medications to be avoided in older people both independent of diagnosis and considering diagnosis [Fick et al. 2003]. However, many of the criteria are controversial [Pitkala et al. 2002, Rochon and Gurwitz 1999] and up to 50% of the proscribed drugs are not listed in European formularies [Fialova et al. 2005, Pitkala et al. 2002, van der Hoof et al. 2005]. IPET contains only 14 criteria and has clear-cut errors principally the avoidance of β -blockers in patients with heart failure [Naugler et al. 2000]. The MAI employs 10 implicit prescribing criteria to measure elements of appropriate prescribing e.g. cost, impractical directions, incorrect dose and duration of therapy [Hanlon et al. 1992]. However, the MAI does not explicitly

refer to specific drugs or drug classes that are problematic in older people, nor does it capture problems of under-use of clinically beneficial medicines.

With this in mind, we aimed to devise a tool with the following essential characteristics: (a) it would be presented as a comprehensive and valid list of potentially inappropriate prescriptions for common conditions in older people, (b) it would be based on current clinical evidence, (c) it would reflect the consensus opinion of a panel of experts in geriatric medicine, clinical pharmacology, psychiatry of old age, pharmacy and general practice and (d) it would include commonly encountered errors of commission, including drug-drug and drug-disease interactions, as well as instances of prescribing omission, i.e. the failure to prescribe drugs that are clearly indicated and likely to benefit older patients. We aimed to design a tool that was easy and time-efficient to use for the busy prescriber in day-to-day practice. The screening tool was given the acronym STOPP/START (Screening Tool of Older Person's potentially inappropriate Prescriptions/Screening Tool to Alert doctors to the Right, i.e. appropriate, indicated Treatment). We aimed to validate STOPP/START in terms of its content and inter-rater reliability.

Methods

Study design

We devised the initial draft version of STOPP/START by compiling lists of well-established instances of potentially inappropriate prescribing in older people according to the main physiological systems affected by the particular drugs or drug-classes in question. The evidence base of each instance was checked using a variety of sources, including the current British National Formulary [BMJ 2006], texts on geriatric pharmacotherapy [Armour and Cairns 2002, Curran and Bullock 2005, O'Mahony and Martin 1999] and extensive literature review. The draft criteria were agreed on a consensus basis within our own research group to begin with and subsequently distributed to a panel of 18 experts in geriatric pharmacotherapy for validation by the Delphi consensus technique [Dalkey

1967]. The Delphi technique is a method of structuring group communication such that individuals within the group can deal with a complex problem, inappropriate prescribing in older people in this instance, and reach consensus by attempting to resolve disagreement. The group of experts independently answers a sequence of questionnaires in which the responses to one questionnaire are refined and used to produce the next questionnaire. The aim is to achieve consensus on an issue, with gradual formation of a considered opinion, while avoiding direct confrontation. The Delphi technique has been used widely in health services research within the fields of technology assessment, clinical practice development, education and training [Beers 1997, Beers et al. 1991, Fick et al. 2003, Walley and Webb 1997].

Expert panel selection

18 experts, with recognized credentials in their specialist areas, were invited by letter to participate in the Delphi process. Study design and aims were explained in detail to each participant. The panel comprised teaching hospital consultants in geriatric medicine (n = 9), clinical pharmacology (n = 3) and old age psychiatry (n = 1), 2 senior academic primary care physicians, and 3 senior hospital pharmacists with a special interest in geriatric pharmacotherapy, representing the range of medical specialties that are regularly involved in geriatric pharmacotherapy. Panelists were from geographically diverse areas of Ireland and the United Kingdom, the majority being affiliated to Irish university medical centers. All panellists completed all rounds of the Delphi process.

Data collection and analysis

The first round questionnaire was posted to each panellist. This consisted of 68 STOPP criteria and 22 START criteria. STOPP criteria were presented as statements describing each instance of potentially inappropriate prescribing in people aged 65 years and over, e.g. "the use of a long-term neuroleptic medication in a patient with Parkinson's disease is potentially inappropriate due to the risk of worsening extrapyramidal symptoms". With

START criteria, similar clinical scenarios were presented, e.g. "warfarin should be prescribed in elderly patients with chronic atrial fibrillation where no contraindication to warfarin exists". All statements were constructed in a similar manner to reduce bias. Panellists were asked to rate their level of agreement with each statement on a 5-point Likert scale [Matell and Jacoby 1971] where 1 = strongly agree, 2 = agree, 3 = ambivalent, 4 = disagree, 5 = strongly disagree, 0 = unable to offer an opinion. Each panellist was invited to add suggestions in relation to dose, frequency and duration of medication, with relevant references, and also to propose instances of inappropriate prescribing not included in the list presented to them. For each statement, the mean Likert scale response and 95% confidence interval were calculated. Statements whose upper limit of the 95% confidence interval was less than 3 were accepted for inclusion in the tool. Statements whose lower limit of the 95% confidence interval were greater than 3 on the Likert scale were rejected from the tool. Statements whose 95% confidence interval included the value of 3 were rephrased in accordance with the suggestions of the panellists to be included in the next round of the Delphi exercise.

Inter-rater reliability

STOPP/START criteria were independently applied by 2 researchers to 100 data sets that were abstracted from the case notes of 100 patients over the age of 65 years admitted to an acute general hospital. The data sets consisted of a list of medical comorbidities, concurrent medications, serum biochemistry profile, blood pressure measurements and electrocardiographs. The proportion of positive and negative agreement was determined. The chance corrected measures of agreement for STOPP and START were determined using the κ -statistic [Cohen 1960].

Results

The Delphi validation process was completed in two rounds between October and December 2006 and full consensus was reached without the need to proceed to a third round. The final consensus-derived STOPP

and START criteria are presented in Tables 1 and 2, respectively. The criteria were arranged according to the relevant physiological systems for ease of use by clinicians, and included specific criteria pertaining to analgesic drugs, drugs that adversely affect older people who fall, and duplicate drug class prescriptions. Each STOPP criterion is accompanied by a concise explanation as to why the prescribing practice may be inappropriate in an older person.

Consensus was achieved on all 22 START criteria and on 65 of 68 STOPP criteria following the first round questionnaire. Consensus could not be reached on 3 STOPP statements following a second round questionnaire. These 3 statements were therefore removed from the list: (a) use of a diuretic with an SSRI due to the significant risk of hyponatremia; (b) bendrofluazide at doses greater than 2.5 mg once daily; (c) use of clopidogrel as first-line antiplatelet therapy where there is no contraindication to aspirin for treatment of stable coronary, cerebral or peripheral vascular disease. Some panellists commented that bendrofluazide, the most widely prescribed thiazide diuretic in the United Kingdom and Ireland, could be used safely in doses of up to 5 mg daily, and that the “inappropriate” use of clopidogrel in this instance was an issue of cost and not of safety.

The majority of STOPP statements pertain to clinically significant drug-drug interactions and drug-disease interactions. Consensus was reached on the upper dose limit of two medications, digoxin and aspirin, above which the risks of toxicity and adverse drug event are unacceptable. The panel agreed that in most older persons, the standard maintenance dose of digoxin should not exceed 125 µg per day owing to the age-related decline in glomerular filtration rate and resultant higher risk of digoxin toxicity. The maintenance dose of aspirin should not exceed 150 mg per day, given the lack of proven benefit and higher risk of significant bleeding with higher doses. The biochemical indicators of significant renal failure upon which the panel agreed, i.e. serum creatinine > 150 µmol/l or estimated glomerular filtration rate (GFR) of < 50 ml/min are based on the recommendations of the current British National Formulary (BNF) [2006]. The panel agreed that physicians should be aware of their patients’

renal function before prescribing drugs such as digoxin, NSAIDs and metformin. Consensus was reached on duration of drug prescription in ten instances, beyond which the prescription is potentially inappropriate owing to increased risk of adverse effects. These are clearly described in Table 1.

Inter-rater reliability

For STOPP criteria the proportion of positive agreement was 87% and the proportion of negative agreement was 13%. The chance-corrected measure of agreement (κ -statistic) was 0.75. For START criteria, the proportion of positive agreement was 84% and the proportion of negative agreement was 16%. The chance-corrected measure of agreement (κ -statistic) was 0.68.

Discussion

STOPP/START is the first physiological systems-based screening tool for potentially inappropriate drug therapy in older people, the greatest consumers of pharmacotherapy globally. The present study describes the validation of STOPP/START criteria for inappropriate prescribing, using the Delphi method. The end product is a set of up-to-date criteria organized according to physiological systems that encompasses both instances of potentially inappropriate prescribing and instances of omission of potentially beneficial pharmacotherapy. STOPP/START focuses on commonly prescribed medicines in older people and the potential problems associated with such prescriptions in the context of the multiple clinical illnesses that older people experience. STOPP/START is not intended to be an exhaustive list of all potential drug/drug interactions as these are available to all prescribers in standard formularies such as the British National Formulary [2006]. We contend that STOPP/START represents a potentially useful screening tool applicable to routine clinical practice. Inter-rater reliability is sufficiently high and average time for deployment is sufficiently low (mean (SD) time 90 ± 35 seconds) to make STOPP/START appropriate to clinical practice. In contrast, Beers’ criteria are not presented in any particular order or structure.

Table 1. **STOPP: Screening Tool of Older People's potentially inappropriate Prescriptions.**
The following drug prescriptions are potentially inappropriate in persons aged ≥ 65 years of age.

A. Cardiovascular system

1. Digoxin at a long-term dose > 125 $\mu\text{g}/\text{day}$ with impaired renal function* (*increased risk of toxicity*) [Cusack et al. 1979, Gooselink et al. 1997, Haas and Young 1999].
2. Loop diuretic for dependent ankle edema only i.e. no clinical signs of heart failure (*no evidence of efficacy, compression hosiery usually more appropriate*) [Alguire and Mathes 1997, Kolbach et al. 2004].
3. Loop diuretic as first-line monotherapy for hypertension (*safer, more effective alternatives available*) [Williams et al. 2004].
4. Thiazide diuretic with a history of gout (*may exacerbate gout*) [Gurwitz et al. 1997].
5. Non-cardioselective β -blocker with Chronic Obstructive Pulmonary Disease (COPD) (*risk of increased bronchospasm*) [van der Woude et al. 2005, Salpeter et al. 2005].
6. β -blocker in combination with verapamil (*risk of symptomatic heart block*) [BNF 2006].
7. Use of diltiazem or verapamil with NYHA class III or IV heart failure (*may worsen heart failure*) [BNF 2006].
8. Calcium channel blockers with chronic constipation (*may exacerbate constipation*) [Dougall and McLay 1996].
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 (*high risk of gastrointestinal bleeding*) [Garcia Rodriguez et al. 2001, Holbrook et al. 2005].
10. Dipyridamole as monotherapy for cardiovascular secondary prevention (*no evidence for efficacy*) [De Schryver et al. 2006].
11. Aspirin with a past history of peptic ulcer disease without histamine H_2 -receptor antagonist or proton pump inhibitor (*risk of bleeding*) [Garcia Rodriguez et al. 2001].
12. Aspirin at dose > 150 mg/day (*increased bleeding risk, no evidence for increased efficacy*) [Fisher and Knappertz 2006].
13. Aspirin with no history of coronary, cerebral or peripheral vascular symptoms or occlusive event (*not indicated*).
14. Aspirin to treat dizziness not clearly attributable to cerebrovascular disease (*not indicated*).
15. Warfarin for first, uncomplicated deep venous thrombosis for longer than 6 months duration (*no proven added benefit*) [Pinede et al. 2001].
16. Warfarin for first uncomplicated pulmonary embolus for longer than 12 months duration (*no proven benefit*) [Pinede et al. 2001].
17. Aspirin, clopidogrel, dipyridamole or warfarin with concurrent bleeding disorder (*high risk of bleeding*) [BNF 2006].

B. Central nervous system and psychotropic drugs

1. Tricyclic antidepressants (TCAs) with dementia (*risk of worsening cognitive impairment*) [Smith 1998, Sommer et al. 2003].
2. TCAs with glaucoma (*likely to exacerbate glaucoma*) [Smith 1998, Sommer et al. 2003].
3. TCAs with cardiac conductive abnormalities (*pro-arrhythmic effects*) [Smith 1998, Sommer et al. 2003].
4. TCAs with constipation (*likely to worsen constipation*) [Smith 1998, Sommer et al. 2003].
5. TCAs with an opiate or calcium channel blocker (*risk of severe constipation*) [Smith 1998, Sommer et al. 2003].
6. TCA's with prostatism or prior history of urinary retention (*risk of urinary retention*) [Smith 1998, Sommer et al. 2003].
7. Long-term (i.e. > 1 month), long-acting benzodiazepines, e.g. chlordiazepoxide, fluzepam, nitrazepam, chlorazepate and benzodiazepines with long-acting metabolites, e.g. diazepam (*risk of prolonged sedation, confusion, impaired balance, falls*) [Gray et al. 2006, Hanlon et al. 1998, Tamblin et al. 2005].
8. Long-term (i.e. > 1 month) neuroleptics as long-term hypnotics (*risk of confusion, hypotension, extrapyramidal side effects, falls*) [Alexopoulos et al. 2004, Maixner et al. 1999].
9. Long-term neuroleptics (> 1 month) in those with parkinsonism (*likely to worsen extrapyramidal symptoms*) [Smith 1998, van de Vijver et al. 2002].
10. Phenothiazines in patients with epilepsy (*may lower seizure threshold*) [Alexopoulos et al. 2004, BNF 2006].
11. Anticholinergics to treat extrapyramidal sideeffects of neuroleptic medications (*risk of anticholinergic toxicity*) [Mintzer and Burns 2000, Tune 2001].
12. Selective serotonin re-uptake inhibitors (SSRIs) with a history of clinically significant hyponatremia (*non-iatrogenic hyponatremia < 130 mmol/l within the previous 2 months*) [Jacob and Spinler 2006].
13. Prolonged use (> 1 week) of first-generation antihistamines, i.e. diphenhydramine, chlorpheniramine, cyclizine, promethazine (*risk of sedation and anti-cholinergic side effects*) [Sutter et al. 2003].

* Serum creatinine > 150 $\mu\text{mol}/\text{l}$, or estimated GFR < 50 ml/min [BNF 2006].

Table 1. Continuation.

C. Gastrointestinal system

1. Diphenoxylate, loperamide or codeine phosphate for treatment of diarrhea of unknown cause (*risk of delayed diagnosis, may exacerbate constipation with overflow diarrhea, may precipitate toxic megacolon in inflammatory bowel disease, may delay recovery in unrecognized gastroenteritis*) [Lustman et al. 1987, Thielman and Guerrant 2004].
2. Diphenoxylate, loperamide or codeine phosphate for treatment of severe infective gastroenteritis, i.e. bloody diarrhea, high fever or severe systemic toxicity (*risk of exacerbation or protraction of infection*) [Thielman and Guerrant 2004].
3. Prochlorperazine (Stemetil) or metoclopramide with parkinsonism (*risk of exacerbating parkinsonism*) [Smith 1998].
4. PPI for peptic ulcer disease at full therapeutic dosage for > 8 weeks (*dose reduction or earlier discontinuation indicated*) [BNF 2006, NICE guideline 2000/022].
5. Anticholinergic antispasmodic drugs with chronic constipation (*risk of exacerbation of constipation*) [Bosshard et al. 2004].

D. Respiratory system

1. Theophylline as monotherapy for COPD (*safer, more effective alternative; risk of adverse effects due to narrow therapeutic index*) [Ramsdell 1995].
2. Systemic corticosteroids instead of inhaled corticosteroids for maintenance therapy in moderate-to-severe COPD (*unnecessary exposure to long-term side effects of systemic steroids*) [Buist et al. 2006, McEvoy and Niewoehner 1997].
3. Nebulized ipratropium with glaucoma (*may exacerbate glaucoma*) [BNF 2006].

E. Musculoskeletal system

1. Non-steroidal anti-inflammatory drug (NSAID) with history of peptic ulcer disease or gastrointestinal bleeding, unless with concurrent histamine H₂-receptor antagonist, PPI or misoprostol (*risk of peptic ulcer relapse*) [Hooper et al. 2004].
2. NSAID with moderate-to-severe hypertension (*risk of exacerbation of hypertension*) [Whelton 2006].
3. NSAID with heart failure (*risk of exacerbation of heart failure*) [Slørddal and Spigest 2006].
4. Long-term use of NSAID (> 3 months) for symptom relief of mild osteoarthritis (*simple analgesics preferable and usually as effective for pain relief*) [Altman et al. 2000].
5. Warfarin and NSAID together (*risk of gastrointestinal bleeding*) [Battistella et al. 2005].
6. NSAID with chronic renal failure* (*risk of deterioration in renal function*) [Cheng and Harris 2005].
7. Long-term corticosteroids (> 3 months) as monotherapy for rheumatoid arthritis or osterarthritis (*risk of major systemic corticosteroid side-effects*) [Altman et al. 2000, Kwoh et al. 2002, Lee and Weinblatt 2001].
8. Long-term NSAID or colchicine for chronic treatment of gout where there is no contraindication to allopurinol (*allopurinol first-choice prophylactic drug in gout*) [Schlesinger 2004, Terkeltaub 2004].

F. Urogenital system

1. Bladder antimuscarinic drugs with dementia (*risk of increased confusion, agitation*) [Kay et al. 2005, Staskin 2005].
2. Antimuscarinic drugs with chronic glaucoma (*risk of acute exacerbation of glaucoma*) [Staskin 2005].
3. Antimuscarinic drugs with chronic constipation (*risk of exacerbation of constipation*) [Staskin 2005].
4. Antimuscarinic drugs with chronic prostatism (*risk of urinary retention*) [Staskin 2005].
5. α -blockers in males with frequent incontinence, i.e. one or more episodes of incontinence daily (*risk of urinary frequency and worsening of incontinence*) [Sarkar and Ritch 2000].
6. α -blockers with long-term urinary catheter in situ, i.e. more than 2 months (*drug not indicated*).

G. Endocrine system

1. Glibenclamide or chlorpropamide with type 2 diabetes mellitus (*risk of prolonged hypoglycemia*) [Cheillah and Burge 2004].
2. β -blockers in those with diabetes mellitus and frequent hypoglycemic episodes i.e. ≥ 1 episode per month (*risk of masking hypoglycemic symptoms*) [Cheillah and Burge 2004].
3. Estrogens with a history of breast cancer or venous thromboembolism (*increased risk of recurrence*) [Beral et al. 2002, Collaborative Group on Hormonal Factors in Breast Cancer 1997, Grady and Sawaya 1998].
4. Estrogens without progestogen in patients with intact uterus (*risk of endometrial cancer*) [Lethaby et al. 2000].

* Serum creatinine > 150 $\mu\text{mol/l}$, or estimated GFR 20 – 50 ml/min [BNF 2006].

Table 1. Continuation.

H. Drugs that adversely affect fallers

1. Benzodiazepines (*sedative, may cause reduced sensorium, impair balance*) [Tinetti 2003].
2. Neuroleptic drugs (*may cause gait dyspraxia, parkinsonism*) [Tinetti 2003].
3. First-generation antihistamines (*sedative, may impair sensorium*) [Sutter et al. 2003].
4. Vasodilator drugs with persistent postural hypotension, i.e. recurrent > 20 mmHg drop in systolic blood pressure (*risk of syncope, falls*) [Leipzig et al. 1999].
5. Long-term opiates in those with recurrent falls (*risk of drowsiness, postural hypotension, vertigo*) [American Geriatrics Society Panel on Persistent Pain in Older Persons 2002, Leipzig et al. 1999].

I. Analgesic drugs

1. Use of long-term powerful opiates, e.g. morphine or fentanyl as first-line therapy for mild-to-moderate pain (*World Health Organization analgesic ladder not observed*) [American Geriatrics Society Panel on Persistent Pain in Older Persons 2002].
2. Regular opiates for more than 2 weeks in those with chronic constipation without concurrent use of laxatives (*risk of severe constipation*) [Walsh 1999].
3. Long-term opiates in those with dementia unless indicated for palliative care or management of moderate/severe chronic pain syndrome (*risk of exacerbation of cognitive impairment*) [American Geriatrics Society Panel on Persistent Pain in Older Persons 2002].

J. Duplicate drug classes

Any duplicate drug class prescription, e.g. two concurrent opiates, NSAIDs, SSRIs, loop diuretics, ACE inhibitors (*optimization of monotherapy within a single drug class should be observed prior to considering a new class of drug*).

STOPP contains 33 instances of potentially inappropriate prescribing not found in the most recent iteration of Beers' criteria [Fick et al. 2003] with the total number of instances cited in STOPP being 65. We believe that this indicates significant deficits in Beers' criteria and that STOPP is more likely to detect potentially inappropriate prescribing in older people. In STOPP, we have deliberately concentrated on commonly prescribed drugs, as opposed to drugs that are outmoded and rarely prescribed, in Western Europe at least. The most recent version of Beers' criteria [Fick et al. 2003] still includes several drugs that are rarely prescribed at the present time (Table 3), in effect making these criteria redundant. Not surprisingly, therefore, Beers' criteria have not found their way into mainstream routine clinical practice in geriatric medicine.

START criteria represent the other side of potentially inappropriate prescribing, i.e. errors of omission of drug therapy likely to be beneficial to the patient which occur for ageist or irrational reasons. This aspect of inappropriate prescribing in older people has been seriously neglected in the literature to date. START criteria, like STOPP, are arranged according to physiological systems for ease of use by the prescriber reviewing an older pa-

tient's pharmacotherapy. Juxtaposition of potential errors of omission with potential errors of prescribing commission, we contend, gives a more holistic and comprehensive assessment of prescribing hygiene reflecting the fact that inappropriate prescribing is as much about the list of medicines that is wrongly left out as it is about what is wrongly left in. In this way, STOPP/START attempts to educate the prescriber in ways of optimizing medication hygiene in frailer older people, in particular, who frequently fall foul of polypharmacy and its directly related problem of ADEs.

STOPP/START criteria have potentially major pharmaco-economic implications. The economic and personal costs of drug-related major morbidity resulting in emergency department referrals, hospitalization and in some cases, death, are very considerable indeed [Hanlon et al. 1997, Juurlink et al. 2003, Klarin et al. 2005, Lazarou et al. 1998]. At the less severe end of the ADE spectrum, there are the economic implications of increased medical consultations, increased medication to counteract unrecognized ADEs and increased spending on over-the-counter drugs. Any screening tool that achieves even a modest (say, 10–20%) reduction in inappropriate prescribing (IP) is likely to be cost-effective,

Table 2. **START: Screening Tool to Alert doctors to Right**, i.e. appropriate, indicated **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 [Hart et al. 1999, Ross et al. 2005, Mant et al. 2007].
2. Aspirin in the presence of chronic atrial fibrillation, where warfarin is contraindicated, but not aspirin [Hart et al. 1999, Ross et al. 2005].
3. Aspirin or clopidogrel with a documented history of atherosclerotic coronary, cerebral or peripheral vascular disease in patients with sinus rhythm [Smith et al. 2006].
4. Antihypertensive therapy where systolic blood pressure consistently > 160 mmHg [Williams et al. 2004, Papademetriou et al. 2004, Skoog et al. 2004, Trenkwalder et al. 2005].
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 greater than 5 years [Brown and Moussa 2003, Amarenco et al. 2004, Smith et al. 2006].
6. Angiotensin converting enzyme (ACE) inhibitor with chronic heart failure [Hunt et al. 2005].
7. ACE inhibitor following acute myocardial infarction [ACE Inhibitor Myocardial Infarction Collaborative Group 1998, Antman et al. 2004].
8. β -blocker with chronic stable angina [Gibbons et al. 2003].

B. Respiratory system

1. Regular inhaled β_2 -agonist or anticholinergic agent for mild-to-moderate asthma or COPD [Buist et al. 2006].
2. Regular inhaled corticosteroid for moderate/severe asthma or COPD, where predicted $FEV_1 < 50\%$ [Buist et al. 2006].
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) [Cranston et al. 2005, Buist et al. 2006].

C. Central nervous system

1. L-DOPA in idiopathic Parkinson's disease with definite functional impairment and resultant disability [Kurlan 1998, Danisi 2002].
2. Antidepressant drug in the presence of moderate/severe depressive symptoms lasting at least three months [Lebowitz et al. 1997, Wilson et al. 2006].

D. Gastrointestinal system

1. Proton pump inhibitor with severe gastroesophageal acid reflux disease or peptic stricture requiring dilation [Hungin and Raghunath 2004].
2. Fiber supplement for chronic, symptomatic diverticular disease with constipation [Aldoori et al. 1994].

E. Musculoskeletal system

1. Disease-modifying antirheumatic drug (DMARD) with active moderate/severe rheumatoid disease lasting > 12 weeks [Kwoh et al. 2002].
2. Bisphosphonates in patients taking maintenance corticosteroid therapy [Buckley et al. 2001].
3. Calcium and vitamin D supplement in patients with known osteoporosis (previous fragility fracture, acquired dorsal kyphosis) [Gass and Dawson Hughes 2006].

F. Endocrine system

1. Metformin with type 2 diabetes \pm metabolic syndrome (in the absence of renal impairment*) [Mooradian 1996, Johansen 1999].
2. ACE inhibitor or angiotensin receptor blocker in diabetes with nephropathy, i.e. overt proteinuria or microalbuminuria (> 30 mg/24 hours) \pm serum biochemical renal impairment* [Sigal et al. 2005].
3. Antiplatelet therapy in diabetes mellitus with coexisting major cardiovascular risk factors (hypertension, hypercholesterolemia, smoking history) [Sigal et al. 2005].
4. Statin therapy in diabetes mellitus if coexisting major cardiovascular risk factors present [Sigal et al. 2005].

* Serum creatinine > 150 μ mol/l, or estimated GFR < 50 ml/min [BNF 2006].

Table 3. Drugs included in Beers' criteria that are rarely used in European Prescribing Practice.

Trimethobenzamide	Methocarbamol	Carisoprolol
Metaxalone	Cyclobenzaprine	Meprobamate
Halazepam	Reserpine	Chlorpropamide
Hydroxyzine	Hyoscyamine	Clidinium
Cyclandelate	Cyproheptadine	Tripelenamine
Guanedrel	Oxaprozin	Guanethidine
Mesoridazine	Isoxsuprine	Thioridazine
Amphetamines	Clonidine	Ethacrynic acid
Dicyclomine	Phenylpropanolamine	Pemolin

given that screening tools are cheap and, if well designed, easy to use. We contend that STOPP/START meets the essential criteria for further study as a potentially effective screening tool for inappropriate prescribing in older people, i.e. IP is a common problem, IP results in major morbidity and mortality, IP is usually preventable and correctable when detected with inexpensive measures to improve prescription hygiene. Further study with STOPP/START is, we believe, well warranted in the form prospective, randomized controlled clinical trials in IP detection, correction and prevention of IP-related adverse clinical events.

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Conflict of interest statement

The authors have no financial interest or conflicts of interest in this study. All authors contributed to study conception and design. Dr. Paul Gallagher, Dr. Stephen Byrne and Dr. Denis O'Mahony recruited the expert panel. Dr. Paul Gallagher and Dr. Denis O'Mahony analyzed and interpreted the data and drafted the manuscript. Ms. Cristin Ryan, Dr. Stephen Byrne and Professor Julia Kennedy critically revised the manuscript. All authors approved the final version of the manuscript.

References

- ACE Inhibitor Myocardial Infarction Collaborative Group.* Indicators for ACE inhibitors in the early treatment of acute myocardial infarction: systematic overview of individual data from 100,000 patients in randomised trials. *Circulation.* 1998; *97*: 2202-2212.
- Aldoori WH, Giovannucci EL, Rimm EB et al.* A prospective study of diet and the risk of symptomatic diverticular disease in men. *Am J Clin Nutr.* 1994; *60*: 757-764.
- Alexopoulos G, Streim J, Carpenter D et al.* Expert consensus panel for using antipsychotic drugs in older patients. Using antipsychotic agents in older patients. *J Clin Psychiatry.* 2004; *65* (Suppl 2): 5-99.
- Alguire PC, Mathes BM.* Chronic venous insufficiency and venous ulceration. *J Gen Intern Med.* 1997; *12*: 374-383.
- Altman RD, Hochberg MC, Moskowitz RW et al.* Recommendations for the Medical Management of Osteoarthritis of the Hip and Knee. American College of Rheumatology Subcommittee on Osteoarthritis Guidelines. *Arthritis & Rheumatism.* 2000; *43*: 1905-1915.
- Amarenco P, Labreuche J, Lavalley P et al.* Statins in stroke prevention and carotid atherosclerosis. Systematic review and up-to-date meta-analysis. *Stroke.* 2004; *35*: 2902-2909.
- American Geriatrics Society Panel on Persistent Pain in Older Persons.* The management of persistent pain in older persons. *J Am Geriatr Soc.* 2002; *50*: 205-224.
- Antithrombotic Trialists' Collaboration.* Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients. *BMJ.* 2002; *324*: 71-86.
- Antman EM, Anbe DT, Armstrong PW et al.* ACC/AHA guidelines for the management of patients with ST-el-

- evation myocardial infarction – executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to revise the 1999 Guidelines for the management of patients with acute myocardial infarction). *Circulation*. 2004; *110*: 588-636.
- Armour D, Cairns C. *Medicines in the elderly*. London: Pharmaceutical Press; 2002.
- Battistella M, Mamdani MM, Juurlink DN *et al*. Risk of upper gastrointestinal haemorrhage in warfarin users treated with nonselective NSAIDs or COX-2 inhibitors. *Arch Intern Med*. 2005; *165*: 189-192.
- Beers MH. Explicit criteria for determining potentially inappropriate medication use by the elderly. An update. *Arch Intern Med*. 1997; *157*: 1531-1536.
- Beers MH, Ouslander JG, Rollinger I *et al*. Explicit criteria for determining inappropriate medication use in nursing home residents. *Arch Intern Med*. 1991; *151*: 1825-1832.
- Beral V, Banks E, Reeves G. Evidence from randomized trials on the long term effects of hormone replacement therapy. *Lancet*. 2002; *360*: 942-944.
- British National Formulary. BMJ Publishing Group Ltd and RPS Publishing; September 2006.
- Bosshard W, Dreher R, Schnegg J *et al*. The treatment of chronic constipation in elderly people. An update. *Drugs Aging*. 2004; *21*: 911-930.
- Brown WV, Moussa M. Perspectives from the antihypertensive and lipid-lowering treatment to prevent heart attack trial – lipid lowering trial and the Anglo-Scandinavian cardiac outcomes trial – lipid lowering arm. *Curr Opin Lipidol*. 2003; *14*: 593-597.
- Buckley L, Hochberg M, Lane N *et al*. Recommendations for the prevention and treatment of glucocorticoid-induced osteoporosis 2001 update. *Arthritis & Rheumatism*. 2001; *44*: 1496-1503.
- Buist AS, Anzueto A, Calverley P *et al*. Global strategy for the diagnosis, management and prevention of chronic obstructive pulmonary disease. <http://www.goldcopd.com>; 2006.
- Cheillah A, Burge M. Hypoglycaemia in elderly patients with diabetes mellitus: causes and strategies for prevention. *Drugs Aging*. 2004; *21*: 511-530.
- Cheng HF, Harris RC. Renal effects of non-steroidal anti-inflammatory drugs and selective cyclooxygenase-2 inhibitors. *Curr Pharm Des*. 2005; *11*: 1795-1804.
- Cohen J. A coefficient of agreement for nominal scales. *Educ Psychol Meas*. 1960; *20*: 37-46.
- Collaborative Group on Hormonal Factors in Breast Cancer. Breast cancer and hormone replacement therapy: collaborative reanalysis of data from 51 epidemiological studies of 52705 women with breast cancer and 108411 women without breast cancer. *Lancet*. 1997; *350*: 1047-1059.
- Cranston JM, Crockett AJ, Moss JR *et al*. Domiciliary oxygen in chronic obstructive pulmonary disease. *Cochrane Database Syst Rev*. 2005; *4*: CD001744.
- Curran S, Bullock R. *Practical Old Age Psychopharmacology: a multiprofessional approach*. Oxford: Radcliffe Publishing; 2005.
- Cusack B, Kelly J, O'Malley K *et al*. Digoxin in the elderly: pharmacokinetic consequences of old age. *Clin Pharmacol Ther*. 1979; *25*: 772-776.
- Dalkey NC. *Delphi*. P-3704 RAND. Santa Monica, CA: RAND Corp; 1967.
- Danisi F. Parkinson's disease. Therapeutic strategies to improve patient function and quality of life. *Geriatrics*. 2002; *57*: 46-50.
- De Schryver EL, Algra A, van Gijn J. Dipyridamole for preventing stroke and other vascular events in patients with vascular disease. *Cochrane Database Syst Rev*. 2006; CD001820.
- Dougall HT, McLay J. A comparative review of the adverse effects of calcium antagonists. *Drug Saf*. 1996; *15*: 91-106.
- Fam AG. Gout in the elderly. Clinical presentation and treatment. *Drugs Aging*. 1998; *13*: 229-243.
- Fialova D, Topinkova E, Gambassi G *et al*. Potentially inappropriate medication use among elderly home care patients in Europe. *JAMA*. 2005; *293*: 1348-1358.
- Fick DM, Cooper JW, Wade W *et al*. 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*: 2716-2724.
- Fisher M, Knappertz V. The dose of aspirin for the prevention of cardiovascular and cerebrovascular events. *Curr Med Res Opin*. 2006; *22*: 1239-1270.
- Furukawa TA, McGuire H, Barbui C. Meta-analysis of effects and side effects of low dosage tricyclic antidepressants in depression: systematic review. *BMJ*. 2002; *325*: 991-999.
- Garcia Rodriguez LA, Hernandez-Diaz S, de Abajo FJ. Association between aspirin and upper gastrointestinal complications. Systematic review of epidemiological studies. *Br J Clin Pharmacol*. 2001; *52*: 563-571.
- Gass M, Dawson Hughes B. Preventing osteoporosis related fractures: an overview. *Am J Med*. 2006; *119* (Suppl 1): S3-S11.
- Gibbons RJ, Abrams J, Chatterjee K *et al*. ACC/AHA 2002 guideline update for the management of patients with chronic stable angina – summary article: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on the Management of Patients with Chronic Stable Angina). *Circulation*. 2003; *107*: 149-158.
- Goldberg RM, Mabee J, Chan L, Wong S. Drug-drug and drug-disease interactions in the emergency department: analysis of a high-risk population. *Am J Emerg Med*. 1996; *14*: 447-450.
- Gooselink A, Van Veldhuisen D, Crigns H. When, and when not, to use digoxin in the elderly. *Drugs Aging*. 1997; *10*: 411-420.
- Grady D, Sawaya G. Postmenopausal hormone therapy increases risk of deep venous thrombosis and pulmonary embolism. *Am J Med*. 1998; *105*: 41-43.
- Gray SL, LaCroix AZ, Hanlon JT *et al*. Benzodiazepine use and physical disability in community dwelling older adults. *J Am Geriatr Soc*. 2006; *54*: 224-230.
- Gurwitz JH, Kalish SC, Bohn RL *et al*. Thiazide diuretics and the initiation of anti-gout therapy. *J Clin Epidemiol*. 1997; *50*: 953-959.
- Haas JG, Young JB. Inappropriate use of digoxin in the elderly. How widespread is the problem and how can it be solved? *Drug Safety*. 1999; *20*: 223-230.
- Hanlon JT, Schmader KE, Sansa GP *et al*. A method for assessing drug therapy appropriateness. *J Clin Epidemiol*. 1992; *45*: 1045-1051.
- Hanlon JT, Schmader KE, Kornkowsky MJ *et al*. Adverse Drug events in high risk older outpatients. *J Am Geriatr Soc*. 1997; *45*: 945-948.
- Hanlon JT, Horner RD, Schmader KE *et al*. Benzodiazepine use and cognitive function among community dwelling elderly. *Clin Pharmacol Ther*. 1998; *64*: 684-692.

- Hart RG, Benavente O, McBride R et al. Antithrombotic therapy to prevent stroke in patients with atrial fibrillation: a meta-analysis. *Ann Intern Med.* 1999; *131*: 492-501.
- Heart Protection Study Collaborative Group. Effects of cholesterol lowering with simvastatin on stroke and other major vascular events in 20,536 people with cerebrovascular disease or other high-risk conditions. *Lancet.* 2004; *363*: 757-767.
- Holbrook AM, Pareira JA, Labiris R et al. Systematic overview of warfarin and its drug and food interactions. *Arch Intern Med.* 2005; *165*: 1095-1106.
- Hooper L, Brown TJ, Elliot RA et al. The effectiveness of five strategies for the prevention of gastrointestinal toxicity induced by non-steroidal anti-inflammatory drugs: systematic review. *BMJ.* 2004; *329*: 948-952.
- Hungin AP, Raghunath A. Managing gastro-oesophageal reflux disease in the older patient. *Digestion.* 2004; *69* (Suppl 1): 17-24.
- Hunt SA, Abraham WT, Chin MH et al. ACC/AHA 2005 guideline update for the diagnosis and management of chronic heart failure in the adult – summary article: A report of the American College of Cardiology/American Heart Association Task Force on practice Guidelines (Writing Committees to Update the 2001 Guidelines for the evaluation and management of heart failure): Developed in collaboration with the American College of Chest Physicians and the International Society for Heart and Lung Transplantation: Endorsed by the Heart Rhythm Society. *Circulation.* 2005; *112*: 1825-1852.
- Jacob S, Spinler SA. Hyponatraemia associated with selective serotonin-reuptake inhibitors in older adults. *Ann Pharmacother.* 2006; *40*: 1618-1622.
- Johansen K. Efficacy of metformin in the treatment of NIDDM: meta-analysis. *Diabetes Care.* 1999; *22*: 33-37.
- Johnson A, Seidemann P, Day R. NSAID-related adverse drug interactions with clinical relevance. An update. *Int J Clin Pharmacol Ther.* 1994; *32*: 509-532.
- Juurlink DN, Mamdami M, Kopp A et al. Drug-drug interactions among elderly patients hospitalised for drug toxicity. *JAMA.* 2003; *289*: 1652-1658.
- Kay GG, Abou-Donia MB, Messer WS Jr et al. Antimuscarinic drugs for overactive bladder and their potential effects on cognitive function in older patients. *J Am Geriatr Soc.* 2005; *53*: 2195-2201.
- Klarin I, Wimo A, Fastbom J. The association of inappropriate drugs use with hospitalisation and mortality: a population based study of the very old. *Drugs Aging.* 2005; *22*: 69-82.
- Kohler GI, Bode-Boger SM, Busse R et al. Drug-drug interactions in medical patients: effects of in-hospital treatment and relation to multiple drug use. *Int J Clin Pharmacol Ther.* 2000; *38*: 504-513.
- Kolbach DN, Sandbrink MW, Hamulyak K et al. Non-pharmacological measures for prevention of post-thrombotic syndrome. *Cochrane Database Syst Rev.* 2004; *1*: CD004174.
- Kurlan R. International symposium on early dopamine agonist therapy of Parkinson's disease. *Arch Neurol.* 1988; *45*: 204-208.
- Kwoh CK, Anderson LG, Greene JM et al. Guidelines for the management of rheumatoid arthritis. 2002 update. American College of Rheumatology subcommittee on rheumatoid arthritis guidelines. *Arthritis & Rheumatism.* 2002; *46*: 328-346.
- Lapane KL, Barbour MM, Van Haaren AB et al. Antiischaemic therapy in patients with coronary heart disease living in long-term care. *Pharmacotherapy.* 1999; *19*: 627-634.
- Lazarou J, Pomeranz BH, Corey PN. Incidence of adverse drug reactions in hospitalised patients: a meta-analysis of prospective studies. *JAMA.* 1998; *279*: 1200-1205.
- Lebowitz BD, Pearson JL, Schneider LS et al. Diagnosis and treatment of depression in late life. Consensus statement update. *JAMA.* 1997; *278*: 1186-1190.
- Lee DM, Weinblatt ME. Rheumatoid arthritis. *Lancet.* 2001; *358*: 903-911.
- Leipzig RM, Cumming RG, Tinetti ME. Drugs and falls in old people: a systematic review and meta-analysis. II. Cardiac and analgesic drugs. *J Am Geriatr Soc.* 1999; *47*: 40-50.
- Lethaby A, Farquhar C, Sarkis A et al. Hormone replacement therapy in post-menopausal women: endometrial hyperplasia and irregular bleeding. *Cochrane Database Syst Rev.* 2000; *2*: CD000402.
- Lindley CM, Tully MP, Paramsothy V et al. Inappropriate medication is a major cause of adverse drug reactions in elderly patients. *Age Ageing.* 1992; *21*: 294-300.
- Lustman F, Walters EG, Shroff NE et al. Diphenoxylate hydrochloride (lomotil) in the treatment of acute diarrhoea. *Br J Clin Pract.* 1987; *41*: 648-651.
- Maixner SM, Mellow AM, Tandon R. The efficacy, safety and tolerability of antipsychotics in the elderly. *J Clin Psychiatry.* 1999; *60* (Suppl 8): 29-41.
- Mangoni AA, Jackson SHD. Age-related changes in pharmacokinetics and pharmacodynamics: basic principles and practical applications. *Br J Clin Pharmacol.* 2003; *57*: 6-14.
- Mant J, Hobbs FD, Flethcher K et al. Warfarin versus aspirin for stroke prevention in an elderly community population with atrial fibrillation (the Birmingham Atrial Fibrillation Treatment in the Aged study, BAFTA): a randomised controlled trial. *Lancet.* 2007; *370*: 460-461.
- Matell MS, Jacoby J. Is there an optimal number of alternatives for Likert scale items? 1: reliability and validity. *Educ Psychol Meas.* 1971; *31*: 657-674.
- McEvoy CE, Niewoehner DE. Adverse effects of corticosteroid therapy for COPD: a critical review. *Chest.* 1997; *111*: 732-743.
- Mintzer J, Burns A. Anticholinergic side effects of drugs in elderly people. *J R Soc Med.* 2000; *93*: 457-462.
- Mooradian AD. Drug therapy of non-insulin dependent diabetes mellitus in the elderly. *Drugs.* 1996; *51*: 931-941.
- Naugler CT, Brymer C, Stolee P et al. Development and Validation of an improved prescribing for the elderly tool. *Can J Clin Pharmacol.* 2000; *7*: 103-107.
- NICE guidelines on Proton Pump Inhibitors. 2000/022. <http://www.nice.org.uk>.
- O'Mahony D, Martin U. Practical therapeutics for the older patient. Chichester: John Wiley & Sons; 1999.
- Papademetriou V, Farsang C, Elmfeldt D et al. Stroke prevention with the angiotensin II type-1 receptor blocker candesartan in elderly patients with isolated systolic hypertension: the Study on Cognition and Prognosis in the Elderly (SCOPE). *J Am Coll Cardiol.* 2004; *44*: 1175-1180.
- Pinede L, Ninet J, Duhaut P et al. Comparison of 3 and 6 months of oral anticoagulant therapy after a first episode of proximal deep vein thrombosis or pulmonary embolism and comparison of 6 and 12 weeks of therapy after isolated calf deep vein thrombosis. *Circulation.* 2001; *103*: 2453-2460.

- Pitkala KH, Strandberg TE, Tilvis RS. Inappropriate drug prescribing in home-dwelling elderly patients: a population based survey. *Arch Intern Med.* 2002; 162: 1707-1712.
- Raj A. Depression in the elderly. Tailoring medical therapy to their special needs. *Postgrad Med.* 2004; 115: 26-28.
- Ramsdell J. Use of theophylline in the treatment of COPD. *Chest.* 1995; 107 (Suppl): 206-209.
- Rash A, Downes T, Portner R et al. A randomized controlled trial of warfarin versus aspirin for stroke prevention in octogenarians with atrial fibrillation (WASPO). *Age Aging.* 2007; 36: 151-156.
- Rochon PA, Gurwitz JH. Prescribing for seniors: neither too much nor too little. *JAMA.* 1999; 282: 113-115.
- Ross HM, Kocovic DZ, Kowey PR. Pharmacologic therapies for atrial fibrillation. *Am J Geriatr Cardiol.* 2005; 14: 62-67.
- Salpeter S, Ormiston T, Salpeter E. Cardioselective β -blockers for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev.* 2005; 4: CD003566.
- Sarkar PK, Ritch AES. Management of urinary incontinence. *J Clin Pharm Ther.* 2000; 25: 251-263.
- Schlesinger N. Management of acute and chronic gouty arthritis: present state of the art. *Drugs.* 2004; 64: 2399-2416.
- Shekelle PG, Maclean CH, Morton SC. ACOVE quality indicators. *Ann Intern Med.* 2001; 135: 653-667.
- Shorr RI, Ray WA, Daugherty JR et al. Concurrent use of non-steroidal anti-inflammatory drugs and oral anticoagulants places elderly persons at high risk for haemorrhagic peptic ulcer disease. *Arch Intern Med.* 1993; 153: 1665.
- Sigal R, Malcolm J, Meggison H. Prevention of cardiovascular events in diabetes. *Clinical Evidence.* 2005; 14: 501-521.
- Skoog I, Lithell H, Hansson L et al. Effect of baseline cognitive function and antihypertensive treatment on cognitive and cardiovascular outcomes. Study on Cognition and Prognosis in the Elderly (SCOPE). *Am J Hypertens.* 2004; 18: 1052-1059.
- Slørdal L, Spigset O. Heart failure induced by non-cardiac drugs. *Drug Saf.* 2006; 29: 567-586.
- Smith D. Side-effects of psychotropic drugs. In: Wheatly D, Smith D (eds). *Psychopharmacology of cognitive and psychiatric disorders in the elderly.* London: Chapman and Hall Medical; 1998, p. 36-54.
- Smith SC, Allen J, Blair N et al. American Heart Association/American College of Cardiology Guidelines for secondary prevention for patients with coronary and other atherosclerotic vascular disease: 2006 Update: Endorsed by the National Heart, Lung and Blood Institute. *Circulation.* 2006; 113: 2363-2372.
- Sommer B, Fenn H, Pompei P et al. Safety of antidepressants in the elderly. *Expert Opin Drug Saf.* 2003; 2: 367-383.
- Spinewine A, Swine C, Dhillon S et al. Effect of a collaborative approach on the quality of prescribing for geriatric inpatients: a randomised, controlled trial. *J Am Geriatr Soc.* 2007; 55: 658-665.
- Staskin DR. Overactive bladder in the elderly: a guide to pharmacological management. *Drugs Aging.* 2005; 22: 1013-1028.
- Stuck AE, Beers MH, Steiner A et al. Inappropriate medication use in community residing older persons. *Arch Intern Med.* 1994; 154: 2195-2200.
- Sutter AI, Lemiengre M, Campbell H et al. Antihistamines for the common cold. *Cochrane Database Syst Rev.* 2003; 3: CD001267.
- Tamblyn R, Abrahamowicz M, du Berger R et al. A 5-year prospective assessment of the risk associated with individual benzodiazepines and doses in new elderly users. *J Am Geriatr Soc.* 2005; 53: 233-241.
- Terkeltaub RA. Clinical Practice. Gout. *N Engl J Med.* 2004; 350: 519-520.
- Thielman NM, Guerrant RL. Clinical practice. Acute infectious diarrhoea. *N Engl J Med.* 2004; 350: 38-47.
- Tinetti M. Preventing falls in elderly persons. *N Engl J Med.* 2003; 348: 42-49.
- Trenkwalder P, Elmfeldt D, Hofman A et al. The Study of Cognition and Prognosis in the Elderly (SCOPE) – major CV events and stroke in subgroups of patients. *Blood Pressure.* 2005; 14: 31-37.
- Tune LE. Anticholinergic effects of medication in elderly patients. *J Clin Psychiatry.* 2001; 62 (Supp 21): 11-14.
- van de Vijver DA, Roos RA, Jansen PA et al. Antipsychotics and Parkinson's disease: association with disease and drug choice during the first 5 years of anti-parkinsonian drug treatment. *Eur J Clin Pharmacol.* 2002; 58: 157-161.
- van der Woude HJ, Zaagsma J, Postma DS et al. Detrimental effects of β -blockers in COPD: A concern for nonselective β -blockers. *Chest.* 2005; 127: 818-824.
- van der Hooft CS, 't Jong GW, Dieleman JP et al. Inappropriate drug prescribing in older adults: the updated 2002 Beers criteria – a population based cohort study. *Br J Clin Pharmacol.* 2005; 60: 2137-2144.
- Verhoeven AC, Boers M, Tugwell P. Combination therapy in rheumatoid arthritis: updated systematic review. *Br J Rheumatology.* 1998; 37: 612-619.
- Walley T, Webb D. Developing a core curriculum in clinical pharmacology and therapeutics: a Delphi study. *Br J Clin Pharmacol.* 1997; 44: 167-170.
- Walsh TD. Prevention of opioid side effects. *J Pain Symptom Manage.* 1999; 5: 363-367.
- Whelton A. Clinical implications of nonopioid analgesia for relief of mild-moderate pain in patients with or at risk of cardiovascular disease. *Am J Cardiol.* 2006; 97: 3-9.
- Whelton PK, Williamson JD, Louis GT et al. Experimental approaches to determining the choice of first-step therapy for patients with hypertension. The ALLHAT Research Group Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial. *Clin Exp Hypertens.* 1996; 18: 569-579.
- White WB. Cardiovascular risk, hypertension and NSAIDs. *Curr Rheumatol Rep.* 2007; 9: 36-43.
- Williams BR, Kim J. Cardiovascular drug therapy in the elderly theoretical and practical considerations. *Drugs Aging.* 2003; 20: 445-463.
- Williams B, Poulter N, Brown M et al. British Hypertension Society guidelines for hypertension management 2004 (BHS-IV): summary. *BMJ.* 2004; 328: 634-640.
- Wilson K, Mottram P, Sivananthan A et al. Antidepressants for depressed elderly. *Cochrane Database Syst Rev.* 2006; 1: CD003491.
- World Health Organisation. Cancer pain relief and palliative care. Report of World Health Organization expert committee. World Health Organization; 1986.
- Zhan C, Sangl J, Bierman AS et al. Potentially inappropriate medication use in the community-dwelling elderly. Findings from the 1996 Medical Expenditure Panel Survey. *JAMA.* 2001; 286: 2823-2829.