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ISSN 0946-1965

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

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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-

Received July 4, 2007;
accepted
September 12, 2007

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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 $> 125 \mu\text{g/day}$ 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 $> 150 \text{mg/day}$ (*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 $< 130 \text{mmol/l}$ 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 $> 150 \mu\text{mol/l}$, or estimated GFR $< 50 \text{ml/min}$ [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	Isoxsurpine	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.

Acknowledgments

The Health Research Board of Ireland has awarded funding by way of a clinical research training fellowship to Dr. Paul Gallagher in support of this study. We wish to thank the members of the expert panel for their contributions to this study. The members of the expert panel and their individual areas of expertise (in parentheses) were: Prof. David Kerins (Clinical Pharmacology and Therapeutics), Prof. Brian Lawlor (Psychiatry of Old Age), Prof. Colin Bradley (General Practice), Prof. Andrew Murphy (General Practice), Prof. Declan Lyons (Geriatric Medicine), Prof. Bernard Walsh (Geriatric Medicine and Therapeutics), Prof. Davis Coakley (Geriatric Medicine), Dr. Shaun O'Keeffe (Geriatric Medicine), Dr. Mike Watts (Geriatric Medicine), Dr. Morgan Crowe (Geriatric Medicine), Dr. Mike O'Connor (Geriatric Medi-

cine), Dr. Dermot Power (Geriatric Medicine), Dr. Brian Carey (Geriatric Medicine), Dr. Michael Barry (Clinical Pharmacology), Dr. Una Martin (Clinical Pharmacology), Ms. Tamasine Grimes (Clinical Pharmacy), Ms. Ann Harnett (Clinical Pharmacy) and Ms. Bernadette Harnett (Clinical Pharmacy).

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.

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