Pharmacology applied to geriatric medicine

STOPP & START criteria: A new approach to detecting potentially inappropriate prescribing in old age

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ABSTRACT

Potentially inappropriate prescribing (IP) is an issue of major importance in the pharmacotherapy of older people globally. To date, Beers' criteria have been in common research usage for defining potentially inappropriate medications (PIMs) in older people. However, Beers' criteria have a number of serious flaws and are of doubtful relevance to routine geriatric pharmacotherapy. For these reasons, new geriatric IP criteria have been devised and validated, called screening tool of older persons' prescriptions (STOPP) and screening tool to alert to right treatment (START) for detection of potential errors of prescribing commission and omission. Prevalence studies in older people in southern Ireland show substantial rates of prescription of one or more PIMs in the primary care setting (22%), in acute hospital care (35%) and in nursing home care (60%) using STOPP criteria. Similarly, prevalence rates of potentially serious prescribing omission are high both in hospital (58%) and in primary care (23%). Prospective data show that STOPP criteria detect adverse drug effects (ADEs) that are causal or contributory to acute hospitalisation in older people 2.8 times more frequently than Beers' criteria. This suggests that ADEs are likely associated with PIMs in older people, contrary to recent research data showing no significant association on the basis of defining PIMs using Beers' criteria. We have recently shown that STOPP/START criteria as an intervention significantly improves medication appropriateness in hospitalised older people. Whether STOPP/START can prevent ADEs and reduce drug costs remains to be elucidated by means of further randomised controlled trials.
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1. Introduction

To date, with regard to inappropriate prescribing (IP) in late life, Beers' criteria have dominated the literature. The criteria are named after the late Dr. Mark Beers, who sadly died last year, and were first published in 1991 [1]. Beers initially devised his criteria with the frail elderly nursing home population of the US in mind. His criteria were subsequently revised and updated in 1997 [2] and again in 2003 [3]. Beers' criteria define potential IP instances in older people, regardless of the clinical setting. The most recent iteration of Beers' criteria is divided into "independent of diagnosis" (ID) and "considering diagnosis" (CD) subsets of criteria for greater ease of use [3].

Dr. Beers deserves considerable credit for his criteria as they represent the first well-organised list of common errors of prescribing in older people. However, there are several deficiencies in Beers' criteria that militate against their widespread use in

European countries. For instance, several of the Beers ID drugs are obsolete and no longer available in Europe (Table 1). Also, several of the drugs in Beers' list are not actually contra-indicated in older people, according to up-to-date evidence-based drug formularies, e.g. the British National Formulary; examples include amitriptyline, nitrofurantoin, amiodarone, doxazosin and propranolol. Furthermore, Beers' criteria do not include several important instances of potential IP (Table 2), e.g. drug-drug interactions or drug class prescription duplication in older people. Importantly, Beers' criteria take no account of prescribing omission errors which may be just as important as prescribing commission errors in the overall consideration of appropriateness, e.g. failure to prescribe anticoagulant drugs in older people with chronic atrial fibrillation considered at high risk for arterial embolism. There are no prospective randomised controlled trials that specifically use Beers' criteria as an intervention to improve medication appropriateness or minimise adverse drug effects (ADEs). Finally, Beers' criteria remain essentially a research tool despite their widespread usage in the published literature on IP in old age and are not used in the routine clinical context to any significant degree.

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Table 1
Drugs listed in Beers' criteria that are rarely used in European 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

2. STOPP/START criteria

Given the deficiencies of Beers' criteria, our research group set about drafting a new and different set of potentially IP criteria in older people, based on the following precepts:

(i) they should capture common and important instances of potentially IP;

(ii) they should be organised according to physiological systems, as is the case with most drug formularies;

(iii) they should give special attention to drugs that adversely affect elderly patients at risk of falls;

(iv) they should give special attention to opiate use in older people;

(v) duplicate drug class prescription (e.g. two ACE inhibitors or two proton pump inhibitors) should be highlighted;

(vi) potentially serious errors of prescribing omission in older people should be addressed;

(vii) the criteria should represent the consensus views of a panel of experts in prescribing in older people.

With these guiding principles, the first draft list of potential errors of prescribing was produced in 2003: potential errors of prescribing commission were grouped together by physiological systems as the "screening tool of older persons" prescriptions' and given the acronym "STOPP"; potential errors of prescribing omission were similarly grouped together as the screening tool to alert to right (i.e. correct) treatment and given the acronym "START". An early prevalidation pilot study of hospitalised older patients in Cork University Hospital indicated that potential IP assessed by STOPP criteria was highly prevalent and that most instances of prescribing errors of commission were detected by the new criteria [4].

The STOPP and START criteria were subsequently validated using a Delphi consensus methodology in 2006. This involved achieving consensus among a group of 18 experts in geriatric medicine, clinical pharmacology, clinical pharmacy, old age psychiatry and primary care. These experts were also invited to suggest additional criteria that were not included in the original drafts of STOPP and START. Sixty-five of the original 68 STOPP criteria and all 22 of the original START criteria received consensus agreement within the expert panel and were subsequently published [5]. The STOPP criteria are detailed in Table 3 and the START criteria in Table 4.

The inter-rater reliability of STOPP/START criteria was subsequently established, with high levels of reliability between physicians [6] and also between pharmacists [7].

3. Potentially inappropriate prescribing prevalence studies using STOPP/START criteria

Using the validated and reliable STOPP/START criteria, our research group has published a series of papers detailing the prevalence of potentially inappropriate medications (PIMs) use in a number of elderly care settings, i.e. acute hospital unit, primary care and long-term nursing care. Although STOPP criteria are fundamentally different from Beers' criteria and therefore not directly comparable, each of the prevalence studies documented prevalence rates of PIMs using both sets of criteria. Table 4 summarizes the STOPP and Beers' criteria prevalence rates in the different care settings from these studies. The data from these studies show that prevalence rates of one or more PIMs are substantial in each care setting in Ireland, ranging from 21% in primary care [8] to 35% in hospital care at the point of admission [9] to 60% in nursing home care [10], and using STOPP criteria (Table 5).

Studies of potentially inappropriate omission of essential pharmacotherapy using START criteria show that between 44 [11] and 57% [12] of hospitalised older people lack one or more indicated essential medicines. In primary care, the prevalence of essential medicine omission using START criteria is 23% [8]. These data indicate that potentially inappropriate omission of essential medicines in older people is at least as prevalent as the inclusion of potentially inappropriate drugs that should probably be avoided. These findings support our contention that STOPP and START criteria should be used in tandem on the basis that inclusion of inappropriate medicines and omission of essential medicines are

Table 2
Some prescriptions to be avoided in elderly patients that are not mentioned in Beers' criteria [3]:.

Loop diuretic for dependent ankle edema only i.e. no clinical signs of heart failure (no evidence of efficacy, compression hosiery usually more appropriate)

Thiazide diuretic with a history of gout (may exacerbate gout)

Aspirin to treat dizziness not clearly attributable to cerebrovascular disease (not indicated)

Tricyclic antidepressants with glaucoma (likely to exacerbate glaucoma)

Long-term (i.e. >1 month) neuroleptics as long-term hypnotics (risk of confusion, hypotension, extrapyramidal side effects, falls)

Anticholinergics to treat extrapyramidal side-effects of neuroleptic medications (risk of anticholinergic toxicity)

Prochlorperazine (Stemetil) with Parkinsonism (risk of exacerbating Parkinsonism)

Proton pump inhibitor for peptic ulcer disease at full therapeutic dosage for >8 weeks (dose reduction or earlier discontinuation indicated)

Theophylline as monotherapy for COPD (safer, more effective alternative; risk of adverse effects due to narrow therapeutic index)

Non-steroidal anti-inflammatory drug (NSAID) with moderate-severe hypertension (risk of exacerbation of hypertension)

NSAID with heart failure (risk of exacerbation of heart failure)

NSAID with chronic renal failure[a] (risk of deterioration in renal function)

Alphablockers in males with frequent urinary incontinence i.e. one or more episodes of incontinence daily (risk of urinary frequency and worsening of incontinence)

Betablockers in those with diabetes mellitus and frequent hypoglycaemic episodes i.e. ≥ 1 episode per month (risk of masking hypoglycaemic symptoms)

Oestrogens with a history of venous thromboembolism (increased risk of recurrence)

Neuroleptics and recurrent falls (may cause gait dyspraxia and Parkinsonism, leading to further falls)

Vasodilator drugs with persistent postural hypotension i.e. recurrent >20 mmHg drop in systolic blood pressure (risk of syncope, falls)

Long-term opiates i.e. >3 months in those with chronic constipation without concurrent use of laxatives (risk of severe constipation)

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

[a] Serum creatinine concentration > 150 μmol/l or estimated glomerular filtration rate < 50 ml/hr.

Table 3
Screening tool of older People's potentially inappropriate prescriptions (STOPP) [5].

The following prescriptions are potentially inappropriate in persons aged ≥ 65 years of age

Cardiovascular system
Digoxin at a long-term dose > 125 μg/day with impaired renal function[a] *(increased risk of toxicity)*
Loop diuretic for dependent ankle oedema only i.e. no clinical signs of heart failure *(no evidence of efficacy, compression hosiery usually more appropriate)*
Loop diuretic as first-line monotherapy for hypertension *(safer, more effective alternatives available)*
Thiazide diuretic with a history of gout *(may exacerbate gout)*
Non-cardioselective betablocker with chronic obstructive pulmonary disease (COPD) *(risk of bronchospasm)*
Betablocker in combination with verapamil *(risk of symptomatic heart block)*
Use of diltiazem or verapamil with NYHA Class III or IV heart failure *(may worsen heart failure)*
Calcium channel blockers with chronic constipation *(may exacerbate constipation)*
Use of aspirin and warfarin in combination without histamine H2 receptor antagonist (except cimetidine because of interaction with warfarin) or proton pump inhibitor *(high risk of gastro-intestinal bleeding)*
Dipyridamole as monotherapy for cardiovascular secondary prevention *(no evidence for efficacy)*
Aspirin with a past history of peptic ulcer disease without histamine H2 receptor antagonist or Proton Pump Inhibitor *(risk of bleeding)*
Aspirin at dose > 150 mg/day *(increased bleeding risk, no evidence for increased efficacy)*
Aspirin with no history of coronary, cerebral or peripheral arterial symptoms or occlusive arterial event *(not indicated)*
Aspirin to treat dizziness not clearly attributable to cerebrovascular disease *(not indicated)*
Warfarin for first, uncomplicated deep venous thrombosis for longer than 6 months duration *(no proven added benefit)*
Warfarin for first uncomplicated pulmonary embolus for longer than 12 months duration *(no proven benefit)*
Aspirin, clopidogrel, dipyridamole or warfarin with concurrent bleeding disorder *(high risk of bleeding)*

Central nervous system and psychotropic drugs
Tricyclic antidepressants (TCA's) with dementia *(risk of worsening cognitive impairment)*
TCA's with glaucoma *(likely to exacerbate glaucoma)*
TCA's with cardiac conductive abnormalities *(pro-arrhythmic effects)*
TCA's with constipation *(likely to worsen constipation)*
TCA's with an opiate or calcium channel blocker *(risk of severe constipation)*
TCA's with prostatism or prior history of urinary retention *(risk of urinary retention)*
Long-term (i.e. > 1 month), long-acting benzodiazepines e.g. chlordiazepoxide, fluazepam, nitrazepam, chlorazepate and benzodiazepines with long-acting metabolites e.g. diazepam *(risk of prolonged sedation, confusion, impaired balance, falls)*
Long-term (i.e. > 1 month) neuroleptics as long-term hypnotics *(risk of confusion, hypotension, extrapyramidal side effects, falls)*
Long-term neuroleptics (> 1 month) in those with parkinsonism *(likely to worsen extrapyramidal symptoms)*
Phenothiazines in patients with epilepsy *(may lower seizure threshold)*
Anticholinergics to treat extrapyramidal side-effects of neuroleptic medications *(risk of anticholinergic toxicity)*
Selective serotonin re-uptake inhibitors (SSRI's) with a history of clinically significant hyponatraemia *(non-iatrogenic hyponatraemia < 130 mmol/l within the previous 2 months)*
Prolonged use (> 1 week) of first generation antihistamines i.e. diphenydramine, chlorpheniramine, cyclizine, promethazine *(risk of sedation and anticholinergic side effects)*

Gastro-intestinal system
Diphenoxylate, loperamide or codeine phosphate for treatment of diarrhoea of unknown cause *(risk of delayed diagnosis, may exacerbate constipation with overflow diarrhoea, may precipitate toxic megacolon in inflammatory bowel disease, may delay recovery in unrecognised gastroenteritis)*
Diphenoxylate, loperamide or codeine phosphate for treatment of severe infective gastroenteritis i.e. bloody diarrhoea, high fever or severe systemic toxicity *(risk of exacerbation or protraction of infection)*
Prochlorperazine (Stemetil) or metoclopramide with Parkinsonism *(risk of exacerbating Parkinsonism)*
PPI for peptic ulcer disease at full therapeutic dosage for > 8 weeks *(earlier discontinuation or dose reduction for maintenance/prophylactic treatment of peptic ulcer disease, oesophagitis or GORD indicated)*
Anticholinergic antispasmodic drugs with chronic constipation *(risk of exacerbation of constipation)*

Respiratory system
Theophylline as monotherapy for COPD *(safer, more effective alternative; risk of adverse effects due to narrow therapeutic index)*
Systemic corticosteroids instead of inhaled corticosteroids for maintenance therapy in moderate-severe COPD *(unnecessary exposure to long-term side-effects of systemic steroids)*
Nebulised ipratropium with glaucoma *(may exacerbate glaucoma)*

Musculoskeletal system
Non-steroidal anti-inflammatory drug (NSAID) with history of peptic ulcer disease or gastro-intestinal bleeding, unless with concurrent histamine H2 receptor antagonist, PPI or misoprostol *(risk of peptic ulcer relapse)*
NSAID with moderate-severe hypertension (moderate: 160/100 mmHg – 179/109 mmHg; severe: ≥ 180/110 mmHg) *(risk of exacerbation of hypertension)*
NSAID with heart failure *(risk of exacerbation of heart failure)*
Long-term use of NSAID (> 3 months) for relief of mild joint pain in osteoarthtitis *(simple analgesics preferable and usually as effective for pain relief)*
Warfarin and NSAID together *(risk of gastro-intestinal bleeding)*
NSAID with chronic renal failure[b] *(risk of deterioration in renal function)*
Long-term corticosteroids (> 3 months) as monotherapy for rheumatoid arthrtitis or osterarthritis *(risk of major systemic corticosteroid side-effects)*
Long-term NSAID or colchicine for chronic treatment of gout where there is no contraindication to allopurinol *(allopurinol first choice prophylactic drug in gout)*

Urogenital system
Bladder antimuscarinic drugs with dementia *(risk of increased confusion, agitation)*
Bladder antimuscarinic drugs with chronic glaucoma *(risk of acute exacerbation of glaucoma)*
Bladder antimuscarinic drugs with chronic constipation *(risk of exacerbation of constipation)*
Bladder antimuscarinic drugs with chronic prostatism *(risk of urinary retention)*
Alphablockers in males with frequent incontinence i.e. one or more episodes of incontinence daily *(risk of urinary frequency and worsening of incontinence)*
Alphablockers with long-term urinary catheter *in situ* i.e. more than 2 months *(drug not indicated)*

Endocrine system
Glibenclamide or chlorpropamide with type 2 diabetes mellitus *(risk of prolonged hypoglycaemia)*
Betablockers in those with diabetes mellitus and frequent hypoglycaemic episodes i.e. ≥ 1 episode per month *(risk of masking hypoglycaemic symptoms)*
Oestrogens with a history of breast cancer or venous thromboembolism *(increased risk of recurrence)*
Oestrogens without progestogen in patients with intact uterus *(risk of endometrial cancer)*

Table 3 (*Continued*)

The following prescriptions are potentially inappropriate in persons aged ≥ 65 years of age

Drugs that adversely affect those prone to falls (≥ 1 fall in past 3 months)
  Benzodiazepines *(sedative, may cause reduced sensorium, impair balance)*
  Neuroleptic drugs *(may cause gait dyspraxia, Parkinsonism)*
  First generation antihistamines *(sedative, may impair sensorium)*
  Vasodilator drugs known to cause hypotension in those with persistent postural hypotension i.e. recurrent > 20 mmHg drop in systolic blood pressure *(risk of syncope, falls)*
  Long-term opiates in those with recurrent falls *(risk of drowsiness, postural hypotension, vertigo)*

Analgesic drugs
  Use of long-term powerful opiates e.g. morphine or fentanyl as first line therapy for mild-moderate pain *(WHO analgesic ladder not observed)*
  Regular opiates for more than 2 weeks in those with chronic constipation without concurrent use of laxatives *(risk of severe constipation)*
  Long-term opiates in those with dementia unless indicted for palliative care or management of moderate/severe chronic pain syndrome *(risk of exacerbation of cognitive impairment)*

Duplicate drug classes
  Any regular duplicate drug class prescription e.g. two concurrent opiates, NSAID's, SSRI's, loop diuretics, ACE inhibitors *(optimisation of monotherapy within a single drug class should be observed prior to considering a new class of drug)*. This excludes duplicate prescribing of drugs that may be required on a PRN basis e.g. inhaled beta 2 agonists (long and short acting) for asthma or COPD, and opiates for management of breakthrough pain

[a] Estimated GFR < 50 ml/minute.
[b] Estimated GFR 20–50 ml/minute.

Table 4
Screening tool to alert doctors to right i.e. appropriate, indicated treatments (START) [5].

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

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

Respiratory system
  Regular inhaled beta 2 agonist or anticholinergic agent for mild to moderate asthma or COPD
  Regular inhaled corticosteroid for moderate-severe asthma or COPD, where predicted FEV1 < 50%
  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)

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

Gastro-intestinal system
  Proton pump inhibitor with severe gastro-oesophageal acid reflux disease or peptic stricture requiring dilatation
  Fibre supplement for chronic, symptomatic diverticular disease with constipation

Musculoskeletal system
  Disease-modifying antirheumatic drug (DMARD) with active moderate-severe rheumatoid disease lasting > 12 weeks
  Bisphosphonates in patients taking maintenance oral corticosteroid therapy
  Calcium and vitamin D supplement in patients with known osteoporosis (radiological evidence or previous fragility fracture or acquired dorsal kyphosis)

Endocrine system
  Metformin with type 2 diabetes ± metabolic syndrome (in the absence of renal impairment[a])
  ACE inhibitor or angiotensin receptor blocker in diabetes with nephropathy i.e. overt urinalysis proteinuria or microalbuminuria (> 30 mg/24 hours) ± serum biochemical renal impairment[a]
  Antiplatelet therapy in diabetes mellitus if one or more co-existing major cardiovascular risk factor present (hypertension, hypercholesterolaemia, smoking history)
  Statin therapy in diabetes mellitus if one or more co-existing major cardiovascular risk factor present

[a] Estimated GFR < 50 ml/minute.

closely and inextricably linked problems in geriatric pharmaco-therapy.

4. Linkage of STOPP and Beers' criteria-related PIMs to ADEs

Until recently, there has been disagreement and consequently uncertainty regarding the link between PIMs and ADEs. This has been largely due to the findings of two large-scale studies of hospitalised older people, both showing no significant association between PIMs (defined by Beers' criteria) and serious ADEs [13,14]. However, we believe that the lack of demonstrable association

between PIMs and ADEs from these studies may be spurious because Beers' criteria may not be sufficiently sensitive for detection of serious ADEs that are causal or contributory to hospitalisation in older people.

As a guiding principal, for any set of potentially IP criteria for older patients to be clinically relevant, they *must* show a high degree of sensitivity to serious ADEs. To test whether STOPP criteria had significantly greater sensitivity for detection of serious ADEs than Beers' criteria, we performed a direct comparison between STOPP criteria and Beers' criteria for inclusion of ADEs. In 715 consecutively admitted older people with acute unselected

Table 5
Prevalence of potentially inappropriate medication use in various clinical settings using STOPP criteria and Beers' criteria.

Criteria	Primary care (%)	Secondary care (%)	Nursing home care (%)
STOPP	21 [8]	34–50 [8,13,22]	60 [10]
Beers	13–18 [8,22]	25–32 [21,23]	37 [10]

illness to Cork University Hospital, we found that PIMs listed in STOPP were causal or contributory to acute admission in 11.5% of cases compared to 6% of cases with Beers' criteria [9]. Although the definition of ADEs in this study was based on trained clinical judgement of two experienced observers rather than on that of a larger consensus panel, nevertheless, these data suggested that STOPP may be more relevant than Beers' criteria in relation to serious ADE detection.

We subsequently performed a more rigorous prospective study looking at the relationship between ADEs causal to acute hospitalisation and PIMs as defined by STOPP and Beers' criteria [15]. In this study, we examined the clinical records of 600 consecutive older patients (median age 77 years, 40% male) admitted to Cork University Hospital with acute illness, looking specifically at the clinical diagnostic and prescription medication data at the point of admission i.e. before any in-patient changes in prescription medicines. Thirty-four percent of patients were taking six or more medicines, 66% were taking more or equal to six medicines. The consensus opinion of a panel of two trained senior geriatricians and two senior pharmacists with special expertise in geriatric pharmacotherapy defined ADEs as a gold standard. Using this method, 329 ADEs were identified in 158 patients, i.e. in 26.3% of the total population. Thirty-six of the 329 ADEs (10.9% of all ADEs) were judged to be the principal cause of the index hospital admission in the 158 affected patients. This equated to 6% of all 600 admissions being the direct result of a serious ADE. A further 183 ADEs were judged to be contributory to hospital admission, making a total of 219/329 ADEs that were causal or contributory to admission i.e. two thirds of all identified ADEs. Avoidability of identified ADEs was then evaluated using Hallas criteria [16]. By these criteria, 107/219 ADEs that were causal/contributory to admission were definitely avoidable and 43/219 ADEs were possibly avoidable, i.e. 150/219 ADEs (68.4%) that were causal/contributory

to admission were definitely or possibly avoidable. Of the 329 identified ADEs, 170 were listed in STOPP (52%) compared with 66 (20%) in Beers' criteria. Ninety-four of 150 definitely/possibly avoidable ADEs (62.7%) were listed in STOPP compared to 34/150 definitely/possibly avoidable ADEs (22.7%) listed in Beers' criteria. Among the 158 patients with identified ADEs, 128 patients (81.0%) were taking one or more STOPP PIMs and 30 patients (19.0%) were not taking STOPP PIMs; 74 patients (46.8%) were taking Beers' criteria PIMs and 84 patients (53.2%) were not taking Beers' criteria PIMs. In other words, STOPP detected definitely/possibly avoidable ADEs 2.8 times more frequently than Beers' criteria. These data show that STOPP criteria are more relevant than Beers' criteria in defining PIMs in older people presenting to hospital with acute illness. They also suggest that PIMs, as defined by STOPP criteria, are significantly associated with serious ADEs, contrary to the findings of Onder et al. [13] and Laroche et al. [14].

5. STOPP/START criteria and medication appropriateness

Another test of the efficacy of STOPP/START criteria as an intervention is to measure their effect on medication appropriateness of older people. Medication appropriateness may be assessed using the medication appropriateness index [17] (MAI) and the assessment of underutilization of medication (AUM) tool [18]. The MAI has been used recently to evaluate the efficacy of structured pharmacist review of hospitalised older people's medication aimed at optimising medication appropriateness, showing that such an intervention improves MAI scores compared with "standard care" in a geriatric assessment unit [19].

In 2008, we posed the same question in relation to applying STOPP/START criteria as an intervention, i.e. does rigorous application of STOPP/START criteria to older hospitalised patients' medication lists result in significantly improved medication appropriateness compared with "standard" care? We adopted a randomised controlled trial (RCT) design, in which 400 consecutive older hospitalised patients participated. Within 72 hours of hospitalisation, two hundred patients were randomised to have their prescription and clinical data screened using STOPP/START criteria with subsequent recommendations to the attending clinicians to modify the prescription medications accordingly. Two hundred patients in the control group received usual hospital
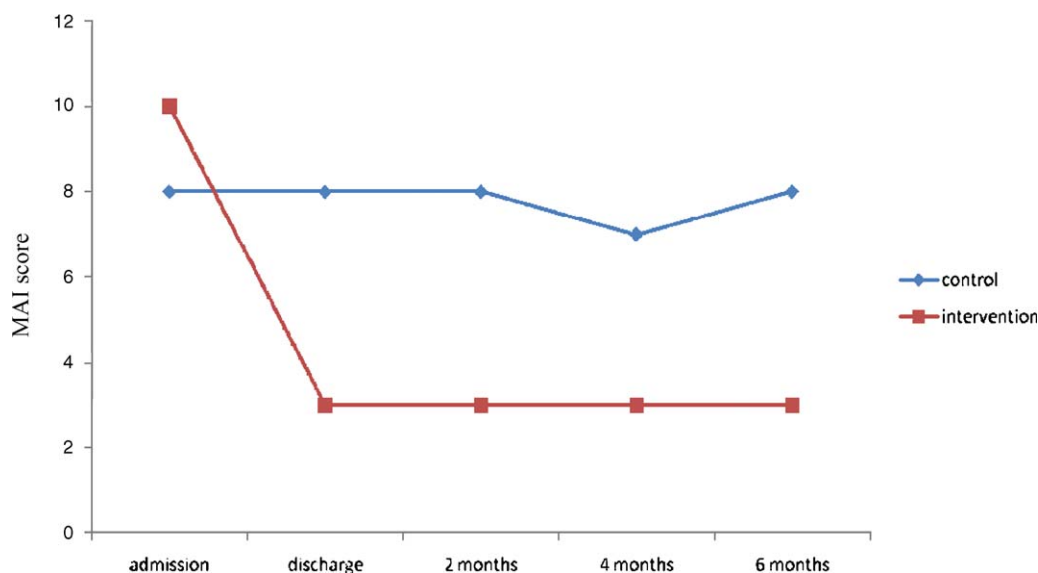

Fig. 1. Results of an RCT of 400 older hospital patients, randomised to rigorous application of STOPP/START criteria (intervention) or standard hospital pharmacotherapy (control) showing a significant change in Medication Appropriateness Index (MAI) [17] scores in the intervention group at discharge compared to controls; the highly significant effect on MAI score ($p < 0.001$) was maintained at 2, 4 and 6 months (the higher the MAI score, the less appropriate the medication).

Percentage of patients with at least one prescribing omission (AUM)

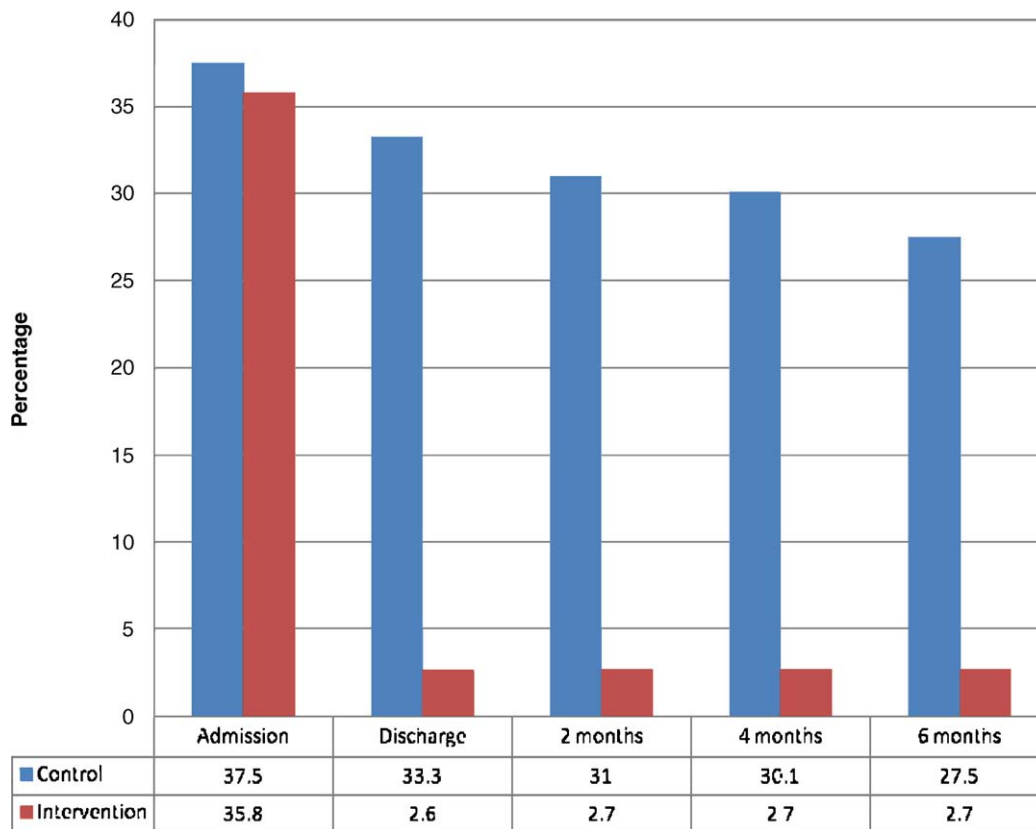|	Admission	Discharge	2 months	4 months	6 months
Control	37.5	33.3	31	30.1	27.5
Intervention	35.8	2.6	2.7	2.7	2.7

Fig. 2. Results of an RCT of 400 older hospital patients, randomised to rigorous application of STOPP/START criteria (intervention) or standard hospital pharmacotherapy (control) showing a significant change in Assessment of Underutilization of Medication (AUM) [18]. Following application of STOPP/START criteria during admission, there is a highly significant improvement in the degree of underutilization of essential medication; this improvement is maintained to the end of the study follow-up at 6 months post-discharge.

physician and pharmacist care, without STOPP/START screening. Only patients who were admitted to hospital under the care of internal medicine physicians (other than geriatricians) were included in the RCT. The primary outcome measures were MAI and AUM scores, which were measured at discharge and at 2, 4 and 6 months post-discharge. The effect of the STOPP/START intervention on prescribing appropriateness at these time points is illustrated in Fig. 1 and Fig. 2. There were highly significant improvements in MAI and AUM scores in the intervention group compared to the control group, confirming our hypothesis that STOPP/START as an intervention significantly improves medication appropriateness in older hospitalised patients [20]. However, there were a number of limitations to this RCT, principally the fact that it was a single-centre, single-blinded and a relatively small-scale.

6. Further research on STOPP/START

Further important research questions relating to the clinical relevance of STOPP/START include:

1. what is the effect of rigorous application of STOPP/START on ADE incidence in older people?
2. what is the effect of rigorous application of STOPP/START on drug cost in older people?
3. what is the effect of rigorous application of STOPP/START on composite health care utilization in older people?
4. what is the effect of rigorous application of STOPP/START on mortality in older people?

The first two questions need to be addressed and answered before the latter two questions can be dealt with. Any set of IP criteria designed for older people should have positive effects on ADE incidence and cost if it is to find any place in day-to-day clinical practice.

STOPP/START criteria were never meant to replace clinical judgement that is based on high-level clinical knowledge and experience; rather they were intended as an aid to routine pharmacotherapy/pharmaceutical care. It is envisaged that STOPP/START criteria are best utilized in tandem with expert medication review both in the hospital setting and in the community setting by physicians and pharmacists. To maintain continuing clinical relevance, STOPP/START criteria need to be reassessed and updated by an expert panel on a routine basis, e.g. every 3 years. With this in mind, it is the intention of the newly formed Drugs and Prescribing special interest group of the European Union Geriatric Medicine Society to organize expert review and updating of STOPP/START, beginning in 2010.

Conflicts of interest

None.

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