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ORIGINAL ARTICLE

Inappropriate medication use in hospitalised oldest old patients across transitions of care

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Abstract

Background Oldest old patients aged 85 years and over are at risk of experiencing potentially inappropriate medications (PIMs) and potential prescribing omissions (PPOs) across transitions of care. Geriatricians also face enormous challenges in prescribing medications for these patients.

Methods A mixed-methods, sequential explanatory design was undertaken of electronic medical records and semi-structured interviews with geriatricians at a public teaching hospital. Data were collected at four time points using the Screening Tool of Older Persons' potentially inappropriate Prescriptions (STOPP) and Screening Tool to Alert doctors to the Right Treatment (START).

Results Of 249 patients, the prevalence of at least 1 PIM varied between 36.9 and 51.0%, while the prevalence of at least 1 PPO varied between 36.9 and 44.6%. The most common PIM was use of proton pump inhibitors while the most common PPO was omission of vitamin D supplements in housebound patients or patients experiencing falls. Poisson regression analysis showed that PIMs were significantly associated with use of mobility aids, 1.430 (95% CI 1.109–1.843, $p=0.006$), and number of medications prescribed at admission, 1.083 (95% CI 1.058–1.108, $p<0.001$). PPOs were significantly associated with comorbidities, 1.172 (95% CI 1.073–1.280, $p<0.001$), medications prescribed at admission, 0.989 (95% CI 0.978–0.999, $p=0.035$), and length of stay, 1.004 (95% CI 1.002–1.006, $p<0.001$). Geriatrician interviews ($N=9$) revealed medication-related, health professional-related and patient-related challenges with managing medications.

Conclusions Inappropriate prescribing is common in oldest old patients. Greater attention is needed on actively de-prescribing medications that are not beneficial and commencing medications that would be advantageous. Tailored strategies for improving prescribing practices are needed.

Keywords Oldest old · Transition · Inappropriate medication · Prescribing · Potentially inappropriate medication · Potential prescribing omission

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Introduction

Globally, the population is ageing. The number and proportion of oldest old people, who are defined as individuals aged 85 years and over, are increasing more rapidly than those in other age groups [1]. Oldest old people comprise about 2% of the population in the United States, while in 2030, this number is projected to increase to 2.5% and 3.7% in 2040 [2]. Oldest old patients often present with several comorbidities that require the use of multiple medications.

Inappropriate medication use involves prescribing potentially inappropriate medications (PIMs) and potential prescribing omissions (PPOs). In relation to PIMs, the risks of using particular medications outweigh their benefits, especially if there are safer and more effective options. With respect to PPOs, these are omitted medications that have a therapeutic use in the absence of contraindications [3, 4]. Inappropriate prescribing can cause an increase in adverse drug events (ADEs), which are situations leading to patient harm with respect to an increase in morbidity, mortality and health care costs [5, 6]. With an ageing population, inappropriate prescribing is an international health care problem [7].

Screening tools for inappropriate prescribing have been formulated to assist clinicians in providing efficient and appropriate prescribing practices, as well as in reducing the prevalence of preventable ADEs [4, 8]. The STOPP (Screening Tool of Older Persons' potentially inappropriate Prescriptions) and START (Screening Tool to Alert doctors to the Right Treatment) criteria were developed in Ireland in 2003 to identify PIMs and PPOs, respectively. The STOPP and START were later validated by a Delphi consensus in 2006 [9]. Version Two of the criteria was released in 2014, comprising 80 STOPP and 32 START criteria [10]. The STOPP and START criteria have been applied in various studies and have been shown to be effective screening tools [11, 12]. Despite their potential benefits and utility, little work has been undertaken using these criteria amongst hospitalised oldest old patients.

The aims of this paper are: to examine the prevalence of inappropriate medication use in oldest old patients across transitions of care using the STOPP and START criteria; to determine which medication categories have a high prevalence of inappropriate medication use in oldest old patients; and to examine challenges associated with medication prescribing in oldest old patients from the perspectives of geriatricians.

Methods

Study design, setting and participants

A mixed-methods, sequential explanatory design was used, involving a retrospective clinical audit of electronic medical records and semi-structured interviews. The study was undertaken at an Australian public, teaching hospital with two sites, comprising 570 beds. This hospital served over 550,000 people living in the northern and western regions of the state of Victoria. At this hospital, doctors were taught about the importance of deprescribing in older patients, and also about the process of doing therapeutic reconciliation.

For the audit, the patient sample was randomly selected by an independent researcher who extracted data such as age, gender, admission dates, and primary diagnostic codes. The inclusion criteria were patients aged 85 years and over, who presented to the emergency department (ED) of the study hospital, and were admitted to the hospital between January 1st 2016 and December 31st 2016 with at least 1 medication on presentation. The exclusion criteria comprised patients who were admitted to the intensive care unit, died before discharge, were palliated prior to discharge, were discharged to other hospitals or private rehabilitation following ED presentation, had incomplete or unobtainable records, had duplicate admission dates in the electronic system, declined medications on ED presentation or were a tourist and therefore medication prescriptions were not reflective of the local situation. There were 1458 potentially eligible patients admitted to the emergency department across the 1-year audit period. Using a random numbers table, medical records were randomly sampled to determine the eligibility for inclusion and till the required sample was obtained.

Using purposive sampling by considering gender and years of working experience, interviews were conducted with geriatricians who worked in the geriatric evaluation and management or general medical units of the hospital.

Procedure

Demographic and medication information were obtained from the ED notes, admission notes, discharge summaries relating to patients' discharge from acute and subacute settings, medication charts and progress notes. Pathology results and observation charts were also perused to obtain details of adverse clinical outcomes experienced by older patients. Data were obtained for four different time points during oldest old patients' hospital stay. These time points were as follows: time point 1: medications on presentation to ED; time point 2: medications on admission to acute care; time point 3: medications on discharge from acute care to subacute care; and time point 4: medications on discharge from acute care directly to home/residential care or on discharge from subacute care to home/residential care. It is important to note that not all patients were discharged from acute care to subacute care.

Data were documented in an Excel spreadsheet (version 2010), which was directly imported into IBM SPSS (version 25). Medications prescribed were noted for each patient

at each of the four time points. The STOPP/START criteria (version 2) were applied and the PIMs and PPOs were documented for each time point. For patients who had an identified PIM, vital sign observations, physical examinations, pathology tests and imaging results were examined to identify adverse clinical outcomes as possible clinical manifestations occurring during the patients' stay. The Adverse Clinical Outcomes Tool was used to record potential adverse clinical outcomes which were developed from the STOPP criteria. Thus, in identifying adverse clinical outcomes, these related to medications that were prescribed and not withdrawn.

Data were collected on patient age, gender, use of walking aids, presence of documented allergy, presence of documented dementia, and presence of documented faecal or urinary incontinence. The Charlson comorbidity index (CCI) was manually calculated using an online calculator [13]. Transition points were defined as the number of changes in the location of a patient during hospitalisation. Change in discharge destination was calculated and defined as a change in the place of dwelling due to higher care requirements, such as moving from home to a residential care facility. Communication barriers were identified and defined by the presence of confusion from delirium or dementia, aphasia, dysphasia, dysarthria, hearing impairment, or an inability to communicate in English without an interpreter. The total length of hospital stay was calculated as the length of stay in acute care and subacute care. Functional Status was defined as patients requiring assistance with activities of daily living (ADL) in each of the domains (personal, domestic and community). Personal ADLs involved showering, dressing, toileting, eating, and grooming. Domestic ADLs involved completing household tasks like cooking and cleaning. Community ADLs comprised driving and shopping. If patients required assistance in any of these areas, they were allocated a score of 1 and a score of 0 if they were independent. The presence of a falls history was defined as having clear documentation of being a recurrent faller or having been referred to the falls clinic. Polypharmacy and excessive polypharmacy were defined arbitrarily as ≥ 5 and ≥ 10 medications.

In organising structured interviews with geriatricians, the questions posed included the barriers to safe prescribing in older patients, and challenges they experienced in ceasing or commencing medications.

Data analysis

Descriptive statistical analysis was performed, with categorical variables analysed using summary counts and percentages. For continuous variables with skewed distributions, medians and inter-quartile ranges were calculated. The following explanatory variables were examined at the univariate level to determine their effects on PIMs or PPOs: age, use of aids, documented allergy, documented dementia, history of falls, incontinence, personal ADLs, domestic ADLs, community ADLs, communication barrier, comorbid conditions, number of medications prescribed on admission, total length of stay, and age. Univariate associations with p values of ≤ 0.25 were included in the Poisson regression modelling. Poisson regression modelling was performed using the number of counts of PIMs or PPOs as the dependent (outcome) variable and explanatory variables. The level of significance utilised was alpha = 0.05.

Using a prevalence rate for PIMs of 54% found in the previous Australian study conducted by Manias et al. [14], and based on a desired 95% confidence interval width of 0.125, the sample size was calculated to be 245 patients. Therefore, data were required to be collected on about 245 patient medical records.

Audio-recorded interviews of geriatricians were transcribed verbatim. Thematic analysis was undertaken, which involved each author independently reading and rereading the data transcripts many times, identifying initial themes and subthemes, and summarising and synthesising the data.

Results

Demographic characteristics

Data on 249 randomly selected medical records were collected (Fig. 1). The demographic characteristics are summarised in Table 1. The median age of patients was 88.5 years, with the oldest patient being 103 years old. The most common diagnosis of admitted patients to acute care was congestive cardiac failure, followed by sepsis, pelvic or femur fracture and cerebral infarction. There were 90 (36.7%) patients who had acute kidney injury on admission.

On presentation to ED, a total of 2,425 medications were prescribed to the entire study population with a median number of 10 medications (range 1–20). On admission to the acute unit, a total of 2254 medications were prescribed with a median number of 9 medications (range 2–10). On admission to the subacute unit, a total of 1,062 medications were prescribed to 108 patients admitted to the subacute unit with a median number of 10 medications (range 3–21). On discharge, a total of 2,391 medications were prescribed with a median of 9 medications (range 1–21). Polypharmacy increased slightly from 90.2% on presentation to ED, to 95.1% at discharge while excessive polypharmacy marginally dropped from 50.8% on presentation to ED, to 48.8% at discharge. All patients had changes to their medications during hospitalisation.

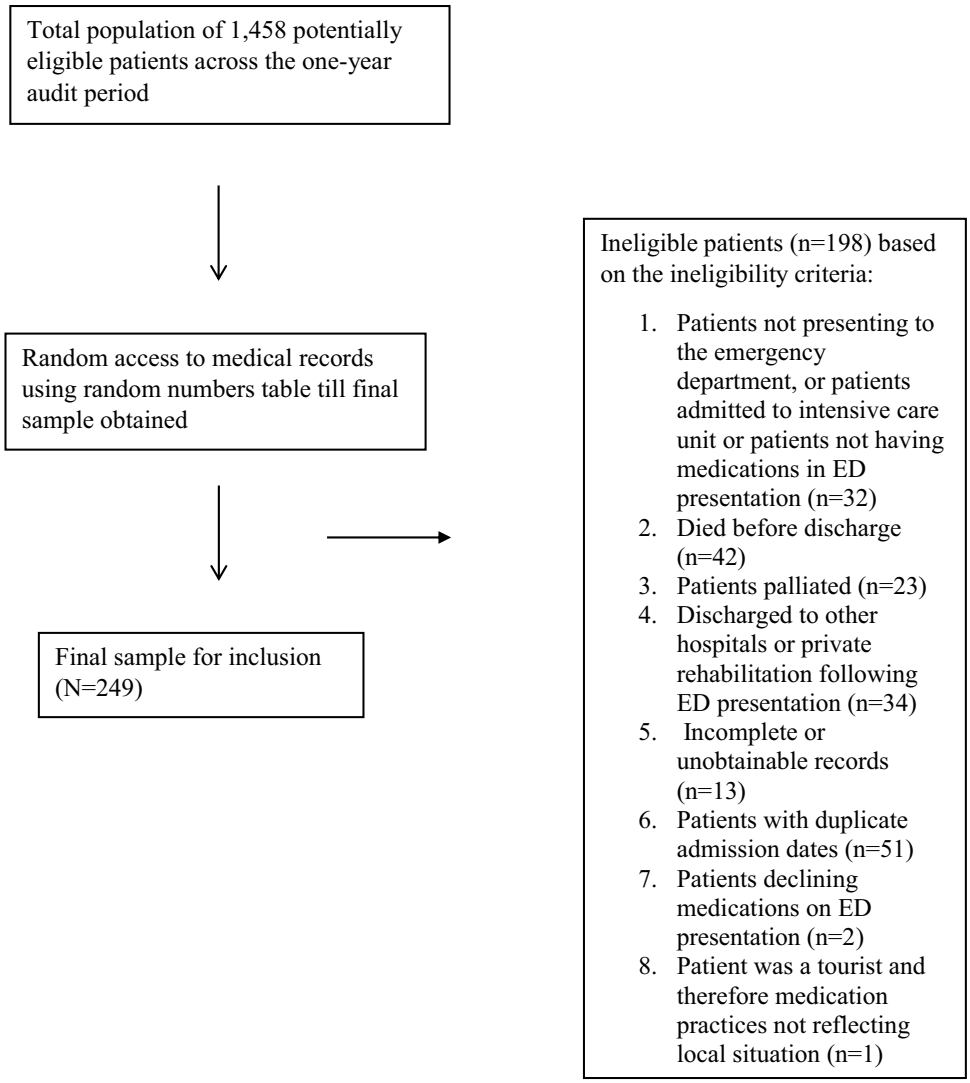

Fig. 1 Flow chart for access of sample

Characteristics of potentially inappropriate medications

Characteristics of potentially inappropriate medications are summarised in Table 2. There were 476 occurrences in the whole sample. The total numbers of PIMs at the four different time points were 195, 123, 51 and 107, respectively. The prevalence of having at least 1 PIM at the different time points was 51.0%, 37.3%, 40.4% and 36.9%, respectively. The most common PIMs were the use of proton pump inhibitors for uncomplicated peptic ulcer disease, followed by use of benzodiazepines, and medications prescribed without an evidence-based clinical indication. The common medications that were prescribed without any clear clinical indication were aspirin, frusemide, spironolactone and amitriptyline.

Characteristics of potential prescribing omissions

For the purpose of PPO characteristics, results reported here exclude the prevalence of vaccination omission as information about vaccinations tended not to be collected by the hospital. For information about PPOs relating to vaccination—omission of documentation about having a pneumococcal vaccine at least once after the age of 65, and omission of a seasonal trivalent influenza vaccine annually—refer to results in the supplementary material. The total numbers of PPOs at the four different time points were 158, 153, 66 and 125 respectively. There were 502 occurrences in the whole sample. The prevalence of having at least 1 PPO at the four different time points was 44.6%, 43.8%, 41.8% and 36.9%, respectively. The most common PPOs were omission of Vitamin D supplements

Table 1 Demographic characteristics ($N=249$)

Variable	*n* (%)
Age, years (*n*, %)	
85–90	173 (69.5%)
91–95	62 (24.9%)
≥96	14 (5.6%)
Age, years	
Median (Q25;Q75)	88 (86;91)
Sex (*n*, %)	
Female	153 (61.4%)
Male	96 (38.6%)
Place of living (*n*, %)	
Home, with someone	143 (57.4%)
Home, alone	79 (31.7%)
Residential care	27 (10.8%)
Use of gait aids (*n*, %)	
4 wheel frame (4WF)	117 (47.0%)
Single point stick (SPS)	44 (17.7%)
2 wheel frame, bedbound, crutches, hoist, wheelchair	7 (2.8%)
Not using aids	81 (32.5%)
Functional status (*n*, %)	
Requiring assistance in at least one area for personal activities of daily living (ADL)	81 (32.5%)
Requiring assistance in at least one domestic ADL	177 (71.1%)
Requiring assistance in at least one community ADL	190 (76.3%)
Communication barrier	
Non English-speaking background	72 (28.9%)
Confusion from delirium or dementia	22 (8.8%)
Aphasia/dysphasia	3 (1.2%)
No communication barrier	149 (59.8%)
Sensory deficits	
Hearing difficulties	45 (18.1%)
Vision difficulties	66 (26.5%)
Both	23 (9.2%)
Language other than English	
Italian	51 (20.5%)
Greek	21 (8.4%)
Other (Polish, Vietnamese, Cantonese, Ukrainian, Mandarin, Dutch, Czechoslovakian, Filipino, German, Maltese, Russian, Haka, Macedonian, Estonian, Croatian, Spanish)	32 (12.6%)
Charlson Comorbidity Index	
Median (Q25 Q75)	7 (5;8)
Geriatric syndromes (*n*, %)	
Falls	118 (47.4%)
Dementia	68 (27.3%)
Incontinence	48 (19.3%)
Urinary incontinence	36 (14.5%)
Faecal incontinence	1 (0.4%)
Double incontinence	11 (4.4%)
Length of stay in days (median, Q25;Q75)	
Acute	8 (6;12)
Subacute geriatric evaluation and management unit	20 (13;32)
Subacute transitional care practice	34 (14;41)
Total	13 (7;33)
Transition points	
Median (Q25;Q75)	3 (3;4)
Transition points (*n*, %)	
3	140 (56.2%)
4	85 (34.1%)
5	20 (8.0%)
6	2 (0.8%)
7	2 (0.8%)
Discharge destination	
Home	188 (75.5%)
Discharge to same destination as admission	212 (85.1%)
Change to higher level of care	37 (14.9%)

in housebound patients or patients experiencing falls, followed by the omission of angiotensin converting enzyme (ACE) inhibitors in patients with systolic heart failure or ischaemic heart disease. The next most common PPOs involved the omission of beta-blockers with ischaemic heart disease (Table 3).

Adverse clinical outcomes

The total number of adverse clinical outcomes across the sample at the 4 different time points was 71, 42, 13 and 19 respectively. The most common adverse clinical outcomes were associated with prolonged use of a proton pump inhibitor, benzodiazepine, neuroleptic medication and non-steroidal anti-inflammatory drugs. As time progressed during the patients' hospitalisation, the prevalence of adverse clinical outcomes decreased from admission to discharge (Table 4).

Poisson regression results

Poisson regression analyses were undertaken to predict the incident count for PIMs and PPOs in relation to explanatory variables (Table 5). Use of mobility aids and a higher number of medications on admission were associated with a higher incident count for PIMs. A higher comorbidity number and a higher length of hospital stay were associated with an increased incident count for PPOs. A higher number of medications on admission was associated with a reduced incidence rate of PPOs.

Table 2 Frequency of incidents across four snapshots of time for the Screening Tool of Older Persons' potentially inappropriate Prescriptions (STOPP)

Criteria	Snapshots of time				Total
	1	2	3	4	
Section A: indication of medication					
1. Any drug prescribed without an evidence-based clinical indication	24	17	6	10	57
3. Any duplicate drug class prescription, e.g. two concurrent non steroidal anti-inflammatory drugs (NSAIDs), selective serotonin reuptake inhibitors (SSRIs), loop diuretics, angiotensin converting enzyme (ACE) inhibitors, anticoagulants (optimisation of monotherapy within a single drug class should be observed prior to considering a new agent)	5			2	7
Section B: cardiovascular system					
1. Digoxin for heart failure with normal systolic ventricular function (no clear evidence of benefit)	2	2	1	2	7
4. Beta-blocker with bradycardia (< 50/min), type II heart block or complete heart block (risk of complete heart block, asystole)	2	1	0	0	3
5. Amiodarone as first-line antiarrhythmic therapy in supraventricular tachyarrhythmias (higher risk of side-effects than beta-blockers, digoxin, verapamil or diltiazem)	1	1	0	0	2
6. Loop diuretic as first-line treatment for hypertension (safer, more effective alternatives available)	5	3	1	6	15
7. Loop diuretic for dependent ankle oedema without clinical, biochemical evidence or radiological evidence of heart failure, liver failure, nephrotic syndrome or renal failure (leg elevation and /or compression hosiery usually more appropriate)	1	1	0	1	3
8. Thiazide diuretic with current significant hypokalaemia (i.e. serum K + < 3.0 mmol/l), hyponatraemia (i.e. serum Na + < 130 mmol/l) hypercalcaemia (i.e. corrected serum calcium > 2.65 mmol/l) or with a history of gout (hypokalaemia, hyponatraemia, hypercalcaemia and gout can be precipitated by thiazide diuretic)	5	1	0	1	7
9. Loop diuretic for treatment of hypertension with concurrent urinary incontinence (may exacerbate incontinence)	1	1	0	1	3
11. ACE inhibitors or Angiotensin Receptor Blockers in patients with hyperkalaemia	7	4	1	1	13
12. Aldosterone antagonists (e.g. spironolactone, eplerenone) with concurrent potassium-conserving drugs (e.g. ACE inhibitors, angiotensin II receptor blockers (ARBs), amiloride, triamterene) without monitoring of serum potassium (risk of dangerous hyperkalaemia i.e. > 6.0 mmol/l – serum K should be monitored regularly, i.e. at least every 6 months)	2	0	0	0	2
Section C: antiplatelet/anticoagulant drugs					
2. Aspirin with a past history of peptic ulcer disease without concomitant proton pump inhbitor (PPI) (risk of recurrent peptic ulcer)	1	1	0	0	2
4. Aspirin plus clopidogrel as secondary stroke prevention, unless the patient has a coronary stent(s) inserted in the previous 12 months or concurrent acute coronary syndrome or has a high-grade symptomatic carotid arterial stenosis (no evidence of added benefit over clopidogrel monotherapy)	1	2	0	0	3
5. Aspirin in combination with vitamin K antagonist, direct thrombin inhibitor or factor Xa inhibitors in patients with chronic atrial fibrillation (no added benefit from aspirin)	1	1	0	1	3
6. Antiplatelet agents with vitamin K antagonist, direct thrombin inhibitor or factor Xa inhibitors in patients with stable coronary, cerebrovascular or peripheral arterial disease (No added benefit from dual therapy)	1	1	0	1	3
8. Vitamin K antagonist, direct thrombin inhibitor or factor Xa inhibitors for first deep venous thrombosis without continuing provoking risk factors (e.g. thrombophilia) for > 6 months, (no proven added benefit)	0	0	1	0	1
10. NSAID and vitamin K antagonist, direct thrombin inhibitor or factor Xa inhibitors in combination (risk of major gastrointestinal bleeding)	7	6	1	8	22
11. NSAID with concurrent antiplatelet agent(s) without PPI prophylaxis (increased risk of peptic ulcer disease)	2	3	0	1	6
Section D: central nervous system and psychotropic drugs					
2. Initiation of tricyclic antidepressants (TCAs) as first-line antidepressant treatment (higher risk of adverse drug reactions with TCAs than with SSRIs or serotonin and noradrenaline reuptake inhibitors (SNRIs))	4	1	1	1	7
5. Benzodiazepines for ≥ 4 weeks (no indication for longer treatment; risk of prolonged sedation, confusion, impaired balance, falls, road traffic accidents; all benzodiazepines should be withdrawn gradually if taken for more than 4 weeks as there is a risk of causing a benzodiazepine withdrawal syndrome if stopped abruptly)	2	0	0	0	2
7. Anticholinergics/antimuscarinics to treat extrapyramidal side-effects of neuroleptic medications (risk of anticholinergic toxicity)	1	1	0	0	2
8. Anticholinergics/antimuscarinics in patients with delirium or dementia (risk of exacerbation of cognitive impairment)	2	1	1	1	5
14. First-generation antihistamines (safer, less toxic antihistamines now widely available)	1	0	0	0	1

Table 2 (continued)

Criteria	Snapshots of time				Total
	1	2	3	4	
Section E: renal system					
1. Digoxin at a long-term dose greater than 125 µg/day if estimated glomerular filtration rate (eGFR) < 30 ml/min/1.73 m2 (risk of digoxin toxicity if plasma levels not measured)	1	0	0	0	1
2. Direct thrombin inhibitors (e.g. dabigatran) if eGFR < 30 ml/min/1.73 m2 (risk of bleeding)	1	1	0	0	2
6. Metformin if eGFR < 30 ml/min/1.73 m2 (risk of lactic acidosis)	3	3	0	1	7
Section F: gastrointestinal system					
1. Prochlorperazine or metoclopramide with Parkinsonism (risk of exacerbating Parkinsonian symptoms)	1	0	0	0	1
2. PPI for uncomplicated peptic ulcer disease or erosive peptic oesophagitis at full therapeutic dosage for > 8 weeks (dose reduction or earlier discontinuation indicated)	52	43	21	40	156
3. Drugs likely to cause constipation (e.g. antimuscarinic/anticholinergic drugs, oral iron, opioids, verapamil, aluminium antacids) in patients with chronic constipation where non-constipating alternatives are available (risk of exacerbation of constipation)	1	1	1	0	3
Section G: respiratory system					
1. Theophylline as monotherapy for chronic obstructive pulmonary disease (COPD) (safer, more effective alternative; risk of adverse effects due to narrow therapeutic index)	1	1	0	0	2
3. Antimuscarinic bronchodilators (e.g. ipratropium, tiotropium) with a history of narrow-angle glaucoma (may exacerbate glaucoma) or bladder outflow obstruction (may cause urinary retention)	0	0	0	1	1
5. Benzodiazepines with acute or chronic respiratory failure i.e. pO2 < 8.0 kPa ± pCO2 > 6.5 kPa (risk of exacerbation of respiratory failure)	1	0	0	0	1
Section H: musculoskeletal system					
2. NSAID with severe hypertension (risk of exacerbation of hypertension) or severe heart failure (risk of exacerbation of heart failure)	3	3	0	1	7
5. Corticosteroids (other than periodic intra-articular injections for mono-articular pain) for osteoarthritis (risk of systemic corticosteroid side-effects)	1	1	0	0	2
8. NSAID with concurrent corticosteroids without PPI prophylaxis (increased risk of peptic ulcer disease)	2	2	0	3	7
Section I: urogenital system					
1. Antimuscarinic drugs with dementia, or chronic cognitive impairment (risk of increased confusion, agitation) or narrow-angle glaucoma (risk of acute exacerbation of glaucoma), or chronic prostatism (risk of urinary retention)	0	0	0	1	1
Section J: endocrine system					
Section K: drugs that predictably increase the risk of falls in older people					
1. Benzodiazepines (sedative, may cause reduced sensorium, impair balance)	32	10	5	13	60
2. Neuroleptic drugs (may cause gait dyspraxia, Parkinsonism)	11	8	6	10	35
3. Vasodilator drugs (e.g. alpha-1 receptor blockers, calcium channel blockers, long-acting nitrates, ACE inhibitors, angiotensin I receptor blockers) with persistent postural hypotension i.e. recurrent drop in systolic blood pressure ≥ 20 mmHg (risk of syncope, falls)	1	1	1	0	3
Section L: analgesic drugs					
1. Use of oral or transdermal strong opioids (morphine, oxycodone, fentanyl, buprenorphine, diamorphine, methadone, tramadol, pethidine, pentazocine) as first-line therapy for mild pain (World Health Organization (WHO) analgesic ladder not observed)	2	1	2	0	5
2. Use of regular (as distinct from pro re nata, as required (PRN) opioids without concomitant laxative (risk of severe constipation)	3	1	2	0	6
Section N: antimuscarinic/anticholinergic drug burden					

Qualitative interview results

Interviews were undertaken with five female and four male geriatricians. Identified themes related to challenges in prescribing medications, challenges confronting geriatricians, and challenges faced by patients (see supplementary material).

Challenges in prescribing medications

Geriatricians referred to challenges in prescribing medications. Time constraints created difficulties in seeking the relevant medication history from specialists and general practitioners (GPs). Oldest old patients came to hospital from residential aged care where there were many GPs managing

Table 3 Frequency of incidents across four snapshots of time for the Screening Tool of Alert doctors to the Right Treatment (START)

Criteria	Snapshots of time				Total
	1	2	3	4	
Section A: cardiovascular system					
1. Vitamin K antagonists or direct thrombin inhibitors or factor Xa inhibitors in the presence of chronic atrial fibrillation	5	3	1	3	12
2. Aspirin (75 mg–160 mg once daily) in the presence of chronic atrial fibrillation, where Vitamin K antagonists or direct thrombin inhibitors or factor Xa inhibitors are contraindicated	4	3	2	1	10
3. Antiplatelet therapy (aspirin or clopidogrel or prasugrel or ticagrelor) with a documented history of coronary, cerebral or peripheral vascular disease	11	9	5	4	29
4. Antihypertensive therapy where systolic blood pressure consistently > 160 mmHg and/or diastolic blood pressure consistently > 90 mmHg; if systolic blood pressure > 140 mmHg and /or diastolic blood pressure > 90 mmHg, if diabetic	2	1	1	0	4
5. Statin therapy with a documented history of coronary, cerebral or peripheral vascular disease, unless the patient's status is end-of-life or age is > 85 years	2	1	1	2	6
6. Angiotensin converting enzyme (ACE) inhibitor with systolic heart failure and/or documented coronary artery disease	25	25	10	27	87
7. Beta-blocker with ischaemic heart disease	22	21	6	17	66
8. Appropriate beta-blocker (bisoprolol, nebivolol, metoprolol or carvedilol) with stable systolic heart failure	1	1	0	1	3
Section B: respiratory system					
1. Regular inhaled beta-2 agonist or antimuscarinic bronchodilator (e.g. ipratropium, tiotropium) for mild-to-moderate asthma or chronic obstructive pulmonary disease (COPD)	6	5	5	4	20
2. Regular inhaled corticosteroid for moderate–severe asthma or COPD, where forced expiratory volume in 1 sec (FEV1) < 50% of predicted value and repeated exacerbations requiring treatment with oral corticosteroids	2	2	1	1	6
Section C: central nervous system and eyes					
2. Non-tricyclic antidepressant (TCA) drug in the presence of persistent major depressive symptoms	1	0	0	0	1
3. Acetylcholinesterase inhibitor (e.g. donepezil, rivastigmine, galantamine) for mild–moderate Alzheimer's dementia or Lewy Body dementia (rivastigmine)	4	5	1	5	15
4. Topical prostaglandin, prostamide or beta-blocker for primary open-angle glaucoma	1	1	0	1	3
Section D: gastrointestinal system					
2. Fibre supplements (e.g. bran, ispaghula, methylcellulose, sterculia) for diverticulosis with a history of constipation	1	1	0	1	3
Section E: musculoskeletal system					
3. Vitamin D and calcium supplement in patients with known osteoporosis and/or previous fragility fracture(s) and/or (Bone Mineral Density T-scores more than − 2.5 in multiple sites)	5	6	5	6	22
4. Bone anti-resorptive or anabolic therapy (e.g. bisphosphonate, strontium ranelate, teriparatide, denosumab) in patients with documented osteoporosis, where no pharmacological or clinical status contraindication exists (Bone Mineral Density T-scores -> 2.5 in multiple sites) and/or previous history of fragility fracture(s)	15	15	5	14	49
5. Vitamin D supplement in older people who are housebound or experiencing falls or with osteopenia (Bone Mineral Density T-score is > -1.0 but < -2.5 in multiple sites)	44	50	22	37	153
7. Folic acid supplement in patients taking methotrexate					
Section F: endocrine system					
1. ACE inhibitor or angiotensin receptor blocker (if intolerant of ACE inhibitor) in diabetes with evidence of renal disease i.e. dipstick proteinuria or microalbuminuria (> 30 mg/24 h) with or without serum biochemical renal impairment	1	1	0	1	3
Section G: urogenital system					
1. Alpha-1 receptor blocker with symptomatic prostatism, where prostatectomy is not considered necessary	2	0	0	0	2
2. 5-alpha reductase inhibitor with symptomatic prostatism, where prostatectomy is not considered necessary	2	1	0	0	3
Section H: analgesics					
1. High-potency opioids in moderate–severe pain, where paracetamol, non steroidal anti-inflammatory drugs (NSAIDs) or low-potency opioids are not appropriate to the pain severity or have been ineffective	0	0	1	0	1
2. Laxatives in patients receiving opioids regularly	2	2	0	0	4

Table 4 Frequency of incidents across four snapshots of time for adverse clinical outcomes

Criteria	Snapshots of time				Total
	1	2	3	4	
Beta-blocker with bradycardia (< 50/min), type II heart block or complete heart block (risk of complete heart block, asystole)—Pulse < 50/min, type II heart block or complete heart block	2	1	0	0	3
Loop diuretic as first-line treatment for hypertension—hypokalaemia (K + < 3.5 mmol/L, hypomagnesaemia, dehydration	3	2	1	1	7
Thiazide diuretic with current significant hypokalaemia, hypercalcaemia or with a history of gout—serum K + < 3.5 mmol/L, serum Na + < 130 mmol/l, serum calcium > 2.65 mmol/l, active gout	5	3	0	2	10
Loop diuretic for treatment of hypertension with concurrent urinary incontinence—presence of urinary incontinence	3	3	1	3	10
ACE inhibitors or angiotensin receptor blockers in patients with hyperkalaemia—worsening hyperkalaemia (K + > 5 mmol/L)	3	2	0	0	5
Aldosterone antagonists (e.g. spironolactone, eplerenone) with concurrent potassium-conserving drugs—worsening hyperkalaemia (K + > 5 mmol/L)	2	0	0	0	2
Antiplatelet agents with vitamin K antagonist, direct thrombin inhibitor or factor Xa inhibitors in patients with stable coronary, cerebrovascular or peripheral arterial disease—abnormal clotting profile	2	2	0	1	5
Benzodiazepines for ≥ 4 weeks—sedation, confusion, impaired balance, and falls	4	1	1	0	6
Anticholinergics/antimuscarinics in patients with delirium or dementia—cognitive impairment	1	1	0	0	2
Digoxin at a long-term dose greater than 125 μg/day if estimated glomerular filtration rate (eGFR) < 30 ml/min/1.73 m^2—clinical manifestations of digoxin toxicity	1	1	0	1	3
Metformin if eGFR < 30 ml/min/1.73 m^2—Muscle weakness, numbness in limbs, dyspnoea, dizziness, light-headedness, nausea, vomiting, gastrointestinal pain, bradycardia	3	2	0	0	5
Proton pump inhibitor (PPI) for > 8 weeks—Hypocalcaemia (normal: 2.1–2.6 mmol/L), hypomagnesemia (normal: 0.75–1.25 mmol/L), *Clostridium difficile* infections, and pneumonia	14	12	5	5	36
Drugs likely to cause constipation (e.g. antimuscarinic/anticholinergic drugs—worsening constipation)	1	1	2	0	4
Antimuscarinic bronchodilators (e.g. ipratropium, tiotropium) with a history of narrow-angle glaucoma or bladder outflow obstruction—glaucoma, urinary retention	0	0	0	1	1
Benzodiazepines with acute or chronic respiratory failure—dyspnoea, confusion, reduced oxygen saturation	1	0	0	0	1
NSAID with severe hypertension—documented heart failure clinical manifestations	4	4	1	2	11
Corticosteroids other than periodic intra-articular injections—documented cataracts, high blood glucose levels, infections, fever, bleeding, frail skin	1	1	0	0	2
Benzodiazepine use—documented prolonged sedation, confusion, impaired balance, falls	14	2	0	1	17
Neuroleptic drug use—documented confusion, gait dyspraxia, prone to falls, hypotension (< 90/60 mmHg), documented extrapyramidal symptoms	6	3	0	2	11
Vasodilator drugs with persistent postural hypotension—drop in systolic blood pressure ≥ 20 mmHg in lying or sitting position, syncope, falls	1	1	2	0	4

them rather than a regular GP, leading to loss of information regarding reasons for prescribing.

Since oldest old patients were often excluded in research studies, geriatricians believed a lack of evidence-based medication management existed in this population. Geriatricians had to extrapolate results from studies in younger patients. A dearth of data existed on the safety profile and efficacy of commonly used medications.

Difficulties arose from patients' inability to afford certain medications. While geriatricians attempted to prescribe medications according to evidence, patients sometimes faced problems with accessing beneficial medications from a lack of government subsidisation.

The nature of adverse effects of certain medications, such as anticoagulants and insulin, meant that geriatricians had to carefully evaluate before commencing these medications. This caution sometimes led to delays in starting potentially beneficial medications.

Challenges in prescribing confronting geriatricians

Geriatricians referred to the differential knowledge about the oldest old sometimes contributed to inappropriate prescribing. While aged care trainee doctors usually had good understanding of safe prescribing, geriatricians perceived that doctors from other specialities and junior doctors may have had gaps in prescribing knowledge. These knowledge gaps could have led to potentially toxic levels of medications and patients taking inappropriate medications over the long-term.

Table 5 Poisson regression analysis for predicting the count of potentially inappropriate medications (PIMs) and potential prescribing omissions (PPOs)

Variable	Exp(B) incident count	*p* Value	95% Confidence intervals
Potentially inappropriate medications (PIMs)			
Use of mobility aids	1.430	0.006	1.109, 1.843
Documented allergy	0.953	0.618	0.789, 1.151
History of falls	1.071	0.484	0.883, 1.299
Incontinence	1.040	0.744	0.822, 1.316
Dependence with personal activities of daily living	0.951	0.649	0.767, 1.180
Dependence with domestic activities of daily living	1.054	0.751	0.763, 1.454
Dependence with community activities of daily living	1.327	0.138	0.913, 1.927
Number of medications on admission	1.083	<0.0001	1.058, 1.108
Total length of stay	0.998	0.451	0.994, 1.003
Potential prescribing omissions (PPOs)			
Dementia	1.019	0.723	0.916, 1.134
History of falls	1.096	0.051	1.000, 1.202
Incontinence	1.088	0.147	0.971, 1.219
Dependence with domestic activities of daily living	0.975	0.722	0.846, 1.123
Dependence with community activities of daily living	1.074	0.359	0.923, 1.249
Comorbidities (up to 6, more than 6)	1.172	<0.0001	1.073, 1.280
Number of medications on admission	0.989	0.035	0.978, 0.999
Total length of stay	1.004	<0.0001	1.002, 1.006

Explanatory variables examined at the univariate level were: age, use of aids, documented allergy, documented dementia, history of falls, incontinence, personal activities of daily living, domestic ADLs, community ADLs, communication barrier, comorbid conditions, number of medications prescribed on admission, total length of stay, and age. Only those variables that had univariate associations with *p* values of ≤ 0.25 were included in Poisson regression modelling

Patients were managed by multiple specialists who sometimes considered their area of expertise rather than patients as a whole. A lack of coordinated care existed between specialists, resulting in patients being prescribed many medications with an increased risk of drug interactions. Patients were also reluctant to discontinue medications prescribed by specialists.

Geriatricians stated that while disease management guidelines were useful, strict observation of guidelines could lead to polypharmacy. Guidelines needed to be tailored to the oldest old, especially since guidelines were mostly based on younger populations. Strict adherence to guidelines could also lead to patients missing out on beneficial medications.

Geriatricians had difficulties in completing timely medication reconciliation on hospital admission. Inadequate information was sometimes available about the type of medications, dosages and indications.

All geriatricians believed that patients needed to be actively involved in decisions and goals of care. Active involvement meant that patients' wishes could be considered in consultations.

As the hospital used a paper-based approach in information management, geriatricians stated there was a potential loss of information regarding medications. This situation increased the risk for medication errors and miscommunication, especially with patient movements between clinical settings.

Geriatricians believed that their medical colleagues were at times over-cautious about prescribing. These colleagues occasionally overestimated the risk of adverse effects, leading to patients missing out on potentially beneficial medications.

Challenges faced by patients

Geriatricians believed that patients were susceptible to adverse effects. Challenges existed in diversity in patterns and severity of patient illness.

Patients were reluctant to cease medications, especially those prescribed by specialists or general practitioners in private practice. This reluctance related to doctors previously informing patients that some medications had to be continued for life. Convincing patients otherwise, was challenging. Families of patients with dementia were also opposed to medication changes because of patients' worsening cognition.

Geriatricians referred to multiple comorbidities leading to polypharmacy. Other challenges related to patient problems with medication adherence. Reasons for non-adherence related to adverse effects experienced by certain medications, and patients' inability to swallow.

Discussion

The study provided comprehensive information about inappropriate prescribing in oldest old patients. The prevalence of having at least one PIM varied between 36.9% and 51.0% while the prevalence of having at least one PPO varied between 36.9% and 44.6% during patients' hospitalisation. Use of mobility aids and an increasing number of medications on admission were associated with a higher incident count for PIMs. A higher comorbidity number and a longer length of hospital stay were associated with an increased incident count for PPOs. A higher number of medications on admission was associated with a reduced incidence rate of PPOs. Interviews with geriatricians identified many complex challenges in prescribing medications for the oldest old, which related to medication characteristics, difficulties confronting geriatricians, and concerns faced by patients.

Marked variability exists in determining PIMs in oldest old patients. Of the small number of studies undertaken in this population group, in community-dwelling people over 3-year cycles (2003, 2007 and 2011), Ble et al. [15] found between 34.9% and 41.1% of patients aged 85 years and over had at least one PIM using Beers (2012 version), while Wauters et al. [16] found 56.1% of community-dwelling people aged 80 years and over had at least one PIM using STOPP (version 2). Using a translated version of the Beers criteria (2012), Lai et al. [17] showed, of patients aged 80 years and over admitted to hospital, 27.1% had at least one PIM while San Jose et al. [18] found 63.3% of patients aged 85 years and over admitted to hospital had at least one PIM using the STOPP (version 2). The baseline level of at least one PIM (51.0%) was therefore similar to those of previous studies using the STOPP (version 2). In the current study, the prevalence was shown to decrease to 36.9% during hospitalisation up to hospital discharge. Previous studies have been cross-sectional in nature while the current study has been able to demonstrate downward trends in PIMs during patients' hospitalisation. In geriatricians' interviews, while there was recognition of the challenges involved in polypharmacy, they were cognisant of reducing inappropriate medication prescribing throughout patients' hospitalisation.

The most common PIMs were the use of PPIs and benzodiazepines. These findings are consistent with previous studies [19–26]. PPIs have been shown to be one of the most commonly prescribed medications in older people [27]. The standard General Practice management for patients with PPIs includes conducting frequent medication optimisation to reduce the dosage or cease PPIs if asymptomatic [27]. Despite these guidelines, active de-prescribing of PPIs is not necessarily practised [28, 29]. The complications associated with long-term use of PPIs include *Clostridium difficile* infections, hypomagnesaemia, renal disease, dementia and pneumonia [30].

Benzodiazepine use was also shown to be a major type of PIM identified. In the study cohort, benzodiazepine use was found to possibly contribute to the presence of adverse clinical outcomes, such as documented prolonged sedation, confusion, impaired balance, falls, dyspnoea, confusion, and reduced oxygen saturation. Although benzodiazepine use appeared to impact on adverse clinical outcomes, the prescription of this medication group decreased during hospitalisation, which appeared to also be associated with a reduction in related adverse clinical outcomes. Past research has shown that oldest old patients who consumed benzodiazepines in hospital were more likely to have cognitive and psychomotor impairment compared with patients aged younger than 80 years [17]. Benzodiazepine use, especially for those prone to falls, was shown to be the most common cause of PIMs in the oldest old patients admitted to hospital [18].

The prevalence of having at least one PPO showed a downward trend for the four time points. If the omission of influenza and pneumococcal infections is included, the prevalence of at least one PPO ranged between 98.4% and 99.1%. There is a need for strategies and guidelines to improve the prescription of appropriate medications for the oldest old. In using the START (version 2), Wauters et al. [16] found a higher prevalence of 67.0% of at least one PPO in community-dwelling people aged 80 years and over, while San José et al. [18] found 53.6% at least one PPO using START (version 1). There are considerable differences between START version 1 and version 2. One of the most obvious is the presence of the two vaccinations relating to influenza and pneumococcal infections.

The most common PPO was vitamin D supplements, which is consistent with the findings of the few international studies in the oldest old population [19–21]. Studies have shown that vitamin D supplements reduce the risk of fractures and falls [31, 32]. Given the high incidence of falls-related ED presentations and the subsequent morbidity and mortality in this group, more vigilance is needed to ensure appropriate prescription of vitamin D supplements. Thereafter, common PPOs were ACE inhibitors in patients with ischaemic heart disease or systolic heart failure and beta-blockers in patients with ischaemic heart disease, respectively, which have previously been identified as common PPOs in the oldest old [19–21]. One study reported that age > 75 years was an independent risk factor

for the under-prescription of ACE inhibitors and beta-blockers [33]. Given that congestive cardiac failure was the most common primary diagnosis in this study sample, more steps need to be taken to prescribe medications such as ACE inhibitors and beta-blockers that have a proven mortality benefit [33].

Poisson regression results demonstrated that an increase in comorbidities was associated with an increased incident count in PPOs and with no effect on PIMs. The current study involved calculation of comorbidity using the Charlson index, which may not be an accurate portrayal of how multimorbidity affects the oldest old. Development of a specific multimorbidity measurement for the oldest old would provide more appropriate measurement, which can be subsequently used to determine its associations with inappropriate prescribing.

Use of mobility aids was associated with an increased incident count of PIMs. Mobility aids comprised four-wheel frames, two-wheel frames, single pronged sticks and crutches. Use of mobility aids was significantly linked with a history of falls. Many of these patients had also used long-term benzodiazepines, which increase the prevalence of confusion and dizziness.

There was a complex picture with the number of medications prescribed on admission, with a significant positive association involving the incident counts of PIMs and a significant negative association involving the incident counts of PPOs. Many studies have previously reported the positive association between the number of medications prescribed and prevalence of PIMs [14, 21, 22, 24, 34]. With an increase in the number of medications, there could be a potential increase in the medication complexity regimen, leading to greater likelihood of adverse events and difficulties in medication reconciliation [35]. Greater attention on medications known to improve therapeutic benefits in the oldest old while at the same time being cognisant of the adverse effects that are likely with other medications, would enable a more balanced approach to prescribing.

As the length of hospital stay increased, patients also experienced an increased prevalence for PPOs. As indicated by the geriatrician interviews, there was a focus on reducing polypharmacy as much as possible during the patients' stay. This situation was evident by the number of PIMs that progressively reduced during patients' hospitalisation. However, at the same time, there was little focus on attempting to commence appropriate medications that are warranted.

There were limitations relating to this study. For the STOPP criteria, patients were assumed to have been on a PPI for > 8 weeks. If possible, the long-term prescription of the medication was verified by checking discharge summaries from other admissions or the medication list from the GP, to reduce the potential overestimation in the prevalence of PPI prescription. If no information was provided about the patients' vaccination status, it was assumed that they did not have pneumococcal or influenza vaccination. Full adherence of patients with their medications was assumed. This was a single-centre study conducted in a tertiary teaching hospital with two sites, and the results cannot be generalised to other healthcare settings. The START and STOPP criteria do not capture the nuances of prescribing for patients on a case-by-case basis. While they are useful guides to safe prescribing, they are not substitutes for clinical reasoning.

This study demonstrated that oldest old patients are discharged with high rates of PIMs and PPOs. Greater attention should be placed on actively de-prescribing medications that are not beneficial while simultaneously commencing medications that would be advantageous. Audits of a larger scale are needed to identify barriers to safe prescribing and implement steps towards improving prescribing practices for this vulnerable population.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Research involving human participants All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent For the retrospective clinical audit of electronic medical records, formal consent was not required. For the semi-structured interviews with geriatricians, informed consent was obtained from all individual participants included in the study.

References

1. United Nations (2015) World population ageing. United Nations, New York
2. Ortman J, Velkoff V, Hogan H (2014) An aging nation: the older population in the United States. Department of Commerce, US Census Bureau, Washington, DC, US
3. Galvin R, Moriarty F, Cousins G et al (2014) Prevalence of potentially inappropriate prescribing and prescribing omissions in older Irish adults: findings from The Irish LongituDinal Study on Ageing study (TILDA). Eur J Clin Pharmacol 70:599–606. https://doi.org/10.1007/s00228-014-1651-8
4. Hamilton HJ, Gallagher P, O'Mahony D (2009) Inappropriate prescribing and adverse drug events in older people. BMC Geriatr 9 (5):https://doi.org/10.1186/1471-2318-1189-1185
5. Hamilton H, Gallagher P, Ryan C et al (2011) Potentially inappropriate medications defined by STOPP criteria and the risk of adverse drug events in older hospitalized patients. Arch Intern Med 171:1013–1019
6. Runciman WB, Roughead EE, Semple SJ et al (2003) Adverse drug events and medication errors in Australia. Int J Qual Health Care 15:i49–i59

7. Sakuma M, Morimoto T (2011) Adverse drug events due to potentially inappropriate medications. Arch Intern Med 171:1959. https://doi.org/10.1001/archinternmed.2011.553
8. Yayla M, Bilge U, Binen E et al (2013) The use of START/STOPP criteria for elderly patients in primary care. Sci World J. https://doi.org/10.1155/2013/165873
9. Gallagher P, Ryan C, Byrne S et al (2008) STOPP (Screening Tool of Older Person's Prescriptions) and START (Screening Tool to Alert doctors to Right Treatment). Consensus validation. Int J Clin Pharmacol Ther 46:72–83
10. O'Mahony D, O'Sullivan D, Byrne S et al (2015) STOPP/START criteria for potentially inappropriate prescribing in older people: version 2. Age Ageing 44:213–218. https://doi.org/10.1093/ageing/afu145
11. Hill-Taylor B, Hayden J, Byrne S et al (2013) Application of the STOPP/START criteria: a systematic review of the prevalence of potentially inappropriate prescribing in older adults, and evidence of clinical, humanistic and economic impact. J Clin Pharm Ther 38:360–372
12. Elliott R, Stehlik P (2013) Identifying inappropriate prescribing for older people. J Pharmac Pract Res 43:312–319
13. Charlson M, Pompei P, Ales K et al (1987) A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 40:373–383
14. Manias E, Kusljic S, Berry C et al (2015) Use of the Screening Tool of Older Person's Prescriptions (STOPP) in older people admitted to an Australian hospital. Aust J Ageing 34:15–20
15. Ble A, Masoli JAH, Barry HE et al (2015) Any versus long-term prescribing of high risk medications in older people using 2012 Beers Criteria: results from three cross-sectional samples of primary care records for 2003/4, 2007/8 and 2011/12. BMC Geriatr 15:146–146. https://doi.org/10.1186/s12877-015-0143-8
16. Wauters M, Elseviers M, Vaes B et al (2016) Too many, too few, or too unsafe? Impact of inappropriate prescribing on mortality, and hospitalization in a cohort of community-dwelling oldest old. Br J Clin Pharmacol 82:1382–1392. https://doi.org/10.1111/bcp.13055
17. Lai X, Zhu H, Huo X, Li Z (2018) Polypharmacy in the oldest old (≥ 80 years of age) patients in China: a cross-sectional study. BMC Geriatr 18:64–64. https://doi.org/10.1186/s12877-018-0754-y
18. San-José A, Agustí A, Vidal X et al (2015) Inappropriate prescribing to the oldest old patients admitted to hospital: prevalence, most frequently used medicines, and associated factors. BMC Geriatr 15:42–42. https://doi.org/10.1186/s12877-015-0038-8
19. Dalleur O, Boland B, De Groot A et al (2015) Detection of potentially inappropriate prescribing in the very old: cross-sectional analysis of the data from the BELFRAIL observational cohort study. BMC Geriatr 15:1
20. San-José A, Agustí A, Vidal X et al (2014) Original article: Inappropriate prescribing to older patients admitted to hospital: a comparison of different tools of misprescribing and underprescribing. Eur J Intern Med 25:710–716. https://doi.org/10.1016/j.ejim.2014.07.011
21. Wauters M, Elseviers M, Vaes B et al (2016) Too many, too few, or too unsafe? Impact of inappropriate prescribing on mortality, and hospitalisation in a cohort of community-dwelling oldest old. Br J Clin Pharmacol. https://doi.org/10.1111/bcp.13055
22. Wahab MSA, Nyfort-Hansen K, Kowalski SR (2012) Inappropriate prescribing in hospitalised Australian elderly as determined by the STOPP criteria. Int J Clin Pharm 34:855–862. https://doi.org/10.1007/s11096-012-9681-8
23. Manias E, Kusljic S, Lam D-L (2015) Use of the Screening Tool of Older Persons' Prescriptions (STOPP) and the Screening Tool to Alert doctors to the Right Treatment (START) in hospitalised older people. Aust J Ageing 34:252–258. https://doi.org/10.1111/ajag.12186
24. Frankenthal D, Lerman Y, Lerman Y (2015) The impact of hospitalization on potentially inappropriate prescribing in an acute medical geriatric division. Int J Clin Pharm 37:60–67. https://doi.org/10.1007/s11096-014-0040-9
25. Blanco Reina E, Ariza Zafra G, Ocaña Riola R et al (2015) Optimizing elderly pharmacotherapy: polypharmacy vs. undertreatment. Are these two concepts related? Eur J Clin Pharmacol 71:199–207
26. Di Giorgio C, Provenzani A, Polidori P (2016) Potentially inappropriate drug prescribing in elderly hospitalized patients: an analysis and comparison of explicit criteria. Int J Clin Pharm 38:462–468. https://doi.org/10.1007/s11096-016-0284-7
27. Miller G, Wong C, Pollack A (2015) Gastro-oesophageal reflux disease (GORD) in Australian general practice patients. Aust Fam Phys 44:701–704
28. Wallerstedt SM, Fastbom J, Linke J et al (2017) Long-term use of proton pump inhibitors and prevalence of disease- and drug-related reasons for gastroprotection—a cross-sectional population-based study. Pharmacoepidemiol Drug Saf 26:9–16. https://doi.org/10.1002/pds.4135
29. Rane PP, Guha S, Chatterjee S et al Prevalence and predictors of non-evidence based proton pump inhibitor use among elderly nursing home residents in the US. Res Soc Adm Pharm 13 (2):358–363. https://doi.org/10.1016/j.sapharm.2016.02.012
30. Eusebi LH, Rabitti S, Artesiani ML et al (2017) Proton pump inhibitors: Risks of long-term use. J Gastroenterol Hepatol 32:1295–1302. https://doi.org/10.1111/jgh.13737
31. Trivedi DP, Doll R, Khaw KT (2003) Effect of four monthly oral vitamin D3 (cholecalciferol) supplementation on fractures and mortality in men and women living in the community: randomised double blind controlled trial. BMJ 326:469. https://doi.org/10.1136/bmj.326.7387.469
32. Broe KE, Chen TC, Weinberg J et al (2007) A higher dose of vitamin D reduces the risk of falls in nursing home residents: a randomized, multiple-dose study. J Am Geriatr Soc 55:234–239. https://doi.org/10.1111/j.1532-5415.2007.01048.x
33. de Groote P, Isnard R, Assyag P et al (2007) Is the gap between guidelines and clinical practice in heart failure treatment being filled? Insights from the IMPACT RECO survey. Eur J Heart Fail 9:1205–1211. https://doi.org/10.1016/j.ejheart.2007.09.008
34. Napolitano F, Izzo M, Di Giuseppe G et al (2013) Frequency of inappropriate medication prescription in hospitalized elderly patients in Italy. PLoS One 8:e82359–e82359
35. Wimmer BC, Bell JS, Fastbom J et al (2016) Medication regimen complexity and polypharmacy as factors associated with all-cause mortality in older people: a population-based cohort study. Ann Pharmacother 50:89–95. https://doi.org/10.1177/1060028015621071