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Potentially inappropriate prescribing and cost outcomes for older people: a national population study

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WHAT IS ALREADY KNOWN ABOUT THIS SUBJECT

- Potentially inappropriate prescribing (PIP) refers to medications that should generally be avoided in older populations and doses or frequencies of administrations that should not be exceeded. Studies of PIP have been primarily based on US indicators of appropriateness such as the Beers criteria due to the lack of European specific indicators.
- PIP has not been assessed in full national samples.
- The total cost of PIP drugs and the cost in relation to overall national pharmaceutical expenditure have not been described.

WHAT THIS STUDY ADDS

- One third of the Irish population aged ≥70 years were prescribed at least one potentially inappropriate medication in 2007 based on European criteria.
- There was a signficant association between polypharmacy and the risk of PIP. Polypharmacy was evaluated as the number of different repeat drug classes (≥ three prescription claims) per claimant.
- The most prevalent PIP drugs were: proton pump inhibitors at maximum therapeutic dosage for >8 weeks (40 mg daily omeprazole, pantoprazole and esomeprazole, 30 mg daily lansoprazole and 20 mg daily rabeprazole); non-steroidal anti-inflammatories for >3 months; long-acting benzodiazepines for >1 month and drug duplication within the same therapeutic class.
- The total expenditure on potentially inappropriate drugs was €45 631 319 in 2007 which is 9% of the overall expenditure on pharmaceuticals in those aged ≥70 years in Ireland.

AIMS

Optimization of drug prescribing in older populations is a priority due to the significant clinical and economic costs of drug-related illness. This study aimed to: (i) estimate the prevalence of potentially inappropriate prescribing (PIP) in a national Irish older population using European specific explicit prescribing criteria; (ii) investigate the association between PIP, number of drug classes, gender and age and; (iii) establish the total cost of PIP.

METHODS

This was a retrospective national population study (n = 338 801) using the Health Service Executive Primary Care Reimbursement Service (HSE-PCRS) pharmacy claims database. The HSE-PCRS uses the WHO Anatomical Therapeutic Chemical (ATC) classification system and details of every drug dispensed and claimants' demographic data are available. Thirty PIP indicators (STOPP) were applied to prescription claims for those ≥70 years in Ireland in 2007. STOPP is a physiological system based screening tool of older persons' potentially inappropriate prescriptions assessing drug–drug and drug–disease interactions, dose and duration.

RESULTS

In our study population PIP prevalence was 36% (121 454 claimants). The main contributors to this were: 56 560 (17%) prescribed proton pump inhibitors at maximum therapeutic dose for >8 weeks, 29 691 (9%) prescribed non-steroidal anti-inflammatories for >3 months, 17 676 (5%) prescribed long-acting benzodiazepines for >1 month and 16 201 (5%) prescribed duplicate drugs. The main determinant of PIP was polypharmacy. The likelihood of PIP increased with a significant linear and quadratic trend ($P < 0.0001$) with the number of drug classes. The maximum net ingredient cost of PIP was estimated to be €38 664 640. Total PIP expenditure was estimated to be €45 631 319, 9% of the overall expenditure on pharmaceuticals in those ≥70 years in 2007.

CONCLUSIONS

The findings identify a high prevalence of PIP in Ireland with significant cost consequences.

Introduction

Optimization of drug prescribing in older populations is a priority due to the significant clinical and economic costs of drug related illness. Inappropriate prescribing in older people is associated with increases in morbidity, adverse drug events, hospitalization and mortality [1, 2]. However the selection of appropriate medication in older people is a challenging and complex process. Older people are particularly vulnerable to inappropriate prescribing because of their multiple drug regimens, co-morbid conditions and age associated physiological changes which can alter their pharmacokinetics and enhance their pharmacodynamic sensitivity to specific drugs [3]. In general, medicines in older people are considered appropriate when they have a clear evidence-based indication, are well tolerated in the majority and are cost-effective. In contrast, medicines that are potentially inappropriate have no clear evidence-based indication, carry a substantially higher risk of adverse side-effects compared with use in younger people or are not cost effective [4].

Appropriateness of prescribing in older people can be assessed by process (i.e. what providers do) or outcome measures (i.e. patient outcomes) which are implicit or explicit [3]. Implicit process measures are based on a clinician's judgment of appropriateness for the individual patient [5]. Explicit process measures are criterion based and are developed from published reviews, expert opinion and/or consensus techniques and should be generalizable across countries [6]. These measures consist of drugs to be avoided in older people, independent of diagnoses or in the context of certain diagnoses [7–9].

The US Beers criteria are the most frequently used and validated explicit process measure [10, 11]. However in the context of European prescribing Beers criteria have several limitations. Some of the limitations include the fact that almost half of the drugs that make up the criteria are unavailable for prescribers [12, 13], several of the drugs are not contra-indicated in older people as per the British National Formulary (BNF), e.g. doxazosin [4], whereas other contra-indicated drugs are omitted [13]. The Beers criteria do not consider drug–drug interactions, duration of treatment, varying indications for certain drugs, e.g. low-dose amitriptyline and neuropathic pain (BNF) and underuse of indicated drugs [3, 4]. Given the limitations of the Beers criteria, a more comprehensive explicit process measure of potentially inappropriate prescribing (PIP) has recently been developed and validated for use in European countries, the Screening Tool of Older Peoples Prescriptions (STOPP) [14].

There have been few studies of PIP in the general population of older people [12, 15, 16]. Previous research is limited by having focused on specific groups in particular settings such as geriatric units, nursing homes and hospitals as well as having measured PIP using Beers criteria. There is also a limited understanding of the risk factors associated with PIP and results from previous studies have been inconclusive [11, 15, 17]. The overall aim of this study was to estimate the prevalence of PIP in the national Irish population aged ≥70 years, in 2007 using thirty STOPP criteria. Additional objectives included: (i) estimation of the prevalence of PIP per individual STOPP criteria by physiological system; (ii) investigation of the association between PIP, number of drug classes, gender and age and; (iii) establishing the total cost of PIP drugs and the cost in relation to overall national pharmaceutical expenditure.

Methods

Study population

The National Shared Services Primary Care Reimbursement Service of the Health Service Executive in Ireland (HSE-PCRS) pharmacy claims database of dispensed medications was used to identify the study population. The HSE-PCRS general medical card scheme provides free health services including medications to eligible persons in Ireland. The HSE-PCRS scheme is means tested for those less than 70 years of age, and free to all those ≥70 years between July 2001 and December 2008. It is estimated that over 97% of this age group nationally avail of the scheme [18].

The HSE-PCRS pharmacy claims database provides details on monthly dispensed medications for each individual within the scheme. Prescriptions are coded using the World Health Organisation Anatomical Therapeutic Chemical (ATC) classification system [19] and prescriber information, defined daily doses (DDD), strength, quantity, method and unit of administration of each drug dispensed, ingredient costs and pharmacist dispensing fees per item dispensed are available. Gender, age group and health board region of each claimant is also recorded, but no diagnosis or outcomes are reported.

Explicit measurement of potentially inappropriate prescribing

STOPP is a physiological system based screening tool and comprises sixty-five clinically significant criteria which take drug–drug and drug–disease interactions, drug doses and duration into consideration [14]. STOPP considers cost-effectiveness as well as clinical effectiveness and includes the removal of any potentially unnecessary drugs. STOPP was validated using the Delphi consensus technique by an eighteen member expert panel in geriatric pharmacotherapy from the UK and Ireland. Inter-rater reliability is high [14, 20].

Thirty STOPP criteria were applied to prescription claims data for all those aged 70 years and older in Ireland in 2007 (supplemental Table S1). The thirty criteria were considered applicable to pharmacy claims data without diagnosis information on a consensus basis by an

expert panel of five members in geriatric pharmacotherapy, clinical pharmacology, pharmacoepidemiology and academic general practice. Prescription drugs for the treatment of certain disease conditions were identified and used as proxies for diagnosis where possible, e.g. dementia (ATC, N06D), Parkinson's disease (ATC, N04), epilepsy (ATC, N03, excluding gabapentin and pregabalin as also prescribed for neuropathic pain, BNF 4.7.3), chronic obstructive pulmonary disease (COPD) (ATC, R03BA, R03BB, R03CC02, R03CC03, R03DA04), glaucoma (ATC, S01ED), type 2 diabetes (ATC, A10B), gout (ATC, M04AA01) [18, 21]. Duplicate classes of medicine (on the same prescription claim) were assessed for five medications – opiates, non-steroidal anti-inflammatory drugs (NSAIDs), selective serotonin re-uptake inhibitors (SSRIs), loop diuretics and angiotensin converting enzyme inhibitors (ACE inhibitors).

Criteria which specified a particular duration were assessed by consecutive months of prescription refills for the period commencing January 2007 to December 2007 (lead-in period October to December 2006 included) e.g. long-acting benzodiazepines >1 month, NSAIDs >3 months. Criteria which specified a particular dosage that should not be exceeded e.g. proton pump inhibitors (PPIs) at maximum therapeutic dosage for >8 weeks (40 mg daily omeprazole, pantoprazole and esomeprazole, 30 mg daily lansoprazole and 20 mg daily rabeprazole) were evaluated by calculating the prescribed daily dose for each claimant according to details on the DDD, strength, quantity, administration, unit of measurement and packsize of the dispensed medication for the specified time period. The duration and dosage of PPI prescribing was assessed for a 1 year continuous period for each claimant e.g. January 2007 to January 2008 (baseline period 8 weeks at maximum therapeutic dosage). PPI dosage was classified as maximum or maintenance dosage at the end of each month according to the calculated prescribed monthly dose.

Claimants were categorized by gender and age group (70–74 years) and (≥75 years). The total number of prescriptions for each different drug class (the first three characters of the ATC code) was calculated for each claimant over the year; each claimant was required to receive at least three prescriptions per different drug class to be included as a measure of a repeat drug class. Polypharmacy was evaluated as the number of different repeat drug classes per claimant ranging from zero (reference group) to ten or more drug classes [15, 22, 23]. Costs were calculated as the net ingredient cost (NIC) of the dispensed drug and the total expenditure which included NIC, value added tax and pharmacist dispensing fee. Costs were adjusted for claimants receiving the same medication for more than one criteria. Costs also excluded the duration of prescribing that was deemed appropriate, e.g. 1 month for long-acting benzodiazepines, 3 months for NSAIDs.

Data analysis

The overall prevalence of PIP and the prevalence per individual STOPP criteria in 2007 were calculated as a proportion of all eligible persons ≥70 years. The association between any (*vs.* no) PIP and polypharmacy (categorized as 0 *vs.* 1, 2, ... 10+ repeat drug classes), age and gender was assessed using logistic regression presenting adjusted odds ratios (OR) and 95% confidence intervals. Finally, the maximum NIC and total expenditure for all potentially inappropriate medications in 2007 were calculated. Data analysis was performed using SAS statistical software package version 9.1 (SAS Institute Inc. Cary, NC, USA). Statistical significance at $P < 0.05$ was assumed.

Results

Population descriptive statistics

In 2007, a total of 338 801 people ≥70 years in Ireland were identified from the HSE-PCRS pharmacy database of which 194 460 (57%) were female and 210 515 (62%) were aged ≥75 years.

Overall prevalence of PIP in 2007

The overall prevalence of PIP in 2007 considering all thirty STOPP criteria was 36% (121 454). A quarter of the population, 83 959 individuals, were prescribed one potentially inappropriate medication, 27 392 (8%) were prescribed two and 10 103 (3%) were prescribed three or more.

Prevalence of PIP according to individual STOPP criteria in 2007

Table 1 presents the prevalence of each of the individual STOPP criteria by physiological system. PPIs at maximum therapeutic dosage for >8 weeks was the most frequently prescribed potentially inappropriate drug (56 560, 17%). In this group, 42 151 (75%) continued on PPI therapy for 6 consecutive months with 23 263 (41%) on PPI therapy for a 1 year continuous period. Of those on PPI therapy for a 1 year continuous period, the majority 22 067 (95%) of individuals were prescribed maximum therapeutic dosage (Figure 1).

The second most frequently prescribed potentially inappropriate drugs were NSAIDs for >3 consecutive months, followed by long-acting benzodiazepines and duplicate drugs on the same prescription claim. NSAIDs and opiates were the most frequently prescribed duplication drugs (Table 1). Other STOPP criteria had lower prevalence rates but some were noteworthy as a proportion of the population taking a particular drug for a particular condition, e.g. one-fifth of those with COPD were prescribed β-adrenoceptor blockers.

Factors associated with overall PIP

There was a strong association between PIP and polypharmacy. The likelihood of PIP increased with a significant

Table 1

Prevalence of potentially inappropriate prescribing by individual STOPP criteria in 2007

Criteria description	*n*	%	Proportionate prescribing per indication (%)*
Cardiovascular system			
Digoxin >125 μg day^{-1} (increased risk of toxicity)	1 211	0.36	4.97
Thiazide diuretic with gout (exacerbate gout)	1 216	0.36	10.34
β-adrenoceptor blocker with COPD† (risk of increased bronchospasm)	7 924	2.34	21.20
β-adrenoceptor blocker with verapamil (risk of symptomatic heart block)	800	0.24	–
Aspirin and warfarin without histamine H_2-receptor antagonist (except cimetidine) or PPI† (high risk of gastrointestinal bleeding)	3 693	1.09	2.69
Dipyridamole as monotherapy for cardiovascular secondary prevention (no evidence of efficacy)	219	0.06	–
Aspirin >150 mg day^{-1} (increased bleeding risk)	5 712	1.69	3.58
Central nervous system and psychotropic drugs			
TCA† with dementia (worsening cognitive impairment)	609	0.18	4.34
TCA and glaucoma (exacerbate glaucoma)	465	0.14	4.44
TCA and opiate or calcium channel blockers (risk of severe constipation)	6 944	2.05	–
Long-term (i.e. >1 month), long-acting benzodiazepines (risk of prolonged sedation, confusion, impaired balance, falls)	17 676	5.22	40.37
Long-term (i.e. >1 month) neuroleptics (risk of confusion, hypotension, extrapyramidal side-effects, falls)	5 688	1.67	13.96
Long-term (i.e. >1 month) neuroleptics with parkinsonism (worsen extrapyramidal symptoms)	1 298	0.38	13.87
Anticholinergics to treat extrapyramidal side effects of neuroleptic medications (risk of anticholinergic toxicity)	1 527	0.45	71.43
Phenothiazines with epilepsy (may lower seizure threshold)	813	0.24	7.69
Prolonged use (i.e. >1 week) of first-generation antihistamines (risk of sedation and anti-cholinergic side-effects)	3 248	0.96	85.71
Gastrointestinal system			
Prochlorperazine or metoclopramide with parkinsonism (risk of exacerbating parkinsonism)	726	0.21	7.66
PPI for peptic ulcer disease at maximum therapeutic dosage for >8 weeks‡ (dose reduction or earlier discontinuation indicated)	56 560	16.69	38.89
Respiratory system			
Theophylline with COPD (risk of adverse effects due to narrow therapeutic index)	4 008	1.18	10.69
Nebulized ipratropium with glaucoma (exacerbate glaucoma)	50	0.01	0.32
Musculoskeletal system			
Long-term use of NSAID† (i.e. >3 months) for pain relief (simple analgesics preferable)	29 691	8.76	23.19
Warfarin and NSAID (risk of gastrointestinal bleeding)	2 535	0.75	–
Urogenital system			
Antimuscarinic drugs with dementia (risk of increased confusion, agitation)	1 568	0.46	7.21
Antimuscarinic drugs with chronic glaucoma (>3 months) (risk of acute exacerbation of glaucoma)	0	<0.01	–
Endocrine system			
Glibenclamide or chlorpropamide with type 2 diabetes mellitus (risk of prolonged hypoglycemia)	976	0.29	3.27
Duplicate drug class prescription (optimization of monotherapy within a single drug class)			
Two concurrent opiates	4 185	1.24	6.18
Two concurrent NSAIDs	7 532	2.22	5.88
Two concurrent SSRIs†	79	0.02	0.19
Two concurrent antidepressants	834	0.25	4.56
Two concurrent loop diuretics	332	0.10	0.58
Two concurrent ACE inhibitors†	3 643	1.08	4.10
All duplicates	16 201§	4.78	–

*Proportionate prescribing per indication, e.g. prevalence of STOPP criteria as a proportion of the overall disease or drug prevalence, e.g. digoxin >125 μg as a proportion of overall digoxin prevalence, β-adrenoceptor-blocker with COPD as a proportion of COPD prevalence. †COPD, chronic obstructive pulmonary disease; PPI, proton pump inhibitor; TCA, tricyclic antidepressant; NSAID, non-steroidal anti-inflammatory drug; SSRI, selective serotonin re-uptake inhibitor; ACE inhibitors, angiotensin converting enzyme inhibitors. ‡Proton pump inhibitor (PPI) at maximum therapeutic dose = 40 mg daily omeprazole, pantoprazole and esomeprazole. 30 mg daily lansoprazole and 20 mg daily rabeprazole. §Adjusted for those receiving more than one duplicate prescription.

linear and quadratic trend ($P < 0.0001$) with the number of different drug classes (Figure 2). PIP was more likely in females *vs.* males after adjusting for age [odds ratio 1.10, 95% confidence intervals (CI) 1.08, 1.12] and those aged ≥75 years compared with 70–74 years after adjusting for gender (OR 1.28, 95% CI 1.26, 1.30). The strength of the association between PIP and gender and age was reduced after additionally adjusting for polypharmacy (gender (F *vs.* M), OR 0.91, 95% CI 0.90, 0.93); (age (≥75 years *vs.* 70–74 years) OR 0.95, 95% CI 0.93, 0.96). No significant collinearity was found between age, gender and polypharmacy.

Factors associated with individual STOPP criteria

There was an association between gender and age and the individual STOPP criteria after adjusting for polypharmacy

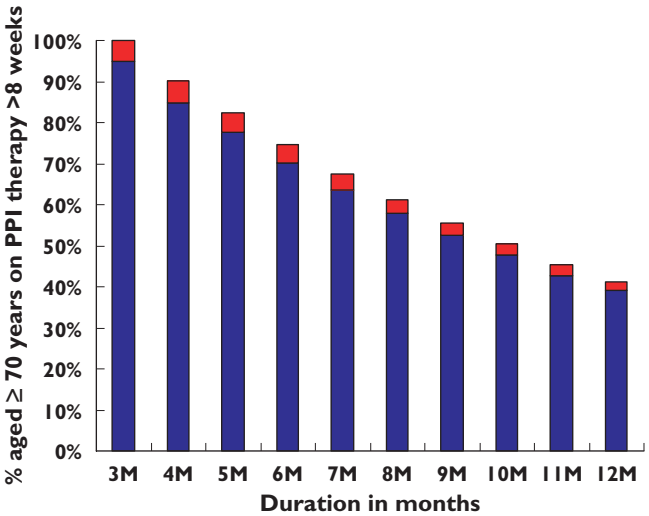

Figure 1

Duration and dosage of PPI therapy for a 1 year continuous period in patients aged ≥70 years on PPI therapy for >8 weeks at maximum therapeutic dosage. 1 year period- January 2007 to January 2008, February 2007 to February 2008. Dosage is the dose at the end of each month. Maximum therapeutic dose = 40 mg daily omeprazole, pantoprazole and esomeprazole, 30 mg daily lansoprazole and 20 mg daily rabeprazole. Maintenance therapeutic dose = 10–20 mg daily omeprazole, 20 mg daily pantoprazole and esomeprazole, 15 mg daily lansoprazole and 10 mg daily rabeprazole. Maintenance dosage (■); Maximum dosage (■)

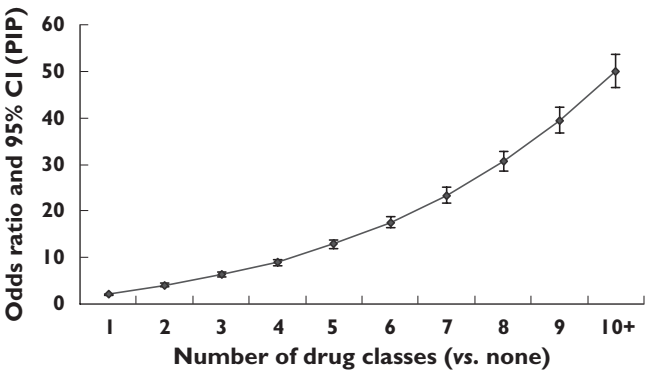

Figure 2

The association between polypharmacy and PIP in 2007. Repeat prescriptions (minimum of three per year). Odds ratio = odds ratio of any potentially inappropriate drug adjusted for gender and age (reference = 0)

(Table 2). Psychotropic drugs such as tricyclic antidepressants (TCAs) and long-acting benzodiazepines, NSAIDs for >3 months duration and duplicate drug classes on the same prescription claim were more likely to be prescribed in females compared with males. Potentially inappropriate cardiovascular drugs, e.g. aspirin >150 mg day^{-1} and respiratory drugs were more likely to be prescribed in males compared with females. The prescribing of digoxin >125 µg, TCAs and antimuscarinic drugs with dementia and duplicate loop diuretics was twice as likely in the older age group (≥75 years) compared with the younger age group (70–74 years).

Cost of potentially inappropriate prescribing in 2007

The total NIC of PIP in 2007 was estimated to be €38 664 640, on average €318 per claimant per year. The total expenditure was estimated to be €45 631 319 which was 9% of the overall expenditure on pharmaceuticals in those aged ≥70 years in Ireland in 2007 [24]. Table 3 presents a breakdown of the NIC and total expenditure on potentially inappropriate medication in 2007 for the highest cost items.

Discussion

Principal findings

This national population based study found that 36% of those ≥70 years received at least one potentially inappropriate medication in 2007 according to the STOPP criteria. The most prevalent PIP drugs were PPIs at maximum therapeutic dosage for >8 weeks, followed by NSAIDs for >3 months and long-acting benzodiazepines for >1 month. The majority of older people prescribed PPIs in 2007 were on PPI therapy for 6 or more consecutive months at maximum therapeutic dosage. Drug duplication on the same prescription claim was also highly prevalent with NSAIDs and opiates as the most frequently prescribed duplication drugs.

Polypharmacy was shown to be strongly associated with PIP. The strength of the overall association between PIP and gender and age was not significant after adjusting for polypharmacy. PIP had a significant impact on the national prescribing budget in 2007 (9% of overall expenditure for those ≥70 years).

Context of PIP in Europe

This study is the first population study to apply the explicit STOPP screening tool for appropriate review of medications in older populations. There have been few studies of PIP in Europe due to the lack of European specific criteria and differences in national drug formularies [13]. Previous population studies in the UK and the Netherlands applied the US Beers criteria and reported lower PIP prevalence rates of 28% and 20%, respectively, with long-acting benzodiazepines and amitriptyline as the most frequently prescribed potentially inappropriate drugs [12, 16].

PPI prescribing for a greater duration and dosage than recommended in the National Institute for Health and Clinical Excellence (NICE) guidelines is not unique to Ireland [25]; 25% to 70% of patients on PPIs have been reported as having no appropriate indication worldwide [26]. PPIs have a high level of efficacy and short-term use is recommended for treating a large range of acid-peptic conditions [25, 26]. Long-term use (≥1 year) in older

Table 2

The association between gender and age and PIP by individual STOPP criteria in 2007

Criteria Description	OR gender* F *vs.* M	95% CI Gender	OR age* ≥75 *vs.* 70–74 years	95% CI Age
Cardiovascular system				
Digoxin >125 μg day^{-1}	0.79	0.70, 0.88	2.20	1.90, 2.55
Thiazide diuretic with gout	0.32	0.28, 0.36	0.83	0.74, 0.93
β-adrenoceptor blocker with COPD†	0.53	0.51, 0.56	0.84	0.80, 0.89
β-adrenoceptor blocker with verapamil	1.07	0.93, 1.24	0.74	0.64, 0.85
Aspirin and warfarin without histamine H_2-receptor antagonist (except cimetidine) or PPI†	0.40	0.37, 0.43	1.02	0.95, 1.09
Dipyridamole as monotherapy for cardiovascular secondary prevention	0.73	0.56, 0.95	2.44	1.73, 3.42
Aspirin >150 mg day^{-1}	0.59	0.56, 0.62	1.05	0.99, 1.11
Central nervous system and psychotropic drugs				
TCA† with dementia	1.68	1.40, 2.01	1.98	1.62, 2.42
TCA and glaucoma	1.18	0.97, 1.43	1.39	1.12, 1.71
TCA and opiate or calcium channel blockers	1.59	1.50, 1.67	0.74	0.70, 0.78
Long-term (i.e. >1 month), long-acting benzodiazepines	1.72	1.65, 1.78	0.89	0.87, 0.92
Long-term (i.e. >1 month) neuroleptics	1.04	0.99, 1.10	0.86	0.81, 0.91
Long-term (i.e. >1 month) neuroleptics with parkinsonism	0.80	0.72, 0.90	0.62	0.55, 0.69
Anticholinergics to treat extrapyramidal side effects of neuroleptic medications	0.96	0.87, 1.06	0.60	0.54, 0.66
Phenothiazines with epilepsy	1.10	0.95, 1.27	0.92	0.79, 1.06
Prolonged use (i.e. >1 week) of first-generation antihistamines	0.98	0.91, 1.05	0.84	0.78, 0.90
Gastrointestinal system				
Prochlorperazine or metoclopramide with parkinsonism	1.16	0.99, 1.35	1.58	1.32, 1.89
PPIs for peptic ulcer disease at maximum therapeutic dosage for >8 weeks‡	0.80	0.78, 0.81	1.05	1.02, 1.07
Respiratory system				
Theophylline with COPD	0.63	0.59, 0.67	1.10	1.03, 1.18
Nebulized ipratropium with glaucoma	0.41	0.23, 0.71	7.30	2.27, 23.51
Musculoskeletal system				
Long-term use of NSAIDs† (i.e. >3 months)	1.25	1.22, 1.28	0.78	0.76, 0.81
Warfarin and NSAIDs	0.57	0.53, 0.62	1.02	0.94, 1.11
Urogenital system				
Antimuscarinic drugs with dementia	1.24	1.11, 1.38	3.19	2.74, 3.70
Endocrine system				
Glibenclamide or chlorpropamide with type 2 diabetes mellitus	0.68	0.54, 0.69	0.96	0.84, 1.10
Duplicate drug class prescription (optimization of monotherapy within a single drug class)				
Two concurrent opiates	1.15	1.07, 1.22	0.96	0.90, 1.03
Two concurrent NSAIDs	1.51	1.44, 1.59	0.62	0.59, 0.65
Two concurrent SSRIs†	2.24	1.31, 3.84	1.78	1.02, 3.10
Two concurrent antidepressants	1.32	1.14, 1.52	0.86	0.75, 1.00
Two concurrent loop diuretics	0.65	0.52, 0.81	2.27	1.70, 3.04
Two concurrent ACE inhibitors†	0.79	0.74, 0.85	0.73	0.68, 0.78
All duplicates	1.19	1.15, 1.23	0.74	0.71, 0.76

*OR Gender = odds ratio adjusted for age and polypharmacy. OR Age = odds ratio adjusted for gender and polypharmacy. Multicollinearity was tested between age, gender and polypharmacy using the collinearity diagnostics statistics (tolerance and variance inflation factor). †COPD, chronic obstructive pulmonary disease; PPI, proton pump inhibitor; TCA, tricyclic antidepressant; NSAID, non-steroidal anti-inflammatory drug; SSRI, selective serotonin re-uptake inhibitor; ACE inhibitors, angiotensin converting enzyme inhibitors. ‡Proton pump inhibitor (PPI) at maximum therapeutic dose = 40 mg daily omeprazole, pantoprazole and esomeprazole. 30 mg daily lansoprazole and 20 mg daily rabeprazole.

patients has been associated with accelerated osteoporosis and an increased risk of hip fracture and *Clostridium difficile* hospital infections [27, 28]. The extent to which older people remain on long-term PPI treatment has significant cost consequences (Table 3).

Long term NSAID use is associated with gastrointestinal adverse effects and hospitalization [29, 30]. Gastroprotective agents are co-prescribed to reduce the risk of adverse effects, if NSAID therapy cannot be stopped [31]. In this study 41% of older patients on PPI therapy of >8 weeks duration were co-prescribed NSAIDs in 2007. NSAID prescribing also had significant cost consequences (Table 3). Long-acting benzodiazepine prevalence rates were higher in Ireland (13%, 5% >1 month) than in population studies from the UK (4%) and the Netherlands (5%) despite the fact that long-acting benzodiazepines have been associated with an increased risk of falls, hip fractures, impaired cognition and dependence problems [12, 16, 32].

PPI therapy withdrawal in older patients requires careful monitoring for disease recurrence but dosage reduction or cessation of treatment is recommended [25, 31]. Long-term users have been shown to cease therapy with no adverse effects to dyspepsia symptom severity and quality of life [33]. Physical therapy and exercise for

Table 3

The highest NIC and total expenditure (>€500 000) for the individual STOPP criteria as a proportion of the overall NIC and total expenditure of PIP in 2007

Criteria description	NIC €	NIC %	Total expenditure €	Total expenditure %
PPI maximum therapeutic dosage for >8 weeks	22 352 240*	58	24 715 010*	54
Neuroleptics >1 month **Neuroleptics >1 month with parkinsonism** **Anticholingerics for neuroleptic side-effects**	5 612 192*†	15	6 079 905*†	13
Duplicates drugs	4 531 160	12	5 499 118	12
NSAIDS >3 months **Warfarin and NSAIDS**	3 969 629*†	11	5 050 640*†	11
TCA and opiate or calcium channel blocker	1 329 275†	3	1 864 433†	4.09
Antimuscarinic drugs with dementia	578 800	1	660 478	1
Long-term (i.e. >1 month) long-acting benzodiazepines	572 009*	1	1 352 209*	3

Supplemental Table S2 outlines costs for the each of the individual STOPP criteria. *Exclude the duration of prescribing that is deemed appropriate, e.g. 8 weeks PPIs. †Adjusted for claimants receiving the same medication per more than one criteria.

musculoskeletal complaints may be more appropriate and effective for some older patients than long-term NSAIDs use or simple or compound analgesics [34, 35]. Gastroprotective agents such as PPIs only reduce the risk of adverse effects but do not eliminate the risk. Withdrawal of long-term benzodiazepine use is limited by dependence problems but gradual discontinuation programmes and intervention strategies have been shown to be successful though labour intensive [31, 36, 37]. Indicators for appropriate initiation of benzodiazepine prescribing may provide a more realistic method to reduce potentially inappropriate use [38].

The strong association between polypharmacy and PIP was in accord with previous studies [15, 39]. The prescription of multiple medications in older adults is associated with an increased risk of unnecessary and non-clinically indicated drugs, drug interactions, adherence problems, increased drug costs and adverse drug events; increasing to 58% for five medications [39]. Contrary to this study, previous studies found that women have an increased risk of being prescribed a potentially inappropriate medication compared with men but similarly found no age effect after adjusting for the number of different medications [11, 15, 17]. Polypharmacy and PIP are also associated with the under-prescribing of indicated medicines but this study did not assess this aspect of medication management in older populations [23, 40, 41].

Costs of PIP

There has also been little research on the costs of PIP in relation to overall government pharmaceutical expenditure. STOPP and the newer explicit screening tools for appropriate medication review, consider cost control alongside improving the quality of prescribing [31]. The discontinuation of potentially inappropriate or marginally effective medications can result in significant savings for prescribing budgets; even for potentially inappropriate medications with relatively low prevalence rates, e.g. neuroleptics >1 month (Table 3). Unnecessary duplication of drugs in the same therapeutic class may have adverse effects and increases costs unnecessarily (Table 3); concurrent use of more than one NSAID has been shown to increase the risk of gastrointestinal toxicity [31]. Studies have shown diuretics, warfarin, NSAIDs, SSRIs, β-adrenoceptor blockers and ACE inhibitors to be the drugs most commonly associated with adverse drug events in older populations [29, 30]. Equally the addition of medications to treat an unrecognized adverse reaction – the 'prescribing cascade' e.g. anticholingerics for neuroleptic side-effects can also result in additional adverse effects and increases costs.

Strengths and limitations

Our study has a number of possible limitations and it is likely that estimates of PIP are conservative. The lack of detailed diagnosis information in the database limited the applicability of all of the STOPP criteria and the investigation of individual patient factors and differences in drug indication. The STOPP criteria were based on dispensed medications and there may be older people who have not yet been diagnosed with a condition, misdiagnosed or who are not receiving prescribed medication for their diagnosis. The pharmacy claims database is related to prescriptions dispensed and is used to reimburse pharmaceutical costs in Ireland; in general claimants' recorded drug use should reflect actual drug use but it is not known whether patients adhered to their medications. In addition, the database does not include over-the-counter (OTC) items, although this is not likely to be a significant factor as the scheme provides free medical treatment and patients must pay for OTC items.

Notwithstanding the limitations this study has provided Irish population based data on PIP in an older population where limited data have been available [42]. Few national population studies have been undertaken to date and they are important in identifying common PIP issues

that may require further investigation, followed by guidelines or incentives to encourage reduction [12, 15, 16]. The application of the STOPP criteria to national population dispensing data rather than prescribing data also provides an opportunity to provide feedback and comparative information on certain key criteria at practice or physician level.

Future research

This study measured an economic outcome, e.g. cost of potentially inappropriate drugs but it did not investigate the association between the STOPP criteria and health outcomes in older populations (e.g. morbidity, mortality). In order to have acceptance in everyday clinical practice explicit process measures of PIP need to be linked to health outcomes. To date there is limited and conflicting evidence [43, 44]. Further research is planned to investigate the association between STOPP and other explicit process measures of PIP and health outcomes, health service utilisation and the overall economic impact of PIP on the health system. Further comparative European population studies are also planned.

Policy implications

Polypharmacy does not imply inappropriate prescribing but it is consistently associated with the risk of PIP (Figure 2) and reducing the number of drugs used by older people through medication review may reduce the risk of PIP, adverse medication outcomes and improve adherence and reduce costs [15, 39]. PIP has been shown to add unnecessary costs to prescribing budgets without providing any additional therapeutic benefits. However while cost control is an important element of a medication review it should not surpass patient safety or access to appropriate medication. Generic prescribing and therapeutic substitution are methods of cost control that do not affect the quality of patient care and offer alternatives when potentially inappropriate medication withdrawal is complex or patients do not concur.

Reduction in PIP requires changes in prescribing behaviour but prescribing guidelines by themselves do not necessarily change behaviour. Computerized screening and clinical decision support tools to implement guidelines by assessing the appropriateness of the medication, the dosage, duration of treatment, drug–disease and drug–drug interactions while balancing the risks of underuse of potentially beneficial drugs are required [3]. While screening tools will never be substitutes for clinical assessment and judgment they can be used to improve prescribing practices and monitor medication use in older populations. Given that life expectancy is increasing worldwide and there will be an associated increase in multimorbidity, polypharmacy, health service utilisation and drug costs, the development and use of comprehensive, practical and computerized prescribing screening tools for appropriate, safe and effective monitoring of drug prescribing is crucial.

Competing interests

None declared.

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Supporting information

Additional supporting information may be found in the online version of this article:

Table S1 STOPP criteria applied to HSE-PCRS prescription claims data for all those aged ≥70 years in Ireland in 2007
Table S2 NIC and total expenditure for the individual STOPP criteria as a proportion of the overall NIC and total expenditure of PIP in 2007

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