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Community pharmacists' evaluation of potentially inappropriate prescribing in older community-dwelling patients with polypharmacy: observational research based on the GheOP³S tool

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ABSTRACT

Background In this study, we aimed to (i) determine the prevalence of potentially inappropriate prescribing (PIP) in community-dwelling older polypharmacy patients using the Ghent Older People's Prescriptions community-Pharmacy Screening (GheOP³S) tool, (ii) identify the items that account for the highest proportion of PIP and (iii) identify the patient variables that may influence the occurrence of PIP. Additionally, pharmacist–physician contacts emerging from PIP screening with the GheOP³S tool and feasibility of the GheOP³S tool in daily practice were evaluated.

Methods A prospective observational study was carried out between December 2013 and July 2014 in 204 community pharmacies in Belgium. Patients were eligible if they were (i) ≥70 years, (ii) community-dwelling, (iii) using ≥5 chronic drugs, (iv) a regular visitor of the pharmacy and (v) understanding Dutch or French. Community pharmacists used a structured interview to obtain demographic data and medication use and subsequently screened for PIP using the GheOP³S tool. A Poisson regression was used to investigate the association between different covariates and the number of PIP.

Results In 987 (97%) of 1016 included patients, 3721 PIP items were detected (median of 3 per patient; inter quartile range: 2–5). Most frequently involved with PIP are drugs for the central nervous system such as hypnosedatives, antipsychotics and antidepressants. Risk factors for a higher PIP prevalence appeared to be a higher number of drugs (30% extra PIPs per 5 extra drugs), female gender (20% extra PIPs), higher body mass index (BMI, 20% extra PIPs per 10-unit increase in BMI) and poorer functional status (30% extra PIPs with 6-point increase). The feasibility of the GheOP³S tool was acceptable although digitalization of the tool would improve implementation. Despite detecting at least one PIP in 987 patients, only 39 physicians were contacted by the community pharmacists to discuss the items.

Conclusion A high prevalence of PIP in community-dwelling older polypharmacy patients in Belgium was detected which urges for interventions to reduce PIP.

Keywords aged, community-dwelling, GheOP³S, inappropriate prescribing, primary care

Introduction

Potentially inappropriate prescribing (PIP) is defined as the prescribing of medication that significantly increases the risk of an adverse drug reaction (ADR), in particular when there is an equally or more effective alternative with lower risk available.[1,2] PIP encompasses three main categories: overuse, underuse and misuse.[3] As PIP is a major risk factor for

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ADRs, it can put substantial pressure on the safety of medication use.[4,5]

A recent systematic review[6] showed that PIP prevalence in community-dwelling European older adults is high (average estimated prevalence: 22.6%, confidence interval (CI): 19.5–26.7%). This shows that PIP is a wide-spread issue. Furthermore, a variety of factors seem to contribute to the prevalence of PIP in older community-dwelling adults, such as polypharmacy, older age, depression, moderate self-rated health quality, low activities of daily living-score and poor economic situation.[4–6] A periodic screening for PIP could be a strategy to diminish its burden.[7] In the literature, there is agreement that such a periodic screening should be applied to older patients with polypharmacy or other additional risk factors. PIP screening in primary care could reduce the risk for ADR and ADR-related hospitalization8 and research showed it is probably cost-neutral.[9,10]

Community pharmacists are ideally placed to perform periodic screening for PIP because of their medication-specific knowledge and the availability of an electronic dispensing record in the pharmacy that ideally includes also all dispensed over-the-counter (OTC) medication. Moreover, multiple studies showed that the community pharmacist can intervene and assist in significantly reducing the occurrence of a lot of specific PIPs. The EMPOWER study, for example, showed that direct-to-consumer education from the community pharmacy effectively reduced overuse of benzodiazepines.[11] Another study, performed in French community pharmacies, shows that providing the community pharmacist with the patients' renal functions can resolve several PIPs concerning incorrect dosing.[12]

However, general screening for PIP in the community pharmacy is more comprehensive and requires an evidence-based screening tool specifically suitable for this setting. The Ghent Older People's Prescriptions community-Pharmacy Screening (GheOP³S) tool[13] is an integrated, recently developed screening tool to detect PIP with high clinical relevance for primary care, taking into account the limited availability of clinical data in the community-pharmacy setting. This tool—consisting of 83 items—addresses PIP on different levels; overuse, underuse and misuse of medication. Additionally, a specific evaluation of the provided pharmaceutical care is included. This multilevel approach is a major advantage over other screening tools, such as the Beers or STOPP/START criteria.[14,15] For each item of the tool, an alternative therapeutic option is offered. Furthermore, pharmacists could perform a medication screening on a regular base or at every moment a change in pharmacotherapy is made.

This observational research was the first to use the GheOP³S tool in the community-pharmacy setting. We aimed (i) to determine the prevalence of PIP in community-dwelling older polypharmacy patients with the GheOP³S tool, (ii) to identify the items that account for the highest proportion of PIP and (iii) to identify the patient variables that may influence the occurrence of PIP. Additionally, (iv) pharmacist–physician contacts resulting from PIP screening with the GheOP³S tool and (v) feasibility of the GheOP³S tool in daily practice were evaluated.

Methods

Study design and setting

This manuscript describes a prospective observational study, carried out between December 2013 and July 2014 in all 204 community pharmacies counselling a pharmacist in training from the Ghent University or the University of Liège, during the academic year of 2013–14 (i.e. a final year pharmacy student, performing obligatory 6-month preregistration community-pharmacy training). Ethical approval was granted by the ethical committees of the Ghent University Hospital (for Flanders) and Centre Hospitalier Universitaire de Liège (for Wallonia). All participants provided written informed consent. The STROBE standardized reporting guidelines for cross-sectional studies were followed to ensure the uniform conduct and reporting of the research.[16]

Participants

All older patients filling a prescription at a participating pharmacy were consecutively approached and invited to participate in the study. They were eligible when meeting the following inclusion criteria: (i) aged 70 years of older, (ii) community-dwelling, (iii) using five of more chronic drugs (i.e. intake follows a fixed regimen) registered in the Belgian Commented Drugs Repertory,[17] (iv) being a regular visitor of the pharmacy and (v) speaking and reading Dutch or French. Each pharmacy planned to recruit five patients. Recruiting patients who regularly visited the pharmacy warranted a patient–pharmacist relationship of respect and trust.

Data collection and outcome measures

Participating patients were interviewed by a pharmacist in training using a structured questionnaire (available upon request). The questionnaire assessed information about demographics, self-rated health,[18] functional status, cognitive impairment (using the Mini-Cog[19]), fall incidents, hospitalizations and emergency visits in the previous year, and current medication use (including detailed information about dose, frequency, time of administration, starting date, etc.).

For current medication use, the electronic dispensing records at the participating pharmacy were consulted as a starting point. In addition, patients were specifically asked about the use of OTC and herbal drugs. The structured interview took place at the pharmacy or at the patient's home (according to patient's preference), and was fully documented on paper.

Using the data from the structured interview and the electronic dispensing record, the pharmacist in training subsequently screened each patient's medication for PIP by applying the GheOP³S tool.[13] The choice to use this screening tool was deliberate. First, the GheOP³S tool makes it possible to screen for PIP in settings where clinical data are not available. Second, the GheOP³S tool is adapted to the European market and addresses all types of PIP. Third, the GheOP³S tool offers the pharmacists a backbone to get started with the process of a medication review. An elaborate document describing rationale, alternative treatment plans and scientific background information of all included items empowers the pharmacists to initiate pharmacist–physician contacts to discuss the considered clinically relevant PIP items.

The GheOP³S tool is subdivided into five different parts: Part 1, potentially inappropriate drugs, independent of diagnosis; Part 2, potentially inappropriate drugs, dependent on diagnosis; Part 3, potential prescribing omissions (PPOs); Part 4, drug–drug interactions (DDIs) of specific relevance and Part 5, general care-related items to be addressed in the community pharmacy. The items in the latter part are not strictly considered to be PIP, according to the definition in the Introduction, but they are considered relevant to be checked for in community-pharmacy practice as they evaluate the appropriateness of the provided pharmaceutical care. With regard to the diagnoses in Part 2, drug proxies were used. Only diagnoses that could unambiguously be derived from the patient's medication (e.g. diabetes from insulin, gout from allopurinol, etc.) were taken into account. In this study, all 83 criteria of the GheOP³S tool were used.

An extensive training session on the use of the GheOP³S tool for PIP screening (with example cases as well as one real-life trial case) was completed by each pharmacist in training before the start of the study. In addition, all screenings included in the study were double-checked by a member of the research team (E.T.). As pharmacist–physician contacts considering PIP are not yet common practice in Belgium, the decision to initiate such a contact from the pharmacy was left to the supervising pharmacist, based on his/her personal judgement of the detected PIPs. All initiated physician contacts and their outcomes were documented. The acceptance of the proposed alternative treatment plans by the pharmacist was categorized as 'accepted', 'partially accepted' or 'not accepted'. Reasons for not accepting the treatment plan were also recorded.

Subsequently, all participating pharmacists evaluated the feasibility of the GheOP³S tool, using a slightly adapted version of the system usability scale (SUS) (Online Supplement 1).[20,21] The SUS is a validated tool for assessing feasibility, consisting of 10 items, each to be scored on a five-point scale. It provides an easy-to-understand overall score from 0 (lowest feasibility) to 100 (highest feasibility). Although no explicit cut-off for feasibility is determined, it is generally accepted that SUS scores >50 are sufficient to consider the tool feasible in current practice.[21] Research by Lewis *et al.* showed that SUS can be divided into two separate factors, specifically representing the usability (8 items) and learnability (2 items) of the evaluated tool.[20]

The participating pharmacists transferred all obtained anonymized patient data and results of the written document through an electronic platform to the Ghent University study centre. Data input was double-checked using the written document by the principal investigator (E.T.) before processing. During this process, each medicine was assigned a seven-digit code in accordance with the Anatomical Therapeutic Chemical Classification System formulated by the World Health Organization Collaborating Centre for Drug Statistics Methodology.[22]

Statistical analysis

Descriptive statistics are provided as counts with percentages, means with standard deviations or medians with interquartile ranges as appropriate. Prevalence of PIP is represented as the proportion of patients with at least one PIP and the median number of PIPs per patient.

Poisson regression was used to investigate the association between different covariates and the number of PIP. Patient covariates considered as predictors in the model were number of drugs, age, gender, body mass index (BMI), smoking status, education, self-rated health status, functional status, living situation, cognitive impairment, emergency department visits, hospitalizations, recent falls and the presence of ADRs. Continuous covariates, such as 'number of drugs', 'age' and 'BMI' were centred ~5, 70 years and 25 kg/m², respectively. After covariate selection, based on 'backward elimination' at the 5% level of significance, the linearity assumption for the continuous covariates in the final model was assessed. Education (Scale: 1–4 with 4 as highest education), functional status (Scale: 0–6 with 6 as worst functional status), self-rated health status (Scale: 1–5 with 5 as best

health rate) and cognitive impairment (Scale: 0–5 with 5 as no cognitive impairment) were set as ordinal variables. Furthermore, a likelihood-ratio-test was performed to test whether overdispersion should be accounted for. Finally, once the final model was developed, likelihood-ratio-testing was performed at the 5% level of significance to test whether two-way interaction terms should be added to the model. Fitting of the models to the observed data and *post hoc* evaluations of the model's goodness-of-fit was performed in R® (R foundation for statistical computing, Vienna, Austria).

Results

Participants

In total, 2228 patients were screened for eligibility. Of note, 726 patients did not meet the inclusion criteria (547 took <5 drugs, 89 were not regular visitors of the participating pharmacy, 45 did not sufficiently understand Dutch or French and 45 were not community-dwelling). Additionally, 486 refused to participate (221 did not have time to participate, 194 were not interested and 71 stated other reasons). Eventually, 1016 older community-dwelling polypharmacy patients were included in the study. Mean age (±SD) was 78.8 (±5.5) years and 58% of the population was female. The total number of medicines taken was 10 568, with a range of 5–29 per patient and a median of 10 per patient (interquartile range 8–12) (Table 1).

Table 1 Basic characteristics of the study population (n = 1016)

Age, mean (SD)	78.8	(5.5)
Age ≥ 85 years, *n* (%)	162	(16%)
Female gender, *n* (%)	592	(58%)
BMI, mean (SD)	26.6	(4.3)
No. of drugs, median (IQR)	10	(8–12)
No. of drugs, mean (SD)	10.4	(3.4)
Current smoker, *n* (%)	57	(6%)
Education[a]		
Primary school	257	(25%)
Secondary school	580	(57%)
Higher education	176	(17%)
Living alone, *n* (%)	434	(43%)
Functional status; need help with, *n* (%)		
Bathing/showering	110	(11%)
Dressing	54	(5%)
Toileting	19	(2%)
Community mobility	117	(12%)
Eating	39	(4%)
Cleaning	382	(38%)
Self-rated health status, *n* (%)		
Excellent	19	(2%)
Very good	104	(10%)
Good	497	(49%)
Fair/moderate	343	(34%)
Poor	53	(5%)
Positive for cognitive impairment (according to the Mini-Cog), *n* (%)	335	(33%)
Emergency department visits		
Patients with emergency department visit in previous year, *n* (%)	229	(23%)
Number of emergency department visits per patient year, median (IQR)	1	(1–2)
Hospitalizations		
Patients with hospitalization in previous year, *n* (%)	394	(39%)
Number of hospitalizations per patient year, median (IQR)	1	(1–2)
Fall incidents		
Patients with fall incident in previous year, *n* (%)	333	(33%)
Number of fall incidents per patient year, median (IQR)	1	(1–3)

[a]Three patients did not answer this question.

Potentially inappropriate prescribing

Considering Parts 1–4 of the GheOP³S tool, a total of 3721 PIPs were detected in 987 (97%) of participants (median: 3; inter quartile range (IQR): 2–5). However, with regard to the full GheOP³S tool, thus also including list five 'General care-related items to be addressed in the community pharmacy', an additional 3186 items considering general care-related items were detected. This led to a total of 6907 items in 1008 (99%) participants (median: 7; IQR: 5–8) (Fig. 1).

The five most prevalent items of each part of the GheOP³S tool are reported in Table 2. The items of Parts 2 and 3 are displayed in two ways; relative to the total population and relative to the overall drug or disease prevalence. For example, of the 130 patients taking narcotic analgesics, 99 (76%) did not receive an appropriate preventative bowel regimen; however, relative to the total population (n = 1016), this considers only 10%. The full list of the prevalence of all GheOP³S criteria is reported as online supplement (Online Supplement 2).

Factors associated with PIP

The estimated parameters from the final Poisson regression model are shown in Table 3. The number of drugs, gender, BMI and functional status were predictive for the observed number of PIPs. From the estimated parameters, we can calculate that a baseline patient (female patient with a functional status of 0, a BMI of 25, taking five drugs) has an

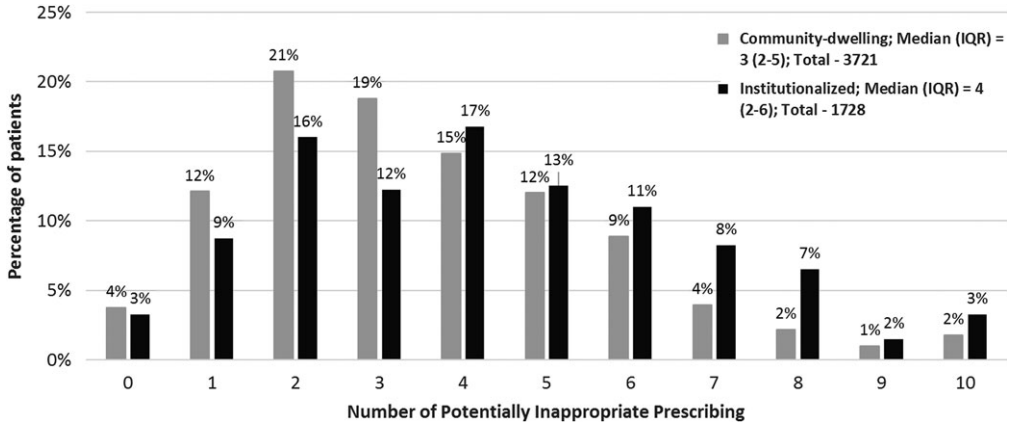

Fig. 1 Distribution of the number of GheOP³S criteria detected per patient (n = 1016; Part 1, potentially inappropriate drugs, independent of diagnosis; Part 2, potentially inappropriate drugs, dependent on diagnosis; Part 3, PPOs; Part 4, DDIs of specific relevance and Part 5, general care-related items to be addressed in the community pharmacy).

estimated average number of PIPs of 2.7 [= ^{e}log (intercept)]. Compared to this 'baseline' patient, a very poor functional status (6 compared to 0) is associated with an average of 30% extra PIPs. Furthermore, male gender and BMI are associated with a decrease of 23% and an increase of 20% (BMI 35 versus 25) in the estimated number of PIPs, respectively. Finally, the number of PIPs increases with the number of drugs taken. For instance, patients taking an additional five drugs have a 30% increase in expected PIPs as compared to otherwise similar patients.

Pharmacist–physician contacts

In total, 22 supervising pharmacists decided to initiate contact with at least one prescribing physician to discuss the detected PIPs. In total, 39 physicians were contacted. Thirteen refused to participate (reasons for refusal: no time (n = 12), not interested (n = 1) and one could not be reached). The remaining 25 physicians agreed to participate and discussed a total of 77 detected PIP items with the pharmacists. For 28 of the 77 items (36%), the alternative treatment plan proposed by the pharmacist was accepted. For two items, the alternative treatment plan was partially accepted. For 47 items, the physician did not accept the proposed treatment plan of the community pharmacists (Table 4).

Usability and feasibility

The mean SUS score was 61.2 (SD: 12.2), with a learnability score of 63.4 (SD: 17.5) and a usability score of 60.7 (SD: 12.9). Reviewing the comments of the users, the most frequent remark was the lack of digitalization or integration of the GheOP³S tool in the software which renders the tool too time-consuming. Mean duration of an evaluation using the GheOP³S tool including the estimation of the clinical relevance of the detected items was 38 min (SD: 27 min).

Discussion

Main findings of the study

In this observational study, we found that in 99% of included patients, at least one GheOP³S-item was detected. Specifically, focusing on PIPs (i.e. Parts 1–4 of the GheOP³S tool), a median of 3 (IQR: 2–5) PIPs per patient was observed. When the general care-related items of Part 5 of the GheOP³S tool were also included, a median of 7 items (IQR: 5–8) per patient was detected. Risk factors most frequently associated with higher number of PIPs were higher number of drugs, female gender, higher BMI and poorer functional status.

What is already known on this topic

Similar studies, also conducted in community pharmacies, are scarce. A study in France using the Laroche list[23] observed that 37.1% of the 393 included patients had at least one PIP,[24] which is markedly lower than the observations in this study. A possible explanation might be that the French Laroche list does not include DDIs, drug-disease interactions (DDisIs) or PPOs.[23] Additionally, in the French study, all older adults were included, regardless of polypharmacy, where in this study, only older adults taking five or more chronic drugs were included.

Studies conducted in other primary care settings but using similar inclusion criteria (older age and five or more chronic drugs), presented higher prevalence numbers for PIP.[25–27] A Spanish study using the START/STOPP criteria,[26] a Danish study using the MAI criteria[27] and an Austrian study

Table 2 The five most prevalent criteria of each part of the GheOP³S tool, $n = 1016$

GheOP³S-item	N, %[a] *(relative to total population)*	N, %[a] *(relative to overall drug or disease prevalence)*
Part 1: potentially inappropriate drugs, independent of diagnosis	*791 (78%)*	
1 Any intermediate acting benzodiazepine or Z-product at full dose or any dose ≥30 subsequent days OR any short- or long-acting benzodiazepine	510 (50%)	
Any intermediate acting benzodiazepine or Z-product at full dose or any dose ≥30 subsequent days	448 (44%)	
Any short- or long-acting benzodiazepine	93 (9%)	
Any intermediate acting benzodiazepine or Z-product at full dose or any dose ≥30 subsequent days and any short- or long-acting benzodiazepine	31 (3%)	
2 Any antidepressant ≥1 year	216 (21%)	
3 Any oral NSAID	146 (14%)	
4 Any PPI at full dose ≥8 weeks	145 (14%)	
5 Any antipsychotic drug ≥1 month	71 (7%)	
Part 2: potentially inappropriate drugs, dependent on diagnosis	*276 (27%)*	
1 Thiazide and loop diuretics with gout	88 (9%)	88/151 (58%)
2 Anticholinergics with constipation	84 (8%)	84/147 (57%)
3 Calcium channel blockers with constipation	43 (4%)	43/144 (30%)
4 Oral corticosteroids >1 week with hypertension	43 (4%)	43/810 (5%)
5 Anticholinergics with benign prostate hyperplasia	40 (4%)	40/93 (43%)
Part 3: PPOs	*727 (72%)*	
1 The patient has an elevated risk for osteoporosis (determined via FRAX tool) and is not prescribed calcium/Vitamin D supplementation	545 (54%)	545/710 (77%)
2 The patient is not reminded and proposed to undergo yearly influenza vaccination	306 (30%)	
3 The patient is taking narcotic analgesics and is not prescribed appropriate preventative bowel regimen (preferably macrogol or lactulose)	99 (10%)	99/130 (76%)
4 The patient is taking oral corticosteroids for ≥1 month and is not prescribed calcium and vitamin D supplementation	39 (4%)	39/54 (72%)
5 The patient is taking an equivalent of 7.5 mg of oral prednisone or more for ≥3 months and is not prescribed calcium/Vitamin D supplementation and bisphosphonates	23 (2%)	23/24 (96%)
Part 4: DDIs of specific relevance	*523 (51%)*	
1 Oral antidiabetics/insulin + beta blocker	226 (22%)	
Oral antidiabetics/insulin + non-selective beta blocker	44 (4%)	
Oral antidiabetics/insulin + cardioselective beta blocker	187 (18%)	
2 Any combination of anticholinergic drug	135 (13%)	
3 RAAS inhibitor + potassium sparing diuretic/potassium supplements/potassium containing drugs	81 (8%)	
4 RAAS inhibitor + oral NSAID	74 (7%)	
5 Oral NSAID + antiplatelet drugs	71 (7%)	
Part 5: general care-related items to be addressed in the community pharmacy	*872 (86%)*	
1 Adherence for all new medication was not checked or discussed at first refill during the past year	701 (69%)	
Adherence for all chronic medication was not checked or discussed during the past year (refill rate)	681 (67%)	
2 Contra-indications that can unambiguously be derived from patient's medication were not added to the electronic patient record	626 (62%)	
3 The patient was not asked which aspects of pharmaceutical care could be improved for him/her	463 (46%)	
4 Polypharmacy patients (chronically taking ≥5 drugs) were not questioned about whether a clear medication scheme was available to him/her	441 (43%)	
5 Dispensation of OTC medication (NSAID, ASA, …) was not added in the electronic patient record	253 (25%)	

ASA, acetyl salicylic acid; NSAID, nonsteroidal anti-inflammatory drugs; PPI, proton pump inhibitor.

[a]Prevalence is expressed as the percentage of patients to whom this item applies, whether relative to the total population or whether relative to the overall disease/drug prevalence.

Table 3 Estimated parameters of the Poisson regression model (outcome: number of PIPs, considering lists 1–4 of the GheOP³S tool) with calculation example

Risk factor	*Estimate*	*95% CI*
Intercept	1.001***	0.932–1.071
No. of drugs (continuous, centred 5)	0.057***	0.049–0.066
Gender (1 = male, 0 (female) as reference)	–0.266***	–0.958 to 0.197
BMI (continuous, centred 25)	0.017***	0.009–0.024
Functional status (Scale 0–6, 0 as reference)	0.043**	0.016–0.070

No., number. ***$P < 0.001$, **$P < 0.01$.

Calculation example: for a man with six chronic drugs, a BMI of 30 and a functional status of 1; the estimated number of PIPs can be determined through the following formula,

Ln (estimated number of PIP) = 1.001 + 0.057 × (6–5) – 0.266 × 1 + 0.017 × (30–25) + 0.043 × (1–0).

Estimated number of PIP = $e^{0.92}$ = 2.5.

using the PRISCUS list[25] detected at least one PIP in, respectively, 76.4%, 94.3% and 37.3% of patients. The low prevalence of the Austrian study should, however, be nuanced with the fact that 93.5% of patients took at least one non-evidence-based medication, that 56.2% had at least one dosing error and that 59.2% had at least one clinically significant DDI.[25]

What this study adds

In the current study, the prevalence of all types of PIP (i.e. overuse, misuse and underuse) was remarkably high. The fact that almost all patients had at least one PIP could raise questions about whether the tool needs to be more discriminatory. During the development of the GheOP³S tool, however, the experts unanimously agreed that it was clinically relevant to check for all of the items included in the GheOP³S tool in ambulatory older patients. Whether the detected 'potential' problems are clinically relevant for the specific individual patient, still needs to be assessed during a pharmacist–physician and follow-up patient consultation. 'Actual' inappropriate prescribing will, therefore, probably be somewhat lower. Nevertheless, these results show that there is a large potential for improvement in the appropriateness of prescribing and provided pharmaceutical care for ambulatory older patients with polypharmacy.

The specific criteria with the highest prevalence are the overuse of benzodiazepines and the underuse of preventive anti-osteoporotic medication, respectively, in 50% and 54% of included patients. A review of studies using STOPP/START criteria also showed that both of these items are

Table 4 Reasons for the family physician not to accept the proposed alternative treatment plan (n = 47)

The family physician did not provide a rationale for not accepting the alternative treatment plan	13
The alternative treatment plan was not feasible due to clinical reasons (e.g. intolerance for alternative)	12
The alternative treatment plan had already been implemented before with insufficient result or relapse	7
The alternative treatment plan was not accepted by the patient	6
Adequate monitoring had already been provided (e.g. frequent measurement of kidney function)	3
Physician is unwilling to change a therapy initiated by a colleague (e.g. specialist or former family physician)	2
PIP was detected on the basis of incorrect data (e.g. flu vaccination was administered but incorrectly registered in pharmacy software)	4

frequently detected.[28] At first instance, it appears that DDisIs are not very prevalent (up to 9% of included patients). However, relative to the number of patients with a certain diagnosis, this is still significant (e.g. 43% of patients using drugs for benign prostate hyperplasia receive anticholinergic medication).

Furthermore, taking into account that only DDIs with high risk for hospitalization were included in the GheOP³S tool, the observed high frequency (i.e. in up to 22% of patients) implies serious potential health consequences and healthcare costs.

Risk factor assessment showed that a higher number of drugs, female gender, a higher BMI and a poorer functional status are associated with a higher prevalence of PIP. Recent systematic research on risk factors for PIP showed that polypharmacy and a poor functional status are indeed consistently positively associated with PIP.[6] BMI could be present due to its association with metabolic syndrome, however, the literature is not consistent considering this risk factor's association with PIP.[29,30] Analogously, with regard to the association between the female gender and a higher prevalence of PIP, no consistency exists in the literature. However, this might be explained by differences in prescribing attitude towards the genders and by differences between genders in educational and socio-economic characteristics.[31]

The evaluation of the feasibility of the GheOP³S tool showed that the tool is functioning well in the current community-pharmacy setting. There is, nevertheless, still room for improvement. It would be interesting to re-evaluate the feasibility of the GheOP³S tool, once the tool is available in a digital format.

The low number of pharmacist-initiated contacts with physicians to discuss the detected PIPs must, however, be seen as a point of concern (only 39 initiated contacts for 987

patients with at least one PIP). These numbers are a real-world representation of the extensively present barriers for collaboration between pharmacists and physicians.[32–34] A Canadian research project identified barriers for pharmacist–physician collaboration which include lack of financial remuneration and insufficient time.[34] Furthermore, although community pharmacists considered patient counselling and advising physicians about drug interactions, dosages and drug information as core tasks, physicians did not perceive this as an important role for the community pharmacist.[34] Other recent research indicated, however, that prescribers prefer pharmacists' input as well as collaborations with other levels of care.[32] Additionally, potential facilitators have been established such as interprofessional experiences and facilitated communication.[33]

Strengths and limitations of this study

This was the first study using the newly developed GheOP³S tool, a community-pharmacy-specific list for settings in which limited clinical data are available. The study was protocol-based and reported following the STROBE statement.[16] Because of the prospective nature and the inclusion of patient interviews, accurate dosing information and complete medication use (i.e. OTC medication, herbal therapies, etc.) were available. Additionally, this was the first study evaluating PIP in community-dwelling older adults in Belgium. The study also evaluated usability and learnability of the GheOP³S tool which is a very important aspect for future implementation research.

On the other hand, this study has some limitations. The first is inherently linked to the use of the GheOP³S tool as screening method. As the GheOP³S tool is an explicit list, it does not take into account all patient factors in evaluating a patient's pharmacotherapy, e.g. the diagnoses and evolution of the patient's diseases, the patient's own preferences and earlier attempts to prohibit the use of potentially inappropriate drugs. The few pharmacist–physician contacts to discuss the detected items made it difficult to estimate which part of the items were of no or limited clinical relevance.

Second, some limitations are linked to the study design. As the study was merely observational, the possible clinical effects of reduced inappropriate prescribing could not be assessed. Moreover, we only evaluated the feasibility of the GheOP³S tool in the community-pharmacy practice, where it also would have been interesting to evaluate how the tool performs in a broader primary healthcare team, including the general practitioner, nurses, physiotherapists, etc. Third, ~20% of potential participants refused study participation. Potential bias caused by those who refused could not be assessed as the ethical committee prohibited data collection in study refusers. The impact on the roll-out of any future intervention based on the current results is therefore unclear.

Finally, generalizability of the results to other countries is difficult. Prescribing patterns vary along healthcare settings, which are very country-specific. However, throughout Belgium, we increased generalizability as much as possible by recruiting a patient sample using all 204 participating pharmacies as one recruitment centre.

Future perspectives

It is clear that a study should be conducted to evaluate the reduction of inappropriate prescribing in older ambulatory patients. Ideally, the impact (clinical and economic) of this improved pharmacotherapy should be measured. To reach this, we need to start with a study to evaluate the discrepancy between the 'potential' inappropriate prescribing detected with the GheOP³S tool and the 'actual' inappropriate prescribing detected after pharmacist–physician consultation. Moreover, such a study could easily integrate an evaluation of all aspects of pharmacist–physician consultations upon PIP detection with the GheOP³S tool (i.e. barriers, modalities, facilitators, etc.).

However, as PIP is a complex matter, it is unlikely that a single intervention will be sufficient to substantially improve the quality of prescribing and patient centred outcomes. Research showed that more integrated approaches are needed to significantly reduce the burden of PIP.[35,36] In that light, developing a complex intervention will be key. A proposition to such an intervention could be as follows. A digital screening of the medication history with the GheOP³S tool happens in the community pharmacy. This screening would yield a list of 'potential' inappropriate pharmacotherapy. Subsequently, in consultation with a multidisciplinary healthcare team, these 'potential' issues are discussed and a list of 'actual' inappropriate pharmacotherapy with recommendations for change is decided on. After consultation with the patient, a final treatment plan is set up. This patient consultation could be performed by any healthcare provider of the multidisciplinary healthcare team. Final decisions are communicated to all healthcare providers that are of the team through a secure electronic platform.

To realize a significant degree of implementation level, the proposed complex intervention would benefit from some optimization in different levels of care: the governmental level, the informatics level and the healthcare providers' level. First, governments could provide incentives to perform medication screening in the ambulatory setting by

financing pilot projects at first and by eventually remunerating this service in case of positive results. Additionally, a clear legal outline of the specific role of each healthcare provider in the medication screening process could empower each one of them to take up their role.[33,34,37] In order to enhance interprofessional collaborations, governments could support the organization of local interdisciplinary conferences.[33] Other strategies could include financial rewards or penalties when specific quality indicators are (not) met.

Second, informatics and software companies could be of major help in facilitating interprofessional communication by developing communication channels that are secure and easy to use.[33] Furthermore, automatizing the screening of medication lists or medication histories, including clinical support systems, could enhance the implementation of this intervention strategy as this would limit the time needed to perform the review. Both limited time and difficult communication are often mentioned as barriers to implement medication review.[32,33]

Finally, healthcare providers should be educated to perform medication review and about their potential role in the process. This includes recognizing each healthcare provider's role while none claiming a position of superiority. As healthcare providers may not always feel confident prescribing for older adults or evaluating their pharmacotherapy, specific courses on geriatric pharmacotherapy should be organized.[32]

With regard to this proposed complex intervention, our study is of help and reveals some pitfalls to which we can further anticipate. To start with, the high prevalence of PIP confirms there is an urge for initiatives such as the proposed complex intervention. The evaluation of risk factors for PIP in the current study show that the intervention should be targeted towards older patients with polypharmacy and poor functional status. Considering the performance of medication screening in the community pharmacy, community pharmacists feel it is feasible using the GheOP³S tool, but could be easier when automatized. Finally, and most importantly, this observational study confirms that the current largest pitfall lies in the extreme low number of initiated pharmacist–physician consultations to discuss detected PIP items. All strategies to improve these collaborations should therefore be exploited. At the same time, we have to be aware of the fact that the current differences in organization, IT systems and inter-variability of healthcare providers will influence the results of the studies that will evaluate this complex intervention.

Conclusion

Screening with the GheOP³S tool revealed a high prevalence of PIP in community-dwelling older polypharmacy patients in Belgium. Drugs or drug groups most often associated with PIP are drugs for the central nervous system such as hypnosedatives, antipsychotics and antidepressants. Also, PPOs are highly present. A higher number of drugs, female gender, a higher BMI and a poorer functional status are risk factors for a higher PIP prevalence. The usability of the GheOP³S tool is acceptable although digitalization of the tool would improve its feasibility. Despite the high number of detected PIPs, however, only a small number of physicians were contacted by the community pharmacists.

Supplementary data

Supplementary data are available at the *Journal of Public Health* online.

References

1 Opondo D, Eslami S, Visscher S *et al.* Inappropriateness of medication prescriptions to elderly patients in the primary care setting: a systematic review. *PloS one* 2012;**7**(**8**):e43617.

2 Fick DM, Cooper JW, Wade WE *et al.* Updating the beers criteria for potentially inappropriate medication use in older adults: results of a US consensus panel of experts. *Arch Intern Medi* 2003;**163**(**22**): 2716–24.

3 Spinewine A, Schmader KE, Barber N *et al.* Appropriate prescribing in elderly people: how well can it be measured and optimised? *Lancet* 2007;**370**(**9582**):173–84.

4 Tache SV, Soennichsen A, Ashcroft DM. Prevalence of adverse drug events in ambulatory care: a systematic review. *Ann Pharmacother* 2011;**45**(**7–8**):977–89.

5 Al Hamid A, Ghaleb M, Aljadhey H *et al.* A systematic review of hospitalization resulting from medicine-related problems in adult patients. *Br J Clin Pharmacol* 2014;**78**(**2**):202–17.

6 Tommelein E, Mehuys E, Petrovic M *et al.* Potentially inappropriate prescribing in community-dwelling older people across Europe: a systematic literature review. *Eur J Clin Pharmacol* 2015;**71**(**12**): 1415–27.

7 Wilson JMG G J. Principles and practice of screening for disease. *J R Coll Gen Pract* 1968;**16**(**4**):318.

8 Leendertse AJ, de Koning GH, Goudswaard AN *et al.* Preventing hospital admissions by reviewing medication (PHARM) in primary care: an open controlled study in an elderly population. *J Clin Pharm Ther* 2013;**38**(**5**):379–87.

9 Donohue JM, Marcum ZA, Gellad WF *et al.* Medicare Part D and potentially inappropriate medication use in the elderly. *Am J Manag Care* 2012;**18**(**9**):e315–e22.

10 Zermansky AG, Silcock J. Is medication review by primary-care pharmacists for older people cost effective? A narrative review of the literature, focusing on costs and benefits. *PharmacoEconomics* 2009;**27**(**1**):11–24.

11 Tannenbaum C, Martin P, Tamblyn R *et al.* Reduction of inappropriate benzodiazepine prescriptions among older adults through

direct patient education the empower cluster randomized trial. *JAMA Int Med* 2014;**174**:6.

12 Pourrat X, Sipert AS, Gatault P *et al*. Community pharmacist intervention in patients with renal impairment. *Int J Clinic Pharm* 2015;**37**(**6**):1172–9.

13 Tommelein E, Petrovic M, Somers A *et al*. Older patients' prescriptions screening in the community pharmacy: development of the Ghent Older People's Prescriptions community Pharmacy Screening (GheOP(3)S) tool. *J Public Health (Oxf)* 2015:e158-70.

14 O'Mahony D, O'Sullivan D, Byrne S *et al*. STOPP/START criteria for potentially inappropriate prescribing in older people: version 2. *Age Ageing* 2015;**44**(**2**):213–8.

15 American Geriatrics Society 2015. Updated beers criteria for potentially inappropriate medication use in older adults. *J Am Geriatr Soc* 2015;**63**(**11**):2227–46.

16 von Elm E, Altman DG, Egger M *et al*. Strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. *BMJ* 2007;**335**(**7624**):806–8.

17 Belgian Center for Pharmacotherapeutic Information B. Commented Drug Repertory. Secondary Commented Drug Repertory 2016. http://www.bcfi.be/

18 DeSalvo KB, Bloser N, Reynolds K *et al*. Mortality prediction with a single general self-rated health question: a meta-analysis. *J Gen Intern Med* 2006;**21**(**3**):267–75.

19 Borson S, Scanlan J, Brush M *et al*. The mini-cog: a cognitive 'vital signs' measure for dementia screening in multi-lingual elderly. *Int J Geriatr Psychiatry* 2000;**15**(**11**):1021–7.

20 Lewis J, Sauro J. The factor structure of the system usability scale. In: Kurosu M (ed). *Human Centered Design*. Berlin Heidelberg: Springer, 2009:94–103.

21 Aaron Bangor PK, James Miller. Determining what individual SUS scores mean: adding an adjective rating scale. *J Usabl Stud* 2009;**4**(**3**):114–23.

22 WHO Collaborating Centre for Drug Statistics Methodology - Norwegian Institute of Public Health. ATC/DDD Index. Secondary ATC/DDD Index 2016. http://www.whocc.no/atc_ddd_index/.

23 Laroche ML, Charmes JP, Merle L. Potentially inappropriate medications in the elderly: a French consensus panel list. *Eur J Clin Pharmacol* 2007;**63**(**8**):725–31.

24 Montastruc F, Laffont M, Bagheri H *et al*. Potentially inappropriate medications in the elderly in France: a study in community pharmacies in 2011–2012. *Eur J Clin Pharmacol* 2013;**69**(**3**):741–2.

25 Koper D, Kamenski G, Flamm M *et al*. Frequency of medication errors in primary care patients with polypharmacy. *Fam Pract* 2013;**30**(**3**):313–9.

26 Filomena Paci J, Garcia Alfaro M, Redondo Alonso FJ *et al*. Inappropriate prescribing in polymedicated patients over 64 years-old in primary care. *Aten Primaria* 2015;**47**(**1**):38–47.

27 Bregnhoj L, Thirstrup S, Kristensen MB *et al*. Prevalence of inappropriate prescribing in primary care. *Pharm World Sci* 2007;**29**(**3**):109–15.

28 Hill-Taylor B, Sketris I, Hayden J *et al*. 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* 2013;**38**(**5**):360–72.

29 Bongue B, Naudin F, Laroche ML *et al*. Trends of the potentially inappropriate medication consumption over 10 years in older adults in the East of France. *Pharmacoepidemiol Drug Saf* 2009;**18**(**12**):1125–33.

30 Klarin I, Wimo A, Fastbom J. The association of inappropriate drug use with hospitalisation and mortality: a population-based study of the very old. *Drugs Aging* 2005;**22**(**1**):69–82.

31 Bierman AS, Pugh MJ, Dhalla I *et al*. Sex differences in inappropriate prescribing among elderly veterans. *Am J Geriatr Pharmacother* 2007;**5**(**2**):147–61.

32 Cullinan S, Fleming A, O'Mahony D *et al*. Doctors' perspectives on the barriers to appropriate prescribing in older hospitalized patients: a qualitative study. *Br J Clin Pharmacol* 2015;**79**(**5**):860–9.

33 Bardet JD, Vo TH, Bedouch P *et al*. Physicians and community pharmacists collaboration in primary care: a review of specific models. *Res Social Adm Pharm* 2015;**11**(**5**):602–22.

34 Kelly DV, Bishop L, Young S *et al*. Pharmacist and physician views on collaborative practice: findings from the community pharmaceutical care project. *Can Pharm J* 2013;**146**(**4**):218–26.

35 Kaur S, Mitchell G, Vitetta L *et al*. Interventions that can reduce inappropriate prescribing in the elderly: a systematic review. *Drugs Aging* 2009;**26**(**12**):1013–28.

36 Meid AD, Lampert A, Burnett A *et al*. The impact of pharmaceutical care interventions for medication underuse in older people: a systematic review and meta-analysis. *Br J Clin Pharmacol* 2015;**80**(**4**):768–76.

37 Hatah E, Braund R, Duffull SB *et al*. General practitioners' views of pharmacists' current and potential contributions to medication review and prescribing in New Zealand. *J Prim Health Care* 2013;**5**(**3**):223–33.