Pharmacist-led medication review in community-dwelling older patients using the GheOP³S-tool: general practitioners' acceptance and implementation of pharmacists' recommendations

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Word count article: 4194

Word count abstract: 299

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Word count references: 1465

No. of figures: 2

No. of tables: 4

No. of supplementary material: 0

Declarations of interest: none

Compliance with Ethical Standards

The ethical committee of Ghent University Hospital granted ethical approval. 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 was obtained from all individual patients included in the study. This article does not contain any studies with animals performed by any of the authors.

Declarations of interest: none

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Abstract

Rationale, aims, and objectives: The Ghent Older People's Prescriptions community Pharmacy Screening (GheOP³S)-tool was recently developed as an explicit screening tool to detect drug-related problems (DRPs) and to help in performing medication reviews. In this study, we aimed (1) to describe the characteristics of the detected DRPs and the subsequent pharmacists' recommendations with their acceptance and implementation rate resulting from a pharmacist-led medication review using the GheOP³S-tool; and (2) to assess the potential impact of the intervention.

Method: Prospective observational study in community-dwelling older patients (≥ 70 years, using ≥ 5 medications). Community pharmacists performed medication reviews resulting in the documentation of 'GheOP³S-related DRPs' and 'other DRPs' with corresponding pharmacists' recommendations. Acceptance was recorded during face-to-face pharmacist-general practitioner (GP) meetings. Implementation was assessed after 3-month follow-up by consulting the electronic pharmacy record, the patient and/or GP. The potential impact on the number of medications, the number of 'GheOP³S-related DRPs', the anticholinergic and sedative burden quantified by the Drug Burden Index (DBI), and medication costs was assessed by a pre-post comparison of the patients' medication lists.

Results: Twenty-one pharmacists detected 470 DRPs with a median (IQR) of 6 (4-8) per patient in 75 patients (about half 'GheOP³S-related DRPs' and half 'other DRPs'). Most prevalent recommendations were stopping (22.9%) and substituting (18.9%) medication. Overall acceptance was 66.9%. At follow-up, 42.9% of all recommendations were implemented. The number of GheOP³S-criteria ($p < 0.001$) and the DBI scores ($p = 0.033$) significantly differed from baseline. This was not the case for the number of chronic medications and medication costs.

Conclusions: This study demonstrates a relatively high acceptance of pharmacists' recommendations, although implementation could be improved. Pharmacist-led medication reviews with multidisciplinary meetings using the GheOP³S-tool can have a potential impact on the number of DRPs and the anticholinergic and sedative burden of patients.

KEYWORDS: drug-related problem; medication review; polypharmacy; community pharmacist; drug burden index; elderly

Introduction

Polypharmacy - often described as the concurrent use of at least five chronic medications ^{1,2} - is common in older people and is often necessary to manage multimorbidity. However, it can also become a problem. **Polypharmacy** inappropriateness may arise if the risk of harm from medications is likely to outweigh the benefits e.g. when pill burden hampers adherence or when medications interact with each other ³, leading to an increased risk of drug-related problems (DRPs) ⁴. A DRP can be defined as an event or circumstance involving medication therapy that actually or potentially interferes with desired health outcomes ⁵. DRPs are associated with higher health-care utilization (e.g. hospitalisations, emergency department visits), reduced quality of life, and increased health-care costs ⁶⁻⁹. Therefore, health-care providers are urged to take action in the prevention of iatrogenic harm related to medications. In this context, the World Health Organization calls for a worldwide commitment to reduce severe and avoidable medication-related harm with 50% by 2022 ¹⁰.

Medication review, consisting of a structured evaluation of a patient's pharmacotherapy, has been proposed as a strategy to identify and resolve DRPs ¹¹. Several studies have shown a positive impact of medication review on the quality of medication use (e.g. the number of (appropriate) medications ^{12,13} and DRPs ¹³) and on disease-specific outcomes (e.g. glycosylated haemoglobin, blood pressure, cholesterol) ¹². However, a forthright effect on major outcomes such as hospitalisation ¹²⁻¹⁴, mortality ^{12,13}, health-related quality of life ^{14,15} and health-care costs ^{13,15} has not yet been demonstrated.

There is an international trend to involve community pharmacists in performing medication reviews, because of their specific medication-related knowledge. However, performing medication reviews is not a common practice in Belgian community pharmacies, nor is it reimbursed by the health insurances. To facilitate the detection of DRPs in a structured way and thereby the implementation of medication review in the Belgian community pharmacy practice, we have recently developed the Ghent Older People's Prescriptions community Pharmacy Screening (GheOP³S)-tool ¹⁶. This is an explicit screening tool for detecting DRPs with high clinical relevance in community-dwelling older people, without the need for clinical patient data. It was specifically designed for use in the community pharmacy setting. The GheOP³S-tool encompasses overuse and misuse (of potentially inappropriate medications), underuse (potential prescribing omissions), drug-drug interactions (DDIs) and pharmaceutical care-related criteria (e.g. monitoring medication adherence).

So far, we have found that GheOP³S-criteria are highly prevalent among older adults with polypharmacy in primary care ¹⁷⁻¹⁹. However, the acceptance and implementation of pharmacists' recommendations resulting from a multidisciplinary medication review process using the GheOP³S-tool has not yet been studied in this population. Therefore, the current study was designed to embed the use of the GheOP³S-tool in a medication review process in community-dwelling older patients with polypharmacy. The main objectives were (1) to investigate the characteristics of the detected DRPs and the subsequent pharmacists' recommendations with their acceptance and implementation by general practitioners (GPs); and (2) to explore the potential impact of this medication review process on the number of medications, the number of 'GheOP³S-related DRPs', the anticholinergic and sedative burden, and medication costs.

Methods

Study design, setting and participants

This study resulted from a collaboration between the Association of Belgian Pharmacies, KU Leuven, Université Libre de Bruxelles and Ghent University, which was set up to investigate the implementation of pharmacist-led medication reviews in primary care in Belgium ²⁰. We conducted a prospective observational study from December 2016 to October 2017 in a convenience sample of 12 community pharmacies in Belgium. These pharmacies employed at least one pharmacist who had previously received training in performing medication review using the GheOP³S-tool and who was willing to engage in a face-to-face discussion with the GP about the results of the medication review. More than one pharmacist per pharmacy could participate.

Since this was the first time that pharmacists would perform multidisciplinary medication reviews using the GheOP³S-tool, the participating pharmacists were asked to search for one or more local GPs who were willing to participate in the study and with whom they had patients in common. The pharmacist and GP selected together community-dwelling patients aged 70 years or older and using five or more chronic medications (defined as medications without a stop date), who could (in their opinion) benefit from a medication review (e.g. patients with a recent hospitalisation, a recent fall, suspected adverse drug reactions (ADRs), suspected problems with adherence). Patients not able to take part in an interview with the pharmacist (e.g. insufficient knowledge of Dutch language, insufficient cognitive skills) were not eligible for inclusion. Selected patients were subsequently invited to participate in the study by the pharmacist. It was planned to recruit at least seven patients per pharmacy practice.

The ethical committee of Ghent University Hospital granted ethical approval. All patients provided written informed consent. This study was reported in accordance with the 'Strengthening The Reporting of Observational Studies in Epidemiology' (STROBE) guidelines ²¹.

Intervention

Before the start of the study, participating pharmacists received protocol training. Pharmacists conducted an intermediate medication review type 2a (which is based on medication history and patient information, according to Pharmaceutical Care Network Europe typology of medication reviews ²²) using the GheOP³S-tool. They were free to use other sources of information (e.g. other medication screening tools, medication interaction checkers, national guidelines) in addition to the GheOP³S-tool.

The medication review process consisted of six steps:

1. **A preparation step** including an extraction of the current medication use and previously reported DRPs (e.g. allergies, contraindications, nonadherence) from the electronic pharmacy record.
2. **A pharmacotherapeutic anamnesis:** a face-to-face patient interview at the pharmacy or at the patient's home to:
  - Collect basic patient characteristics (age, gender, weight, length, functional status, self-rated health). Self-rated health was determined by the question “How in general would you rate your health?” with response options of “excellent, very good, good, fair, or poor) ²³.
  - Collect smoking status, alcohol use, diet and cognitive function using the Mini-Cog test ²⁴. The Mini-Cog test consists of three questions: (1) to recall three unrelated words, (2) to draw a clock as a recall distractor and (3) to recall the three previously unrelated words. Recalling zero words or recalling $\leq$ two words and drawing an abnormal clock, was suggestive for cognitive impairment.
  - Check the accuracy of the current medication list and potential medication indications.
  - Identify experienced ADRs and (practical) problems with medication intake.
  - Assess medication adherence.
  - Discuss the patient's experiences, expectations and preferences about their medication.
  - Assess the patient perceived medication effectiveness.
3. **A pharmacotherapeutic analysis** consisting of:
  - Medication screening with the GheOP³S-tool to detect ‘GheOP³S-related DRPs’. Pharmacists were advised to exclude the GheOP³S-criteria concerning direct oral anticoagulants (in light of the emerging evidence ²⁵), and to elevate the threshold for the 10-year probability of major osteoporotic fractures from 10 to 20% ²⁶ for the GheOP³S-criterion ‘patient has an elevated risk for osteoporosis and is not prescribed calcium/vitamin D supplementation’.
  - Identification of ‘other DRPs’ using other sources of information (including DRPs detected during the patient interview). Additional information (e.g. confirmation of diagnosis) could be acquired by contacting the GP or in the next step, the face-to-face discussion with the GP.
  - Development of a pharmaceutical care plan with the pharmacist's recommendations to improve medication appropriateness.

4. **A face-to-face pharmacist-GP meeting** to discuss the relevance (for the individual patient) of the pharmacist's recommendations, to seek agreement on the interventions in the pharmaceutical care plan and to prioritize all identified DRPs with their interventions in an agreed action plan. Priorities were discussed between the pharmacist and GP, taking into account the information pharmacists received during the patient interview (e.g. the patient's preferences or expectations) and the instructions given in the study protocol (e.g. What is currently a problem for the patient?, Is the patient's safety compromised?, Which conditions could be treated more effectively?, What is the life expectancy of the patient?).
5. **A discussion between the patient** and pharmacist and/or GP to seek agreement on proposed interventions, resulting in a final action plan. In addition, the patient received an updated medication list (including agreed medication changes) from the pharmacist.
6. **A follow-up moment** (three months after step five) to evaluate the implementation of pharmacist's recommendations. Pharmacists assessed the implementation rate by consulting the electronic pharmacy record (e.g. to check whether medications were actually stopped or started), the patient (e.g. to check whether information was transmitted) and/or the GP (e.g. to check whether therapy monitoring was carried out).

During the study, pharmacists were supported by the researcher who monthly called them to discuss possible problems or questions and to assess the progress of the study. A financial incentive of 60 € per included patient was provided to the participating pharmacists at the end of the study.

Data collection

Pharmacists recorded all patient data and interventions in a case report form (CRF) developed by the research team (available upon request). They also recorded for each patient how much time they spent to each step of the intervention.

Data analysis

All medications were coded using the Anatomical Therapeutic Chemical Classification System (ATC) formulated by the World Health Organisation Collaborating Centre for Drug Statistics Methodology ²⁷. All DRPs and pharmacists' recommendations were classified by the researcher and peer reviewed through discussion with a second pharmacist using the Pharmacists' Documentation of Interventions in Seamless Care (PharmDISC) classification system ²⁸.

Primary outcomes were the number and type of DRPs; the subsequent pharmacists' recommendations; and the GPs' acceptance and implementation rate of pharmacists'

recommendations. DRPs were categorized as either 'GheOP³S-related DRPs' when it was clear from the CRF that the detection of the DRP resulted from screening with the GheOP³S-tool; or as 'other DRPs' when the detected DRP was not recorded in the CRF as a GheOP³S-criterion. Acceptance and implementation were categorized as: 'full', 'partial', 'not', and 'not recorded'. Acceptance was classified as 'partial' when: (1) the GP accepted dose tapering but no full stop, or (2) the GP accepted to switch medication but preferred another medication than the one proposed by the pharmacist, or (3) if only one recommendation was accepted in case of a combined recommendation (e.g. pharmacist advised to taper two benzodiazepines and GP wanted to taper only one). Implementation was classified as 'partial' when: (1) the GP accepted to stop medication using tapering, but the medication appeared to be not fully stopped at 3-month follow-up, or (2) if only one recommendation was implemented in case of a combined recommendation. Acceptance and implementation rate were determined by the ratio of the number of relevant pharmacists' recommendations that were fully or partially accepted/implemented by the GP to the total number of relevant pharmacists' recommendations.

In addition, the potential impact of the intervention was assessed by comparing patient's medication list between baseline (after the patient interview) and 3-month follow-up in terms of:

- a) The number of medications.
- b) The number of 'GheOP³S-related DRPs'.
- c) The Drug Burden Index (DBI) score of all oral chronic medications, which was used as a proxy for medication safety. The DBI is based on a linear additive model and quantifies the cumulative anticholinergic and sedative medication burden in older adults ²⁹. A higher anticholinergic and sedative burden can increase the risk of impaired cognitive and physical function and the frequency of falls ^{30,31}. Scores were calculated using the formula $DBI = \sum D/(D + \delta)$, where D is the daily dose of every anticholinergic or sedative medication used by the patient and δ is the minimum recommended daily dose as listed by the Belgian Commented Medications Repertory ³². Medication was considered anticholinergic when present in the GheOP³S-tool ('medications with high risk for anticholinergic side-effects', based on the list of Duran et al. ³³), or sedative based on ATC-code (N01A, N02A, N05, N06A, N07CA and R06).
- d) Medication costs per day (in euro): these costs were calculated for both the patient (out-of-pocket medication cost) and the Belgian health-care insurance system (National Institute for Health and Disability Insurance, NIHDI) (third party reimbursement). Topical agents and as needed medications were excluded.

Statistical analysis was performed using SPSS® Statistics version 25. A Wilcoxon signed rank test was used to compare the medians of two discrete variables (number of chronic medications and number of GheOP³S-criteria). A Mann-Whitney U Test was used to compare the acceptance and implementation rate of recommendations related to 'GheOP³S-related DRPs' and 'other DRPs'. A paired t-test was used to compare the means of two (paired) continuous variables (DBI scores and medication costs). Comparisons were made between data at baseline (after the patient interview) and 3-month follow-up. A two-tailed P-value of < 0.05 was considered significant.

Results

Sample characteristics

In the 12 participating community pharmacies, 21 pharmacists collaborated with 44 GPs. Eighty-nine patients were invited for study participation, of which 10 (11.2%) refused to participate, resulting in 79 included patients (Figure 1A). Four patients were excluded from analysis, resulting in a final sample of 75 patients (Figure 1A). Pharmacist and patient characteristics are detailed in Table 1.

Intervention characteristics

a) Baseline DRPs and resulting pharmacists' recommendations

Pharmacists detected a total of 470 DRPs in 75 patients with a median (IQR) of 6 (4-8) per patient. The most prevalent types of DRPs (according to the PharmDISC classification system) were 'contraindication' (19.1%), 'interaction' (15.3%) and 'missing patient documentation or information' (10.0%) (Table 2). Forty-nine percent of DRPs were 'GheOP³S-related DRPs' (n = 230). Screening with the GheOP³S-tool mainly attributed to the detection of DRPs related to overuse/misuse (PharmDISC categories C1.2 contraindication, C1.3 interaction, C4.3 inappropriate therapy duration and C3.2 overdose, see Table 2), and underuse (PharmDISC category C1.1 no concordance with guidelines, only suboptimal therapy possible, Table 2). Fifteen GheOP³S-criteria accounted for more than three-quarters (76.5%) of all detected GheOP³S-criteria. Most prevalent GheOP³S-criteria (n, % of patients) were: 'any intermediate acting benzodiazepine or Z-drug at full dose or any dose $\geq$ 30 subsequent days' (34, 45.3%), 'any antidepressant $\geq$ 1 year' (21, 28.0%), 'the patient has an elevated risk for osteoporosis and is not prescribed calcium/vitamin D supplementation' (21, 28.0%), 'any proton pump inhibitor (PPI) at full dose $\geq$ 8 weeks' (12, 16.0%), 'oral antidiabetics/insulin + cardioselective β -blocker' (10, 13.3%) and 'any combination of anticholinergic medications' (10, 13.3%). 'Other DRPs' constituted 51.1% (n = 240) of all detected DRPs. About one fourth (25.7%, 121/470) of all DRPs were exclusively identified on the basis of patient interviews (e.g. untreated symptoms, ADRs, nonadherence, administration technique errors).

The most common pharmacists' recommendations were to stop medication (22.9%), to substitute medication (18.9%), to monitor therapy (14.5%) and to adjust dose (12.8%) (Table 2). Pharmacists did not record their recommendation for 24 DRPs (5.1%, 24/470) (Figure 1B1).

b) Acceptance of pharmacists' recommendations

During the pharmacist-GP meetings, 20 of 446 (4.5%) pharmacists' recommendations were judged as not relevant for the specific patient (Figure 1B2). These were all recommendations for laboratory

parameter monitoring that had already been provided by the GP (n = 17), or recommendations related to medication that had already been stopped or started in the period between the pharmacotherapeutic analysis by the pharmacist and the pharmacist-GP meeting (n = 3). For 33 (7.7%, 33/426) recommendations the pharmacist did not record the acceptance. The GPs (fully or partially) accepted **66.9%** (285/426) of the recommendations (Figure 1B3). Recommendations with high acceptance rate (> 70%) were 'optimization of administration/route' (82.4%, 14/17), 'therapy started' (80.0%, 32/40) and 'therapy monitoring' (78.9%, 45/57) (Table 3).

The main reasons for not accepting pharmacists' recommendations were: the GP perceived medication as still necessary or beneficial and the GP perceived the recommendation to be of inferior priority (but still relevant) at the moment (Table 4). Acceptance rates of recommendations related to 'GheOP³S-related DRPs' (67.2%, 135/201) and recommendations related to 'other DRPs' (66.7%, 150/225) did not statistically differ (Mann-Whitney U Test, $z = -0.455$, $p = 0.684$).

c) Implementation of pharmacists' recommendations

Overall, **42.9%** (183/426, Figure 1B4) of pharmacists' recommendations were (fully or partially) implemented at 3-month follow-up. This corresponds to **56.1 %** of accepted pharmacists' recommendations. For 22 recommendations the implementation was not recorded (5.2%, 22/426). 'Application instruction' (100.0%, 8/8), 'clarification/addition of information' (100.0%, 6/6) and 'in-depth counselling of patient' (100.0%, 6/6) were the recommendations with the highest implementation rates (Table 3). Main reasons for non-implementation of accepted recommendations were: the patient refuses recommended medication change and postponement of the intervention (Table 4). Implementation rates of recommendations related to 'GheOP³S-related DRPs' (33.3%, 67/201) and 'other DRPs' (51.6%, 116/225) did not statistically differ (Mann-Whitney U Test, $z = -1.289$, $p = 0.218$).

d) Time investment

The median (IQR) time investment per medication review was 180 (150-244) minutes. The anamnesis or patient interview was the most time-consuming step. The median (IQR) time investment per step in the medication review process was: preparation step 30 (30-45) minutes, anamnesis 60 (50-90) minutes, medication review (screening with the GheOP³S-tool, detection of 'other DRPs' and formulating recommendations) 50 (30-70) minutes, pharmacist-GP meeting 15 (10-28) minutes, discussion with the patient 15 (10-30) minutes and 3-month follow-up 10 (5-20) minutes.

Potential impact of the intervention

The number of chronic medications had remained unchanged between baseline and 3-month follow-up, while the number of 'as needed' medications had slightly decreased ($p = 0.002$) (Figure 2a). At 3-month follow-up, the number of 'GheOP³S-related DRPs' ($p < 0.001$) significantly decreased (Figure 2b). Furthermore, the DBI score was slightly lower at follow-up (versus baseline) ($p = 0.033$), but the medication costs had remained unchanged (Figure 2c-d).

Discussion

In this study, we investigated a community pharmacist-led medication review process (including a face-to-face meeting with both the patient and the GP) in older patients with polypharmacy using the GheOP³S-tool. The GheOP³S-tool served as a structured evidence-based aid to detect DRPs with high clinical relevance for older patients and to initiate medication review in a community pharmacy setting without the patient's clinical information.

The high number of detected DRPs (median (IQR) of 6 (4-8) per patient) highlights the relevance of performing medication reviews in this population. Most prevalent detected DRPs comprised overuse and misuse of potentially inappropriate medications, missing patient documentation or information and underuse.

Our study showed a relatively high (67%) overall acceptance rate of pharmacists' recommendations. This is in accordance with other studies investigating pharmacist-led medication reviews^{34,35} and demonstrates that GPs were indeed (this was an inclusion criterion) willing to collaborate during the face-to-face meetings. Less challenging recommendations (e.g. optimization of administration, start medication, therapy monitoring) were most likely to be accepted. In most cases of non-acceptance, the GP perceived that the medication needed to be continued or that the recommendation was currently of inferior priority. Although we did not investigate the clinical relevance of these recommendations, a possible explanation for not accepting certain recommendations could be 'inertia'³⁶. This means that the GP perceives stopping medication as a lower value recommendation than continuing medication (e.g. because of fear for negative consequences or minimization of the medication inappropriateness). The fact that certain DRPs and their related recommendations were perceived to be of inferior priority, underlines the need for prioritizing actions (e.g. to make a top 3 of agreed actions) instead of engaging to implement all recommendations. Some of the 'not recorded' acceptance or implementation could be a result of this prioritization, but this was not clear from the CRF. Nonetheless, periodic medication reviews should regularly reassess the willingness to act upon these recommendations.

Remarkably, about half (56%) of the accepted recommendations were implemented. Other studies have reported similar implementation rates^{37,38}. The two main reasons for not implementing accepted recommendations were patient refusal or postponement of the intervention. It seemed that adjustments in the use of potentially inappropriate medications such as benzodiazepines/Z-drugs, antidepressants, proton pump inhibitors and anticholinergics were not that easy to implement for both the GP and the patient. A systematic review performed by Reeve et al. (2013) emphasizes the role of patients in this process and described several patient reported barriers³⁹. Patients can perceive the

cessation of medication as inappropriate (e.g. when medication is perceived as currently necessary/beneficial or when the patient accepts his medical condition and therefore the need for medication). In addition, patients could fear the return of the condition or withdrawal symptoms when medication is stopped⁴⁰. Consequently, it is crucial that patients are well informed about the proposed interventions. This information should be streamlined between the pharmacist and GP, so both can convey the same message towards the patient. Accordingly, more intensive collaboration between pharmacist and GP to reinforce trust and their professional relationship could lead to higher acceptance and implementation rates³⁷. In addition, introducing extra follow-up moments could increase the actual implementation of interventions that were postponed.

About half of the detected DRPs were related to GheOP³S-criteria. Most prevalent GheOP³S-criteria comprised the overuse or misuse of potentially inappropriate medications and underuse. Most frequently involved medications were benzodiazepines, antidepressants, calcium/vitamin D, PPIs and anticholinergics, which is also regularly reported in other studies^{41,42}. Pharmacists also detected a large number of 'other DRPs' (51%), which consisted of a variety of DRP types. Prevalent 'other DRPs' encompassed DRPs such as 'missing patient documentation or information' (e.g. untreated symptoms or medications not present in the electronic pharmacy record), 'adverse effect' and 'financial burden'. These types of DRPs cannot be detected by merely screening a medication list with the help of an explicit screening tool. Patient involvement by including a patient interview in the medication review process is a key factor to detect these additional types of DRPs^{43,44}. This is supported by our finding that 26% of all detected DRPs were only detected on the basis of the patient interview. Notwithstanding the different types of 'GheOP³S-related DRPs' and 'other DRPs', the acceptance and implementation rate of pharmacists' recommendations for both types of DRPs was similar.

An essential factor that needs to be tackled to implement medication reviews on a larger scale is the considerable time investment. Pharmacists reported a median of 180 minutes to complete the whole review, which has also been reported in literature on pharmacist-led medication reviews^{45,46}. The patient interview and medication screening were the main contributing factors. We believe that more education about communication (e.g. techniques to guide the conversation) and more training and experience in performing medication reviews could counter this. Facilitated interdisciplinary information exchange with access (before starting a medication review) to already available patient information (e.g. diagnoses, previous and most recent laboratory parameters, actual medication use with start/stop dates of medications, contraindications, reported ADRs) could lead to more accurate information and could therefore decrease time investment. Development of a software application of the GheOP³S-tool should facilitate medication screening in the pharmacy. In addition, the substantial time investment advocates targeting high-risk patients (e.g. prescribed 10 or more medications⁴⁷,

using high-risk medication ^{4,47}, multimorbidity ⁴⁸, cognitive impairment ⁴, nonadherence ⁴, renal impairment ⁴, experience of ADRs ⁴, high frailty score ⁴) instead of all older patients with polypharmacy.

At follow-up, we observed a positive impact on the number of 'GheOP³S-related DRPs' and the anticholinergic and sedative burden (DBI scores), which could have clinical implications for the patient.

Our study has several strengths. First, this is the first study exploring the use and potential impact of the GheOP³S-tool during a multidisciplinary medication review in an ambulatory primary care setting. Second, this study combined the use of an explicit screening tool, the GheOP³S-tool, with a patient-centred approach (e.g. including patient interviews) to detect additional DRPs.

Although the results of the present study are promising, there are some limitations that should be taken into account. First, participating pharmacists were presumably more motivated as most of them volunteered to participate (participation bias). Pharmacists probably selected GPs who were more likely to engage in a pharmacist-GP collaboration and patients of whom they thought could benefit from a medication review (selection bias). This could have led to higher acceptance rates and could limit the generalizability. Second, the observational design of this study could only detect a 'potential' impact of the intervention on different outcomes. In addition, we were not able to assess medication appropriateness or clinical relevance of pharmacists' recommendations due to incomplete data. Noteworthy, the detection of DRPs in this study was primarily based on data from the electronic pharmacy record (e.g. dispensed medications, certain contraindications, allergies) and from the patient interview (e.g. the actual medication use, problems and experiences with medications). Pharmacists could contact the GP for additional information during the pharmacotherapeutic analysis, but they had no access to the GP's medical records. In addition, studies investigating medication review processes often have different designs and settings, which hinders a forthright comparison in acceptance and implementation of pharmacists' recommendations.

Future larger sampled (longer-term) studies should determine the impact of this medication review process on patient-centred outcomes. A full cost-effectiveness analysis should also be performed in the future.

Conclusion

This study demonstrates that a multidisciplinary pharmacist-led medication review including a patient interview, screening with the GheOP³S-tool and face-to-face pharmacist-GP meetings detects a high number of DRPs. The acceptance rate of pharmacists' recommendations was relatively high, although this did not translate into a similar implementation rate. At follow-up, the number of 'GheOP³S-related DRPs' and the anticholinergic and sedative burden of patients were reduced, which illustrates the potential positive impact of pharmacists performing medication reviews in collaboration with GPs. Future studies should focus on higher-risk patients to efficiently allocate time, ensure patient involvement (shared decision making) and collaboration between pharmacists and GPs to establish trust and streamline information.

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Figure 1. Study flowchart with (A) Recruitment of participants and (B) Intervention characteristics

DRP: drug-related problem; **GP:** general practitioner; **GheOP³S:** Ghent Older People's Prescriptions community Pharmacy Screening

*Eligible patients: patients on which both the pharmacist and GP agreed a medication review could be beneficial

Figure 2: Potential impact of the intervention assessed using (a) number of medications per patient; (b) number of detected 'GheOP³S-related DRPs'; (c) DBI scores; (d) medication cost (Black: at baseline; grey: at 3-month follow-up).

* Wilcoxon signed rank test

** McNemar's test

*** Paired t-test

DBI: Drug Burden Index; **DRP:** drug-related problem; **GheOP³S:** Ghent Older People's Prescriptions community Pharmacy Screening

Acknowledgments

We would like to thank Marie Carrein for her contribution in the data analysis and the participating community pharmacists and GPs for their support in recruiting study participants.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. The Association of Belgian Pharmacies provided the participating pharmacies a financial incentive of 60 € per included patient at the end of the study.

Conflict of interest

The authors declare that they have no conflict of interest.

Ethical approval

The ethical committee of Ghent University Hospital granted ethical approval. Informed consent was obtained from all individual patients included in the study. 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 was obtained from all individual patients included in the study. This article does not contain any studies with animals performed by any of the authors.