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Reduction of Potentially Inappropriate Medications Using the STOPP Criteria in Frail Older Inpatients: A Randomised Controlled Study

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Abstract

Background Hospital admissions may provide an opportunity to discontinue potentially inappropriate medications (PIMs) in older patients. Little is known about the effect of using the Screening Tool of Older People's potentially inappropriate Prescriptions (STOPP) in this context. This study aimed to test the hypothesis that specific STOPP recommendations from an inpatient geriatric consultation team (IGCT) to the hospital physician leads to reductions in PIMs for patients at discharge.

Methods This was a randomised controlled study in 146 frail inpatients (in 2011). The intervention consisted of STOPP recommendations made by the IGCT to ward physicians to discontinue PIMs, in addition to the standard geriatric advice.

Results Intervention ($n = 74$) and control ($n = 72$) groups were similar in terms of patient characteristics (median age 85 years; median number of daily drugs, seven) and PIM distribution (68 and 57 PIMs in 53 and 51 % of patients, respectively). At discharge, the reduction in PIMs was twice as high for the intervention group as for the control group (39.7 and 19.3 %, respectively; $p = 0.013$). The proportion of patients who still had one or more PIM at discharge did not differ between groups. In the 50 patients followed-up a year later, the majority of PIMs that had been stopped during hospitalisation had not been restarted after discharge (17/28; 61 %). The clinical relevance of PIMs identified at baseline in those patients was considered major (29 %), moderate (37 %), minor (5 %), deleterious (8 %), or not assessed (11 %). Discontinuation rate was not associated with clinical importance.

Conclusion Specific STOPP recommendations provided to hospital physicians doubled the reduction of PIMs at discharge in frail older inpatients. To further improve the appropriateness of prescribing in older patients, clinicians should focus on the STOPP criteria that are of major clinical importance, and general practitioners should be actively involved.

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Key Points

Using STOPP at hospital reduces inappropriate prescribing at discharge.

The relevance of the STOPP recommendations depends on the context of the patient.

Focussing on STOPP criteria of major clinical importance and actively involving general practitioners are recommended.

1 Introduction

Inappropriate prescribing is well described in older patients [1–5]. It increases the risk of adverse drug events and thereby morbidity, mortality, and costs of care [2, 6]. Furthermore, the hospitalisation period is a time when the prescribing process is exposed to possible introduction of errors [7]. Multiple prescribers can be involved in the care of the patient, bringing complexity and communication challenges. For example, the patient is at a higher risk of medication discrepancies [8] or unnecessary medication at hospital discharge [9]. Nevertheless, hospital admission can be a good opportunity for medication review.

Upon admission to a geriatric unit, patients usually benefit from a comprehensive geriatric assessment (CGA) [10], which consists of a “multidisciplinary process to achieve a coordinated and integrated plan for treatment, taking into account the patient’s medical, psychosocial and functional capability” [11]. In non-geriatric wards, frail older patients receive a CGA from an inpatient geriatric consultation team (IGCT) [11]. The IGCT also offers recommendations for improving patient management [12]. IGCTs have been implemented in various countries (mainly in Europe) as a way to improve care for geriatric patients not admitted to geriatric wards [13]. In Belgium, IGCTs benefit from federal funding. A recent meta-analysis showed that IGCTs have favourable effects on mortality up to 8 months after discharge [13]; however, little is known about the efficacy of geriatric counselling on the discontinuation of potentially inappropriate medications (PIMs).

Validated tools for detecting inappropriate prescribing could be useful in aiding IGCTs to assess patients’ medications. The Screening Tool of Older People’s potentially inappropriate Prescriptions (STOPP) is a European tool addressing overprescribing in older patients [14, 15]. STOPP is increasingly being used in observational studies to describe the prevalence of inappropriate prescribing [5, 16–20]. STOPP has several advantages over other explicit criteria, including its structure by system and its good inter-rater reliability. Its European origin also improves its applicability to our Belgian setting. Moreover, STOPP has been shown to be efficient at detecting inappropriate prescriptions that are related to adverse drug events [17, 18]. To our knowledge, only one randomised controlled trial to date has evaluated the effect of applying the STOPP criteria. Significant improvements in prescribing appropriateness were documented [21].

The objective of this study was to evaluate the effect of STOPP criteria recommendations from an IGCT on discontinuation of PIMs in older inpatients discharged from a hospital medical ward.

2 Methods

2.1 Design

We conducted a randomised controlled study on consecutive frail older medical patients admitted from February to June 2011 to a 975-bed teaching hospital (Cliniques universitaires Saint-Luc) in Brussels, Belgium. The study protocol was approved by the local Ethics Committee (Commission d’Éthique Biomédicale Hospitalo-Facultaire, Faculté de Médecine, Université catholique de Louvain; 2011/25JUI/323-B403201111806). Informed consent from study participants was not considered necessary for this study.

2.2 Inclusion and Exclusion Criteria

Inclusion criteria for patients were: (1) 75 years of age or older; (2) risk of frailty defined by a an Identification of Seniors At Risk (ISAR) score of $\geq 2/6$ (one point for each of the following: needing help with activities of daily life; an increase in this need related to the current illness; memory problems; significantly altered vision; hospitalisation in the previous 6 months; and daily use of three or more medications at home [22]); (3) admission to a medical ward; and (4) availability of a CGA (confirming the frailty profile of the patient) performed by the IGCT. Surgical admissions were not included because the revision of chronic medications by surgeons was not considered to be part of standard care. Patients whose discharge letter contained incomplete medication data were excluded from the analysis.

2.3 Inpatient Geriatric Consultation Team

The IGCT performs CGAs on patients with an ISAR score $\geq 2/6$ [22], at the request of non-geriatric ward physicians. In our hospital, the IGCT is a multidisciplinary team consisting of nurses, geriatricians, a dietician, an occupational therapist, a physiotherapist, a speech therapist, and a psychologist. Although clinical pharmacists worked on the acute geriatric unit of the hospital, no pharmacist collaborated with the IGCT at the time of the study due to lack of resources. This situation is similar in many other Belgian hospitals. The initial evaluation of the patient is made by a nurse, who then refers the patient on to other team members, depending on the patient’s needs. The IGCT management of a patient is an established process that includes multidisciplinary rounds. Patients are screened for geriatric syndromes, including recent falls (two or more falls in the last 6 months), polypharmacy (five or more daily medications), cognitive disorder (known dementia and/or an impaired Mini-Mental State Examination [MMSE] score of

<24/30) [23], malnutrition (a body mass index of <21 kg/m² and/or a mid-arm circumference <23 cm), living alone, and functional dependency in activities of daily life (a Katz score of $\geq 9/24$ [24]). A geriatrician supervises the CGA for each patient. Recommendations are communicated orally to the ward team and are available in the electronic medical record. The patient's IGCT report is also sent to their general practitioner (GP) at discharge.

2.4 Randomisation

Eligible patients were allocated by the IGCT nurse to the control or intervention group by simple randomisation using drawing of lots [25] (without matching for age or geriatric profile). After randomisation, the nurse assigned each patient to the geriatrician that had been allocated to their intended group. In order to avoid contamination bias, two of the four geriatricians involved in the IGCT during the study period were allocated to the intervention group because they used the STOPP criteria in their current practice, while the other two, who had never worked with the STOPP criteria, were allocated to the control group. Geriatricians for both groups were of a similar age, education level, and level of clinical experience. They were used to working in the same team and performed CGA using the same structured approach and reporting data according to the same structured electronic medical record.

In the control group, the IGCT provided standard care. Each patient's medications were routinely reviewed by the IGCT geriatrician, using an implicit approach (i.e. no explicit tool was used). In the intervention group, in addition to the usual IGCT care, the geriatricians performed the following two steps: (1) using 64 STOPP criteria ('duplicate drug classes' was not considered because the concept of duplication is perceived differently by the clinicians) to systematically screen the list of medications being taken by the patient on admission for PIMs; and (2) oral and written recommendations made to the ward physician during hospitalisation for the discontinuation of PIMs. Apart from these two steps, both the control and the intervention group benefitted from the same CGA.

The attending ward physician (who is responsible for prescriptions during hospitalisation and at discharge), the evaluator (OD), and the patients were blinded to group assignment. The IGCT nurse provided the evaluator with a list of the patients included in the study, which did not specify allocation group. The evaluator gathered data on the primary outcome.

2.5 Outcome Measures

The primary outcome was the proportion of PIMs discontinued (or corrected in case of dosage-related or duration-

related PIMs) between hospital admission and discharge (according to the discharge letter). Secondary outcomes were: (1) characteristics associated with discontinuation of PIMs at discharge; (2) the proportion of PIMs that were still discontinued 1 year after discharge; and (3) the clinical significance of the STOPP-related recommendations.

One year after hospital discharge, a follow-up questionnaire was sent to the GPs of all patients included in the study who had presented with PIMs on admission. In order to maximise response rate, a single question was asked: "Could you please indicate if the patient is currently receiving the following drug(s)", followed by a list of the PIMs identified on admission. Anonymity was guaranteed. A stamped return envelope was provided and a reminder was sent 2 months later [26].

In the patients followed at 1 year, the clinical relevance of STOPP-related recommendations made during their hospital stay was evaluated by three experts (a geriatrician [BB], a GP [JMD], and a clinical pharmacist [AS]). This evaluation used a 6-point rating scale that had been employed in a previous study (minor: no benefit or minor benefit; moderate: improvement of the appropriateness of the level of practice or prevention of an adverse drug event of moderate importance; major: prevention of serious morbidity—including readmission—and serious adverse drug event; extreme: life-saving; deleterious: increased risk of health adverse event; non-applicable) [27]. The panel had access to the full record and their judgement was based on rich contextual information (indications for medications, dose, duration, life expectancy). Members first rated each recommendation independently and then met to discuss discrepancies.

2.6 Sample Size

We calculated the study size defining a 50 % discontinuation rate of PIMs at discharge in the intervention group as clinically relevant according to the perception of the research team, assuming a 20 % discontinuation rate in the control group, using the standard levels for type I and II errors ($\alpha = 0.05$ and $\beta = 0.8$), and assuming that the average number of PIMs in this population was 0.7 per patient, based on our previous study [18]. On this basis, 112 patients (56 per arm) were required. We aimed at 150 patients (75 per arm).

2.7 Statistical Methods

The control group and the intervention group were compared using the Student's *t*-test for normally distributed variables, the Mann–Whitney Wilcoxon test for non-normally distributed continuous variables, and the Chi-squared test or Fisher's exact tests for categorical comparisons.

Statistical analyses were performed using SPSS, version 20 for Windows (IBM Corporation, Armonk, NY, USA) and R software, version 2.12.0 (Free Software Foundation, Inc., Boston, MA, USA).

3 Results

3.1 Patient Characteristics

Figure 1 shows the patient flow from enrolment to follow-up. A total of 158 eligible patients were randomised. Twelve patients subsequently had to be excluded, resulting in 146 frail older patients for analysis (median age [P_{25} ; P_{75}] 85 years [81; 88], 63 % women, median ISAR score [P_{25} ; P_{75}] 3 [3; 4]). The intervention ($n = 74$) and control ($n = 72$) groups did not differ in terms of patient sociodemographics, geriatric features (ISAR score median 3, functional dependency [50 %], recent falls [45 %], malnutrition [29 %]), and number of medications (median, seven) [see Table 1].

Half of all patients were taking PIMs at home (see Table 1). Overall, 125 PIMs were detected. Eighty percent of PIMs belonged to the same six classes of medications aimed at the central nervous system and the cardio-vascular system. These were: benzodiazepines (n PIMs = 41; 33 % of all PIMs), antiplatelet agents (n PIMs = 19; 15 %), opiates (n PIMs = 13; 10 %), β -blockers (n PIMs = 10; 8 %), tricyclic antidepressants (n PIMs = 9; 7 %), and neuroleptics (n PIMs = 8; 6 %) [see Table 2]. In the intervention group, the IGCT geriatrician made recommendations that the 68 PIMs detected be discontinued.

3.2 Discontinuation of Potentially Inappropriate Medications (PIMs) at Discharge

The discontinuation at discharge of PIMs present on admission was twice as high in the intervention group as in the control group (39.7 vs. 19.3 %; odds ratio [OR] 2.75 [95 % confidence interval (CI) 1.22–6.24]; $p = 0.013$). This 20.4 % absolute difference in PIM discontinuation rate showed that five PIMs needed to be screened and advised to be stopped in order to yield one additional PIM discontinuation at hospital discharge. Although detecting differences in PIM discontinuation according to drug classes was beyond the scope of this study, our result showed that the PIM discontinuation rate of benzodiazepines tended to be higher in the intervention than in the control group (34.6 vs. 6.7 %; $p = 0.063$) [see Table 2].

At the patient level, the reduction in the prevalence of PIMs (i.e. patients having one or more PIM) did not differ between the intervention group and the control group (23.1 vs. 16.1 %; OR 1.5 [95 % CI 0.49–4.89]; $p = 0.454$).

However, the proportion of patients with at least one improvement to their drug treatment was higher for the intervention group than for the control group (25.7 vs. 13.9 %; $p = 0.034$).

3.3 One-Year Follow-Up and Clinical Importance of PIMs

The GPs of the 76 patients for whom PIMs were detected on admission were contacted after 1 year. Of these, 93 % responded. One-year follow-up data was thus obtained for 50 patients (see Fig. 1). The intervention group ($n = 26$) and the control group ($n = 24$) were comparable in terms of patient age, geriatric profile, and PIMs ($n = 48$ vs. 36) on admission.

The clinical importance of these 84 PIMs was evaluated by the panel of experts as follows—major: 29 % (e.g. ‘benzodiazepine or neuroleptics in patients who have had falls’); moderate: 37 % (e.g. ‘long-term opiates in those with recurrent falls’, ‘long-term neuroleptics (>1 month) in those with parkinsonism’); minor: 5 % (e.g. ‘theophylline as monotherapy in chronic obstructive pulmonary disease’). Seven recommendations were considered to be deleterious (8 %: ‘ β -blockers in those with diabetes mellitus and frequent hypoglycaemic episodes’ in patients with ischaemic disease [$n = 4$]; ‘vasodilator drugs with persistent postural hypotension’ [$n = 2$]; and ‘long-term opiates in those with recurrent falls’ in patients with severe pain requiring morphine [$n = 1$]). Other recommendations (21 %) were not discussed by the panel because of the low prevalence of the criteria due to insufficient information in patients’ medical records.

The 1-year follow-up showed that in both groups, the majority of PIMs that had been stopped during hospitalisation had not been restarted after hospital discharge (38 % [8/21] PIMs had restarted in the intervention group and 43 % [3/7] in the control group; $p = 0.999$). The higher the clinical importance, the lower the discontinuation rate: 25.0 % of major PIMs were discontinued compared with 32.3 % of moderate and 75.0 % of minor PIMs; however, deleterious PIM recommendations were mostly rejected (71.4 %).

4 Discussion

This study illustrates the positive role that systematic screening using the STOPP criteria can play in improving the appropriateness of medications in frail older inpatients. However, it also illustrates the limitations of this screening process. Half of frail older inpatients had PIMs on admission, according to STOPP. Identification and counselling by the IGCT successfully doubled the reduction of PIM

Fig. 1 Patient flow. *CGA* comprehensive geriatric assessment, *GP* general practitioner, *PIM* potentially inappropriate medication

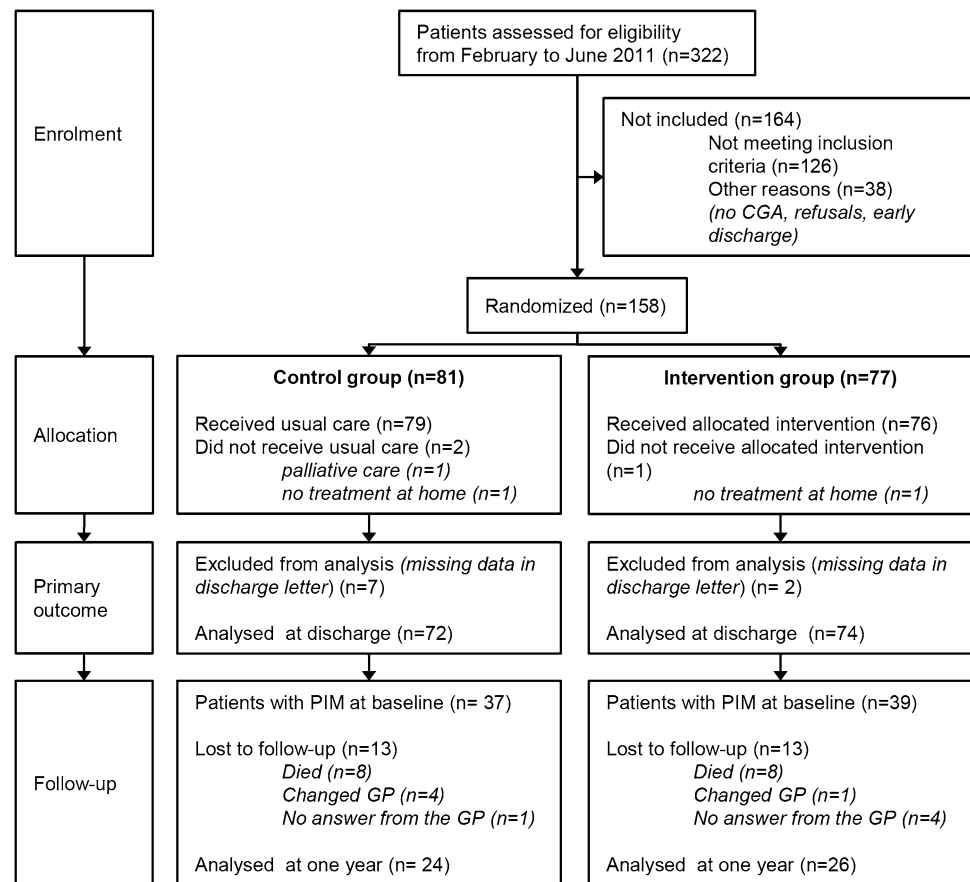


Table 1 Patient characteristics upon admission

	Control (N = 72)	Intervention (N = 74)	p-value
Sociodemographic data			
Female sex [n (%)]	49 (68.1)	43 (58.1)	0.213
Age [years; median (P25; P75)]	86 (81; 89)	84 (81; 87)	0.122
Living at home [n (%)]	65 (90.3)	66 (89.2)	0.829
Living at home and alone [n (%)]	28 (39.4)	30 (40.5)	0.892
Geriatric features			
ISAR score [median (P25; P75)]	3 (3; 4)	3 (3; 4)	0.457
Cognitive disorder [n (%)]	14 (19.4)	12 (16.4)	0.637
Malnutrition [n (%)]	20 (28.2)	22 (29.7)	0.836
Recent fall [n (%)]	28 (39.4)	37 (50.0)	0.201
Katz score [median (P25; P75)]	8 (7; 12)	8 (7; 11)	0.566
eGFR			
<50 ml/min [n (%)]	33 (45.8)	31 (41.9)	0.631
Drugs used at home			
Median (P ₂₅ ; P ₇₅)	7 (5; 9)	7 (5; 9)	0.987
Polypharmacy (≥5 drugs/day) [n (%)]	59 (81.9)	61 (82.4)	0.939
PIMs			
Patients with ≥1 PIM [n (%)]	37 (51.4)	39 (52.7)	0.874
Median (P ₂₅ ; P ₇₅)	1 (0; 1)	1 (0; 1)	0.710

eGFR estimated glomerular filtration rate, *ISAR* Identification of Seniors At Risk Score, *PIMs* potentially inappropriate medications

Table 2 Potentially inappropriate medications (PIMs) on admission and at discharge

PIM medication class ^a	Control group PIMs		Intervention group PIMs	
	Admission [n]	Discharge [n (% of admission PIMs)]	Admission, n	Discharge [n (% of admission PIMs)]
Total	57	46 (81)	68	41 (60)
Benzodiazepines	15	14 (93)	26	17 (65)
Antiplatelet	10	8 (80)	9	7 (78)
Opiates	5	3 (60)	8	5 (62)
β -blockers	4	4 (100)	6	5 (83)
TCA	4	3 (75)	5	2 (40)
Neuroleptics	4	4 (100)	4	3 (75)
Others	15	10 (67)	10	2 (20)

TCA tricyclic antidepressants

^a Context in which the drugs were considered to be PIMs: benzodiazepines with a long-acting profile used long-term, or in patients who had experienced falls; aspirin in patients with a past history of peptic ulcer disease without gastric protection, at a dose >150 mg/day, for primary cardiovascular prevention, to treat dizziness not clearly attributable to cerebrovascular disease, in patients with concurrent bleeding disorder, or in combination with warfarin without gastric protection; long-term opiates in patients who had experienced falls, or powerful molecules as first-line therapy for mild-to-moderate pain, prescribed for more than 2 weeks in patients with chronic constipation without the concurrent use of laxatives, or in patients with dementia; β -blockers in combination with verapamil, in diabetic patients with frequent hypoglycaemic episodes, or non-cardioselective β -blockers with chronic obstructive pulmonary disease; TCAs in patients with dementia, glaucoma, cardiac conductive abnormalities, or constipation, in patients also taking an opiate or calcium channel blocker, or in patients with prostatism or prior history of urinary retention; neuroleptics as long-term hypnotics, in patients who had experienced falls, or in patients with parkinsonism

prescriptions at discharge; however, many PIMs persisted at discharge and the proportion of patients with PIMs at discharge did not differ between groups. Most treatment modifications made during hospitalisation were maintained after discharge. This reinforces our opinion that hospital admission can be a good opportunity for medication review in older patients, but also highlights the important role GPs have to play in the further optimisation of prescribing.

This is one of the first studies to document the impact of IGCT on PIMs. Previous evaluative research on IGCTs has mainly focused not specifically on medications but on outcomes such as mortality, readmissions, or functional status [13]. Hogan et al. [28] showed a decrease in the total number of oral medications after the intervention of an IGCT, but appropriateness of prescribing was not evaluated. All the geriatricians involved in the IGCT at our hospital had worked with a consistent focus on the appropriateness of pharmacotherapy prior to this study. The CGA of the patient by the IGCT includes an evaluation of the drug regimen. This study shows that giving this medication review a framework, using STOPP, allows for improved discontinuation of inappropriate medications. Dissemination of geriatric pharmacotherapy knowledge in non-geriatric wards is useful. The limited effectiveness of the IGCT found in the present study is likely due to the advisory role of this structure. Geriatricians suggested modifications to prescriptions but did not modify the prescriptions personally. Compliance with the recommendations by the ward teams therefore remains a key determinant of effectiveness. This corresponds with what has been reported by other studies [10, 29]. Reasons to

reject recommendations could be further explored in future studies. Possible means of improving compliance are direct control by the IGCT over prescribing, selected patients and prioritised recommendations, mutual acknowledgement of specific competences between the ward and the IGCT, and the involvement of a clinical pharmacist.

The STOPP criteria are increasingly being used to describe the inappropriate use of medications by older patients in both primary and secondary care [16]. The prevalence of patients with at least one PIM in our study (52 %) corresponds with observations made in other cohorts with community-dwelling patients admitted to acute care (prevalence 35–59 %) [17–20, 30]. However, these studies were observational in nature, while ours was experimental. To our knowledge, there has been only one randomised controlled trial to date evaluating the effect of implementing the STOPP criteria in clinical practice, and that study was conducted by the authors of this tool. This therefore potentially affects the generalisability of the results [16]. The authors reported significant improvements in the appropriateness of treatment at discharge, according to the Medication Appropriateness Index (MAI) [21, 31]. The present study shows some similarities with this previous study: a similar study population, criteria applied by a physician, and subsequent oral and written counselling to the attending medical team. However, the previous study did not assess the clinical relevance of recommendations, as the present study has.

Our analysis provides new data on the validity and operationalisability of the STOPP criteria. In contrast to the criteria that were considered to be highly relevant by the

panel of experts (i.e. ‘benzodiazepines in patients who have had falls’ and ‘selective serotonin re-uptake inhibitors in patients with a history of hyponatraemia’), several other criteria were rated as deleterious when applied to individual cases. We would suggest considering either removing these criteria from the list or editing the list by adding explicit reasons for not applying the criteria in order to improve validity. This also confirms the notion that explicit tools should enhance but not replace good clinical judgement [1]. Finally, the proper application of several criteria required detailed information that was not always available in the electronic medical records (e.g. pain assessment or psychiatric history). This weakness was also emphasised when the STOPP criteria were applied in a community pharmacy setting [32]. The indication, dose, and therapy duration should all be taken into account as part of the medication review. The modest sample of PIMs assessed does not allow us to draw conclusions from the inverse relationship between the clinical importance of PIMs and discontinuation at 1 year observed in our results. However, it is true that the feasibility of discontinuation of PIMs varies according to the drug involved and the withdrawal plan required.

The high prevalence of PIMs at discharge in both groups shows that there is still room for improvement. Discontinuation of PIMs should be carried out as part of an integrated and interdisciplinary approach to optimise pharmacotherapy in older patients. This process should also involve the GP. We suggest a multistep approach—first, screening for patients who are most at risk of adverse drug events, then performing a medication review, possibly by a clinical pharmacist, with the help of the STOPP. Clinical pharmacists, working with a multidisciplinary geriatric team, have previously been shown to improve the appropriateness of prescribing in older patients [33] and to have an effect on STOPP drugs [34]. The implementation of STOPP should be embedded within the CGA for the following reasons: a systematic structured review of medication should be part of the global patient assessment; the other components of the CGA (medical, social, and functional) enhance the drug treatment review; and the process of the CGA is a good opportunity to implement the use of the tool.

This study has certain limitations. First, this was a monocentric study. The generalisation of these results to other IGCTs may therefore not be straightforward. In our setting, the IGCT had an advisory role only. The effect might have been greater had the team had direct control over prescriptions, which is the case in a few other IGCTs in Belgium [10]. Second, we did not evaluate the appropriateness of prescribing using other tools such as the MAI. This was because our main objective was to focus on the use of and effect of the STOPP criteria, specifically.

However, measuring the effect of the intervention on the MAI score would have strengthened our results. We also did not evaluate the effect on clinical outcomes such as adverse drug events, although we did provide interesting data on clinical relevance. The prevalence of PIMs was underestimated because ‘duplications’ were not taken into account. ‘Duplications’ have been reported to be highly prevalent by previous studies [19]. Finally, the optimisation of underprescribing using the Screening Tool to Alert doctors to the Right Treatment (START) was not evaluated [14, 35]. Furthermore, more extensive studies are needed to confirm our findings.

5 Conclusion

This study provides new insights on the use of STOPP criteria in the hospital setting through an IGCT. Discontinuation of PIMs at discharge is higher if the IGCT actively recommends discontinuing PIMs according to STOPP. In order to further improve the appropriateness of prescribing, it seems to be essential that the use of STOPP be adapted to the individual situation of the patient, that the most important criteria be focused on, and that there be active collaboration with GPs. Further data are also needed on the feasibility of discontinuing PIMs and on the predictive validity of explicit tools, namely the effect on relevant clinical, economic, and humanistic outcomes.

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