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A comparison of two tools to screen potentially inappropriate medication in internal medicine patients

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Summary

What is known: Potentially inappropriate medication (PIM) is an important issue for inpatient management; it has been associated with safety problems, such as increases in adverse drugs events, and with longer hospital stays and higher healthcare costs.

Objective: To compare two PIM-screening tools—STOPP/START and PIM-Check—applied to internal medicine patients. A second objective was to compare the use of PIMs in readmitted and non-readmitted patients.

Method: A retrospective observational study, in the general internal medicine ward of a Swiss non-university hospital. We analysed a random sample of 50 patients, hospitalized in 2013, whose readmission within 30 days of discharge had been potentially preventable, and compared them to a sample of 50 sex- and age-matched patients who were not readmitted. PIMs were screened using the STOPP/START tool, developed for geriatric patients, and the PIM-Check tool, developed for internal medicine patients. The time needed to perform each patient's analysis was measured. A clinical pharmacist counted and evaluated each PIM detected, based on its clinical relevance to the individual patient's case. The rates of screened and validated PIMs involving readmitted and non-readmitted patients were compared.

Results: Across the whole population, PIM-Check and STOPP/START detected 1348 and 537 PIMs, respectively, representing 13.5 and 5.4 PIMs/patient. Screening time was substantially shorter with PIM-Check than with STOPP/START (4 vs 10 minutes, respectively). The clinical pharmacist judged that 45% and 42% of the PIMs detected using PIM-Check and STOPP/START, respectively, were clinically relevant to individual patients' cases. No significant differences in the rates of detected and clinically relevant PIM were found between readmitted and non-readmitted patients.

What is new and conclusion: Internal medicine patients are frequently prescribed PIMs. PIM-Check's PIM detection rate was three times higher than STOPP/START's, and its screening time was shorter thanks to its electronic interface. Nearly half of the PIMs detected were judged to be non-clinically relevant, however, potentially overalerting the prescriber. These tools can, nevertheless, be considered useful in daily practice. Furthermore, the relevance of any PIM detected by these tools should always be carefully evaluated within the clinical context surrounding the individual patient.

Thierry Fumeaux and Nicolas Schaad contributed equally to the supervision of this work.

1 | BACKGROUND

The concept of potentially inappropriate medication (PIM) was introduced by Beers et al. 30 years ago.[1] The current definition of PIM includes the following: overprescription (a drug prescribed without a valid indication or with a contraindication); underprescription (a clinically indicated drug that was not prescribed); drug-drug or drug-disease interaction; and misprescription (referring to an indicated drug that has been incorrectly prescribed, such as duplicate therapy, inappropriate follow-up and incorrect medication dose or duration).[2,3]

In the literature, the rate of PIM varies greatly but is always significant (12.5%–77.3%).[2,4-7] Most of the published data have focused on geriatric patients, and it has been estimated that 21%–43% of elderly internal medicine patients, with comorbidities and polymedication, will be prescribed at least one PIM during their hospitalization.[8] General internal medicine patients are therefore at a high risk of PIM.[9]

A PIM thus represents a significant safety issue, one which has been associated with adverse drugs events, longer hospital stays, increased resource utilization, higher hospital readmission rates and increased healthcare costs.[2,3,10-13]

A recent systematic review[14] identified 14 different screening tools developed between 1991 and 2015 for detecting PIM. These included the Beers,[1] McLeold,[15] Laroche,[16] Norgep,[17] PRISCUS List[18] and STOPP/START criteria.[19] All these tools were developed specifically for geriatric populations, with STOPP/START mostly used in European countries.

PIM-Check is a more recently developed screening tool specially dedicated to hospitalized, adult, general internal medicine patients.[20] PIM-Check includes 160 statements (related to overprescribing, underprescribing, drug-drug interaction and suboptimal prescribing practice). Information on the major medical conditions and the list of medication used can be entered into the electronic version. This tool was developed using a Delphi methodology and the collaborative work of international experts in internal and hospital medicine. More details on the development and use of PIM-Check's electronic version are available in Appendix S1. Until recently, no validation of its use had been published.

This study's main objective was to compare the detection of PIM using STOPP/START and PIM-Check on a population of general internal medicine patients. We also aimed to compare the rate of PIMs detected in readmitted and non-readmitted patients.

2 | METHOD

2.1 | Study design and setting

This was a retrospective observational study of a randomly selected population of patients hospitalized in the general internal medicine ward of the regional non-university hospital in Nyon, Switzerland, in 2013. The analysis included 100 patients, half of whom were readmitted patients.

Readmitted patients were selected using the SQLape© (*Striving for high Quality Level and Analyzing of Patient Expenditures*) algorithm,[21] which is used nationwide in Switzerland to benchmark rates of potentially avoidable hospital readmissions as a quality of a care indicator.[22] SQLape© is based on administrative data and the 10th revision of the International Classification of Disease codes (ICD-10) for admissions and readmissions, to identify avoidable readmissions occurring within 30 days of discharge; it has a reported sensitivity and specificity of 96%.[23] Among all the patients (n = 95) who underwent a potentially avoidable readmission in 2013, 50 were randomly selected. Fifty age- and sex-adjusted non-readmitted patients were randomly sampled in the same period (the non-readmitted group).

2.2 | Data collection

Entry and discharge dates and dates of birth were extracted directly from the administrative database. Clinical information (active diagnosis, comorbidities, allergies, vaccinal status, laboratory results and lifestyle habits) was extracted from patients' electronic records (Cerner Soarian Clinicals®), and medication data came from electronic prescription software (Predimed®). A score for the burden of chronic disease, the Charlson comorbidity index, was calculated on the comorbidities reported in each patient's medical record.[24]

To guarantee patient confidentiality, all the data collected were anonymized and stored in a specific database (Access® version 2010; Microsoft Corp, Redmond, WA, USA).

2.3 | Screening tools

The STOPP/START and PIM-Check criteria were applied by a pharmacy student (SS) with no prior specific training in their use. STOPP/START was developed and validated as a screening tool for geriatric populations.[19] The updated French-language version was used[25,26] with some prespecified usage criteria (detailed documentation is presented in Appendix S1). PIM-Check was more recently developed and is applicable to hospitalized internal medicine patients.[20] All clinical information (medications used and major medical conditions) was entered into the tool's electronic version (www.pimcheck.org—version 1.1; March 2016). Laboratory results and major clinical observations cannot be automatically entered into either STOPP/START or the electronic version PIM-Check. Both tools were applied to the medical conditions and the list of medication used during the last 24 hours of the hospital stays.

2.4 | Ethical approval

The Human Research Ethics Committee of the Canton Vaud (CER-VD) approved the study protocol (#355/13) and its analysis of medication's implication in hospital readmissions.

2.5 | Outcome measures

The total number and various subtypes of PIM detected for each patient were counted, and the time required for each screening process was measured. Any PIM detected was then reviewed by a senior clinical pharmacist (ALB) and designated as clinically relevant or not, based on each patient's clinical context. The reasons for the non-validation of detected PIMs were documented and categorized as either missing data, not applicable to the clinical context, a PIM detection error or irrelevant (for PIM-Check's electronic version only, due to inadequate settings).

After the identification of a PIM, associations with potential causal factors (age, length of stay, number of comedications and Charlson comorbidity index)[24] were determined.

In a secondary analysis, the rates of PIMs validated by the senior clinical pharmacist were compared for readmitted and non-readmitted patients.

2.6 | Statistical analysis

All descriptive statistics (means, proportions, standard deviations and confidence intervals) were performed using Excel® (version 2010; Microsoft Corp, Redmond, WA, USA) and STATA® (version 13.1; StataCorp, Lakeway Drive, Texas, USA). All other statistical analyses (Student's/chi-square test and McNemar, binomial negative multivariate analysis) were performed using open-source R software (version 3.1.2, for Windows). P-values under .05 were considered statistically significant.

3 | RESULTS

3.1 | Patient sample

The sample included 100 patients (Table 1), with a total of 702 prescriptions for the whole population (mean of 7 drugs per patient, range 1-20).

3.2 | Primary outcome

The mean time for an analysis using PIM-Check was significantly shorter than with STOPP/START (4 ± 1 minutes vs 10 ± 3 minutes, respectively; $P < .05$). Totals of 1,348 and 537 PIMs were detected using PIM-Check and STOPP/START, respectively, with means of 13.5 and 5.4 PIMs per patient ($P < .001$); at least one PIM was detected for each patient. The categories of PIM detected are presented in Table 2. PIM-Check detected at least one overprescription in more patients than STOPP/START (86% vs 70%, respectively; $P = .003$),

but it detected at least one underprescription in fewer patients than STOPP/START (94% vs 100%, respectively; $P = .04$). Drug-drug interactions or suboptimal prescribing practice was not comparable, as the STOPP/START criteria do not detect them.

After evaluation, the clinical pharmacist considered that 45% and 42% of the PIMs detected using PIM-Check and STOPP/START, respectively, were clinically relevant. The reasons why some of the PIMs detected were not validated by the clinical pharmacist are displayed in Figure 1, and the proportion of validated PIMs for each tool is reported in Table 3.

Overall, after validation by the clinical pharmacist, PIM-Check detected 2.7 times more PIMs than STOPP/START (606 vs 223, respectively).

Table 4 reports the five most frequently validated types of PIM with each tool, classified by incidence and percentage of clinical validation.

After multivariate analysis, the number of drugs taken ($P < .018$) and the Charlson comorbidity index ($P < .034$) were both associated with the number of PIMs detected and validated using PIM-Check. Only the number of prescribed drugs taken was associated ($P < .02$) with the number of PIMs detected and validated using STOPP/START.

3.3 | Secondary outcome

There was no significant difference between the number of PIMs detected by each tool for patients who had experienced a potentially avoidable readmission and age- and sex-adjusted patients who had not been readmitted: 6.3 vs 5.8 PIMs detected for readmitted and non-readmitted patients, respectively, with PIM-Check ($P = 0.51$); and 2.2 vs 2.2 PIMs detected for readmitted and non-readmitted patients, respectively, with STOPP/START ($P = 0.95$).

4 | DISCUSSION

Our retrospective analysis of a sample of hospitalized internal medicine patients showed that PIMs are a common problem. They were detectable in all patient prescriptions when using screening tools such as PIM-Check or STOPP/START. PIM-Check detected 2.5 times more PIMs than STOPP/START (1,348 vs 537, respectively) and did this three times faster. PIM-Check therefore could be a better candidate than STOPP/START for screening for PIMs in hospitalized internal medicine patients, especially with regard to how quickly it produces results. Furthermore, PIM-Check's other advantage is that despite the similar percentage of validated, clinically relevant PIMs, the absolute number of relevant PIMs detected was higher, suggesting a greater power to reduce the overall number of PIMs. However, fewer than half of the PIMs detected by the student pharmacist were judged clinically relevant and validated by the clinical pharmacist, complicating the use of these tools. For both tools, the time needed for the untrained pharmacy student to analyse each patient was slightly longer than, but comparable to, that described in previously published data; as suggested, for clinical use,

Patients' characteristics	Study population (n = 100)	Readmitted group (n = 50)	Non-readmitted group (n = 50)
Age, mean (SD)	77.1 (13.8)	77.4 (13.9)	76.9 (13.7)
>65 years old,	84 (84%)	42 (84%)	42 (84%)
Female	66 (66%)	33 (66%)	33 (66%)
Length of stay, mean (SD)	5.6 (3.9)	6.6 (4.6)	4.6 (2.9)
1-6 days	71 (71%)	31 (62%)	40 (80%)
>6 days	29 (29%)	19 (38%)	10 (20%)
Number of drugs, mean (SD)	7.0 (3.6)	6.8 (3.1)	7.1 (3.8)
≥10 drugs	22 (22%)	9 (18%)	13 (26%)
Charlson comorbidity index:			
1-2	53 (53%)	23 (46%)	30 (60%)
3-4	20 (20%)	12 (24%)	8 (16%)
>4	9 (9%)	5 (10%)	4 (8%)
Comorbidity			
Cardiovascular disease			
Heart failure	20 (20%)	13 (26%)	7 (14%)
Myocardial infarction	10 (10%)	6 (12%)	4 (8%)
Peripheral vascular disease	3 (3%)	1 (2%)	2 (4%)
Cerebrovascular disease	11 (11%)	6 (12%)	5 (10%)
Dementia	15 (15%)	7 (14%)	8 (16%)
Chronic pulmonary disease	17 (17%)	7 (14%)	10 (20%)
Connective tissue disease	1 (1%)	1 (2%)	0 (0%)
Peptic ulcer disease	3 (3%)	1 (2%)	2 (4%)
Mild liver disease	6 (6%)	4 (8%)	2 (4%)
Hemiplegia	1 (1%)	1 (1%)	0 (0%)
Moderate-to-severe renal failure	17 (17%)	11 (22%)	6 (12%)
Diabetes			
Without organ damage	13 (13%)	3 (6%)	10 (20%)
With organ damage	6 (6%)	5 (10%)	1 (2%)
Cancer			
Solid tumour	19 (19%)	10 (20%)	9 (18%)
Leukaemia	2 (2%)	1 (2%)	1 (2%)
Lymphoma	1 (1%)	0 (0%)	1 (2%)
Metastatic solid tumour	2 (2%)	1 (2%)	1 (2%)

Results are presented as n (%) if not otherwise specified.

these tools could be applicable in less than 5 minutes.[4,27] Physicians already familiar with these screening tools can significantly shorten this time.[28]

The different detection rates of PIMs that these tools described in our population were mainly related to their construction: as previously described, PIM-Check includes 160 statements (36 related to overprescribing, 74 related to underprescribing, 16 related to drug-drug interaction and 34 related to suboptimal prescribing practice);[20] STOPP/START includes 115 statements (81 related to overprescribing (STOPP) and 34 related to underprescribing (START)),[25,26] with none on drug-drug interaction or suboptimal prescribing practice. Overall, 65% of the statements used by PIM-Check are not included in STOPP/

START and, inversely, 43% of the STOPP/START statements are not found in PIM-Check. These differences are mainly due to the types of populations for which the tools were developed and validated (internal medicine patients and geriatric patients).

A high rate of PIM has been found previously in elderly hospitalized internal medicine patients: using STOPP/START, Beers Criteria and ACOVE-3, at least one PIM was detected for 87.6% of patients.[29] Other studies have shown similar results using STOPP/START alone, ranging from 21% to 79% for STOPP criteria and from 23% to 74% for START criteria.[5,30,31] It is of note that there are as yet no published data available for PIM-Check regarding the detection of PIM in similar populations.

TABLE 2 Number of potentially inappropriate medications (PIMs) detected individually by each screening tool for all patients (n = 100)

	PIM-Check	STOPP/START
Number of PIMs detected	**1348**	**537**
Overprescription	264	171
Underprescription	633	366
Drug-drug interaction	131	-
Suboptimal prescribing practice	320	-
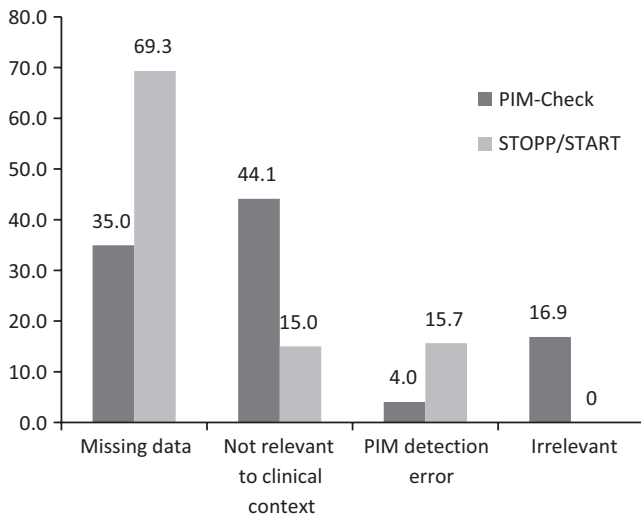
FIGURE 1 Reasons for the non-validation of detected potentially inappropriate medications (PIMs) using each screening tool (PIM-Check: n = 742; STOPP/START: n = 314)

An experienced clinical pharmacist evaluated all the screened PIMs, considering their clinical relevance and each patient's specific context. A high proportion of the PIMs detected were found to be not directly relevant, regardless of the screening tool used. Very few published data are available regarding the evaluation of PIMs as detected using these screening tools, but similar results have been found when drug-related problems were detected using a medication review, with a similar proportion of alerts judged to be not clinically relevant and therefore not reported to the prescribers.[32] In the present study, the experienced clinical pharmacist validated more of the PIMs detected

as overprescribing, drug-drug interactions and suboptimal prescribing practice than as underprescribing. One reason for this is that the information needed to validate a tool's detection of underprescription was often not available in the patient's medical record used by the pharmacist. As already shown, a precise medical history is needed for 88% of the START criteria.[33] The second reason why the pharmacist did not validate all the PIMs detected was that the drug was not adapted to the patient's clinical situation, based on all the available information. The main challenge to using these tools therefore is the need for accurate and complete medical information.[33,34]

With regard to the non-validation of the PIMs detected because they were "non-relevant to the clinical context," these items were not considered as appropriate to the patient's specific context, despite the fact that they are usually considered useful. For example, consider a patient suffering from heart failure but without a prescription for ACE inhibitors. In this context, PIM-Check would display the statement "Heart failure: Start ACEI or ARB." However, when the medication review was performed, the patient's blood pressure was not high enough to cope with the use of this medication. The statement would therefore be considered non-relevant for the specific patient's clinical context. To limit the number of non-relevant alerts, specific information about clinical observations, such as blood pressure and heart rate, must be integrated into the tool, as must major laboratory test results (eg sodium, potassium, creatinine).

The number of "irrelevant PIM" detected would not have been greatly reduced by an experienced pharmacist using PIM-Check. This subgroup of non-validated PIMs was related to unsuitable settings in the version 1.1 of PIM-Check. These settings were signalled to the developers of the electronic version of PIM-Check and corrected immediately after the conclusion of the present study.

The distribution of the types of PIM detected in our study was in line with previously published data, including the overprescription of benzodiazepines and PPIs, and evidence of the underprescription of oral anticoagulants and vitamin D supplements.[5,8,30–32,35–37] Moreover, our results confirmed previous data describing polymedication and comorbidities as risk factors for PIM.[29,38,39] Due to their designs, these two screening tools do not focus on similar types of PIM. To provide a better detection rate, the possibility of combining their use should be explored.

For the most frequently validated PIMs detected using both tools, the per cent of validation varied substantially (from 52% to

TABLE 3 Percentage and number of PIMs validated using both screening tools

	PIM-Check		STOPP/START	
	% validation	Validated PIMs (n)	% validation	Validated PIMs (n)
All PIMs detected	**45%**	**606**	**42%**	**223**
Overprescription	59%	156	78%	134
Underprescription	31%	196	24%	89
Drug-drug interaction	50%	66	-	-
Suboptimal prescribing practice	59%	188	-	-

TABLE 4 Five most frequently validated types of PIM, with the number and validation percentage, for each tool

	Number of PIMs validated	Number of PIMs before validation	Validation percentage
Five most frequently validated types of PIM with PIM-Check			
Overprescription: PPI—re-evaluate treatment dose and duration	40	42	95.2
Drug-drug interaction: Strong enzyme inducers and inhibitors	27	52	51.9
Overprescription: Be careful with drugs that prolong the QT interval	24	25	96.0
Overprescription: PPI—prescription with no valid indication	23	29	79.3
Underprescription: Diabetes mellitus—adjust therapy according to HbA1c targets	19	19	100
Five most frequently validated types of PIM with STOPP/START			
Overprescription: Medication prescribed without clinical indication (PPI, aspirin or statins)	43	51	84.3
Underprescription: Vitamin D supplements (cholecalciferol 800-1000 UI/day) in patients housebound or at risk of falls	29	38	76.3
Overprescription: PPI—at maximal dosage >8 weeks	20	20	100
Overprescription: Benzodiazepines for more >4 weeks	17	19	89.5
Underprescription: Oral anticoagulant with atrial fibrillation	7	13	53.8

100%) depending on the patient's specific clinical context, practitioners' prescribing practices (ie dosing HbA1c in diabetes patients during hospitalization) or the lack of information, as previously mentioned.

Finally, the rates and types of the PIMs detected were similarly distributed across both groups of patients in our population sample—those readmitted and not readmitted to hospital—as it has been previously reported in the literature.[40-42]

Our study has several strengths. First, both tools were used in similar conditions by one investigator, on the same population of patients, in a general internal medicine unit where physicians and pharmacists had been collaborating for years to improve the prescription process. Thus, the individual influences of the characteristics of the investigator, the patients and the physician in charge are expected to be very low. This type of analysis is also the best way to match real clinical conditions. Second, we chose a retrospective design to limit the influence of PIM screening on prescriptions by the physician in charge, which may have decreased the number of PIMs and limited the power of the analysis. Third, the tools were used by a pharmacy student with no clinical experience. This showed that they could be handled by inexperienced personnel—an ideal characteristic for screening tools. Fourth, the sample was randomly chosen from a population of patients presenting with the typically wide array of clinical conditions found in general internal medicine. Fifth, to the best of our knowledge, this is the first study to report on results comparing the PIM-Check electronic screening tool (specifically developed for internal medicine patients) and STOPP/START (mainly validated in geriatric populations).

Despite these strengths, our results must be interpreted with caution due to some methodological limitations. First, due to the study's retrospective design, missing data in patient records limited our ability to accurately evaluate each PIM detected using the screening tools. Some specific information, such as treatment durations or vaccinal status, is difficult to retrieve, even in prospective studies. Second, the analysis was performed on a random sample of patients, without a prior power calculation. Nevertheless, the high rate of PIMs detected allowed a very robust analysis. Third, the process of evaluating every PIM was performed by a single senior clinical pharmacist: before generalizing these results, a replication study should be performed based on a multidisciplinary evaluation process involving pharmacists and physicians. Another limitation was that we only evaluated the PIMs detected using the screening tools. Thus, the rate of undetected or false-negative PIMs could not be measured and the specificity of the screening tools could not be assessed. Finally, due to the small sample population studied, the comparison between the rates and types of PIM among readmitted and non-readmitted patients should only be considered exploratory and a hypothesis generator.

In conclusion, the present study shows that PIM is very common in general internal medicine, but that detection is possible using screening tools such as PIM-Check and STOPP/START, even by clinically inexperienced staff. These tools do seem to be highly sensitive, detecting PIM in the vast majority of patients, although almost half of the cases of PIM detected were not considered to be directly clinically relevant and there is an increased risk of overalerting the prescribing physician. The number of drugs prescribed and comorbidities could act as indicators for selecting the patients who would benefit most from screening using such tools. Before recommending their widespread clinical introduction, the effects of the regular use of such tools on the rate of PIM should be tested prospectively in clinical studies, using patient-centred outcomes such as significant adverse drug events or readmission rates. In this perspective, PIM-Check seems the more promising tool, as it is more sensitive and takes less time to use than STOPP/START. Both tools are interesting means of decreasing the risk of PIM, especially if their use is associated with a careful validation of their alerts by an experienced physician and/or a clinical pharmacist, taking into account the specific clinical context of the patient.

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SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.