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# Prevention of potentially inappropriate medication in internal medicine patients: A prospective study using the electronic application PIM-Check

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## Summary

**What is known**: Potentially inappropriate medication (PIM) is a risk factor for drug-related problems (DRPs) and an important inpatient safety issue. PIM-Check is a screening tool designed to detect PIM in internal medicine patients.

**Objective**: This study aimed to determine whether PIM-Check could help to identify and reduce DRPs.

**Method**: Prospective interventional study conducted on patients admitted to internal medicine wards in a university hospital between 1 September 2015 and 30 October 2015. Adult patients were included if they were hospitalized for more than 48 hours. Patients received either usual care (period 1 = control) or usual care plus medication screening by the wards' chief residents using PIM-Check (period 2 = intervention). An expert panel, composed of a clinical pharmacist, a clinical pharmacologist and two attending physicians in internal medicine, blinded to patient groups, identified DRPs.

**Results**: A total of 297 patients were included (intervention: 109). The groups' demographic parameters were similar. The expert panel identified 909 DRPs (598: control; 311: intervention). The mean number of DRPs per patient was similar in the control (3.2; 95% CI: 2.9-3.5) and intervention groups (2.9; 95% CI: 2.4-3.3) ($P$ = .12). PIM-Check displayed 33.4% of the 311 DRPs identified in the intervention group.

**What is new and conclusion**: In this study, PIM-Check had limited value, as the average number of DRPs per person was similar in both groups. Although one-third of DRPs counted in intervention group had been identified by PIM-Check, this did not lead to a reduction in DRPs. This lack of impact of PIM-Check on drug prescription may be explained by the number of alerts displayed by the application and hospital physicians' reluctance to modify the treatments for chronic conditions previously prescribed by general practitioners.

KEYWORDS
clinical decision support system, internal medicine patients, medication review, potentially inappropriate medication

  

## 1 | WHAT IS KNOWN AND OBJECTIVE

Potentially inappropriate medication (PIM) is a concept first proposed by Beers et al.[1] in the early 1990s; it focusses on geriatric patients. Potentially inappropriate prescribing refers to the quality of prescribing, including a drug's pharmacological appropriateness, data on safety and effectiveness.[2] The contemporary definition of PIM includes overprescription (medication without a valid indication or with a contraindication), underprescription (failure to prescribe a clinically indicated drug), misprescription (improper drug selection) and unwanted drug interactions.[2,3]

Potentially inappropriate medication is well described as a risk factor for drug-related problems (DRPs), which are an important issue for hospital inpatient safety and may lead to adverse drug events, increased length of stay, hospital admissions or readmissions and, therefore, increased healthcare costs.[2-4] Several studies have highlighted PIM as a frequent problem among geriatric patients. The incidence of PIM varies between 12.5% and 77.3% of patients, depending on the population studied and the tool used to detect it (eg Beers Criteria, STOPP-START and Priscus list).[2,5-8]

General internal medicine patients are also at a high risk of PIM.[9] Indeed, polymedication and multiple comorbidities are frequent among medicine patients, especially older ones. Indeed, most of tools developed to detect PIM were specifically conceived for geriatrics populations. A specific tool focusing on internal medicine patients—PIM-Check—was recently developed and validated using a Delphi method involving 40 experts from four French-speaking countries.[10] PIM-Check is available as an electronic application and alerts focus on overprescription, underprescription, misprescription and drug-drug interactions (DDIs).[10]

As previously suggested, integration into daily practice requires such PIM-screening tools to be easy to use and rapid, usually within the 5 minutes available for performing a medication review.[5,11] This prospective study's objective was to determine whether PIM-Check could help physicians to identify and prevent DRPs in internal medicine patients. The secondary objective was to assess this electronic application's ease of use for physicians during their daily practice.

## 2 | METHOD

### 2.1 | Study design and setting

This prospective study took place at the Geneva University Hospitals (Switzerland) in the general internal medicine department. Patients were prospectively recruited over two consecutive months, between 1 September 2015 and 30 October 2015. Patients included during September formed the control group and those included during October formed the intervention group.

Adult patients were included if they were hospitalized for more than 48 hours in one of the seven general internal medicine department wards taking part in the study. Patients who died during their hospital stay were excluded from the analysis.

During the October intervention period, patients were included in the study if their hospital admission process was supervised by one of the nine chief residents trained to use the electronic tool and an admission medication review utilized the PIM-Check.

### 2.2 | Interventions

During the *control period*, patients received usual care, and medication reviews were performed as usual by residents and chief residents during their medical rounds, without other specific support.

During the i*ntervention period*, patients received usual care plus specific medication screening by the chief residents using the PIM-Check application (version 1.0, 2015), within 24 hours of admission. If necessary, therefore, potential medication changes could be done within 48 hours of admission. After this delay, patients received usual care throughout their hospital stay. Chief residents had been specifically trained to use the electronic application (a one-hour training session).

The PIM-Check electronic tool's screening function was used for the medication review. It allowed a specific analysis of each patient's PIM, taking into account their comorbidities and medication. Of the 160 alerts registered in the tool, only those corresponding to preselected criteria are displayed.

### 2.3 | Outcome measures

Within 48 hours of hospital admission, anonymized data on every medication, laboratory result, comorbidity and active diagnosis were collected from the electronic medical records of every patient in the two groups. A score for the burden of chronic disease—the Charlson Comorbidity Index—was calculated from the chronic comorbidities listed in each patient's medical record.[12] All information related to the patients' dates of hospitalization was removed from their data sets, however.

#### 2.3.1 | Primary outcome

The study's primary outcome was the mean number of DRPs per patient 48 hours after hospital admission. These were identified by an expert panel comprising a senior clinical pharmacist, a senior clinical pharmacologist and two attending physicians from the internal medicine department. The panel analysed every patient's data, blinded as to the study period and group.

Each DRP identified was classified according to the Swiss Association of Public Health Administration and Hospital Pharmacists' (GSASA) classification.[13] The DRP subtypes were recorded (ie non-conforming with guidelines or contraindication, overprescription or duplicate therapy, DDIs, adverse drug events, inappropriate route of administration or galenic formulation, overdosage, underdosage, inappropriate monitoring, inadequate dosage according to physiological state, inappropriate treatment duration,

inappropriate time or frequency of administration, drug prescribed was unavailable, missing patient data and non-administered treatment). Therefore, the definition used in this study is a wide definition of all problems encountered with medication treatment and not only focused on PIM, defined as overprescription, underprescription, misprescription and unwanted drug-drug interaction. Therefore, the PIM-Check tool was not expected to eliminate all DRP encountered in the intervention group.

The clinical pharmacist assessed the clinical relevance of each DRP using a study-specific classification system (see Table S1), ranking them from 1 to 3 as: 1) DRP presenting a significant risk to the patient; 2) DRP presenting a moderate risk; and 3) DRP presenting a low risk to the patient or potential for long-term therapy optimization.

All the cases were discussed during weekly expert panel meetings, and DRPs were only noted as "identified" if validated by all the panel's members.

### 2.3.2 | Secondary outcomes

#### Electronic detection of DRPs in the intervention group using the PIM-Check application

The electronic detection of DRPs using the PIM-Check application was recorded on a specific server to ensure data protection and analyse the alerts generated by the application. The number of alerts displayed by the application was recorded. DRPs identified by the application for patients in the intervention group and validated by the expert panel were also recorded.

#### Usability of the electronic application

The electronic application's usability was evaluated from the results of a specific survey sent to all the chief residents in charge of patients during the intervention period. The following items were evaluated using a five-point Likert scale: (i) overall assessment of the electronic application (ie the application's relevance, whether it responds to a need and overall satisfaction); (ii) usability of the electronic application (ie ease of use, speed of display and graphic design); (iii) agreement with the alerts generated by PIM-Check (ie level of agreement, specificity and implementation); and (iv) further use (ie other medication review events using PIM-Check, such as at admission, during the stay and prior to discharge, or whether they would recommend it to other colleagues).

### 2.4 | Ethics committee approval

This study was submitted to the University Hospitals of Geneva's Ethical Committee on Health Research (CCER), which validated it as a quality improvement project. Therefore, no specific additional patient approval was considered necessary.

### 2.5 | Statistical analysis

Analyses were performed using a per-protocol design (ie only data on patients who participated in the whole study protocol were used) using GraphPad PRISM® for Mac (version 6.0, GraphPad, CA, USA). All data were summarized with descriptive statistical analyses (means, proportions and 95% confidence intervals) and specific statistical analyses (the Student's *t* test, chi-square test and Mann-Whitney non-parametric test). All reported *P*-values are two-tailed, and significance was assumed if *P*-value < .05.

## 3 | RESULTS

### 3.1 | Population characteristics

Four hundred and two patients fulfilling the inclusion criteria were hospitalized in the internal medicine wards during the study period. The study finally included 297 patients, with a mean age of 67 years old (range: 18-100). Of these, 188 of 200 patients (94%) were included for the control group, together with 109 of 202 patients (54%) for the intervention group. For these 109 patients included in the intervention group, the chief residents used the electronic tool PIM-Check for the medication review during the admission process.

As described in Table 1, the mean age, Charlson Comorbidity Index and number of drugs prescribed were similar for both groups.

A total of 3055 medications were prescribed to the overall study population, with a mean (SD) of 10.3 (4.5) per patient.

### 3.2 | Primary outcome: DRPs in the control and intervention groups

The percentages of patients presenting with at least one DRP were 88.3% (166/188) and 90.8% (99/109) in the control and intervention groups, respectively. The total number of DRPs detected in the overall study population was 909, with a mean of 3.1 DRPs (95% CI: 2.8-3.3) per patient. The mean number of DRPs in each group was similar: 3.2 DRPs per patient (95% CI: 2.9-3.5) and 2.9 DRPs per patient (95% CI: 2.4-3.3) for the control and intervention groups, respectively (*P*-value: .12). The distribution of DRPs in both groups is presented in Figure S1. The repartition of DRP subtypes among patients in the control and intervention groups was similar and is presented in Table 2.

The most frequent DRP subtypes were non-conforming with guidelines/untreated indication, followed by overprescription/duplicate therapy and then DDIs.

The clinical relevance of DRPs was similar in both groups: 32.3% and 37.0% posed a major risk, 43.8% and 39.2% posed a moderate risk and 23.9% and 23.8% posed a low risk, in the control and intervention groups, respectively (*P*-value = .3).

Among the 3055 drugs prescribed, 1104 (36.1%) were involved in the 909 DRPs. The most frequent drug classes involved were as follows: drugs for acid-related disorders (n = 101), antidepressants (n = 90), vitamin and mineral supplements (n = 90), drugs

**TABLE 1** Patient characteristics of the overall study population

| | Study population (n = 297) | Control group (n = 188) | Intervention group (n = 109) | *P*-value[a] |
|---|---|---|---|---|
| Age, mean (SD) | 67 (16) | 66 (17) | 68 (16) | .34 |
| >65 years old | 178 (59.9) | 110 (58.5) | 68 (62.4) | |
| >85 years old | 36 (12.1) | 19 (10.1) | 17 (15.6) | |
| Female sex, | 127 (42.8) | 82 (43.6) | 45 (41.3) | .69 |
| Charlson comorbidity index, mean (SD) | 2.2 (2.2) | 2.2 (2.2) | 2.3 (2.2) | .82 |
| 0-1 pts | 146 (49.2) | 95 (50.5) | 51 (46.8) | |
| 2-4 pts | 99 (33.3) | 61 (32.4) | 38 (34.9) | |
| >4 pts | 52 (17.5) | 32 (17.0) | 20 (18.3) | |
| Charlson comorbidities | | | | |
| Heart failure | 12 (4.0) | 5 (2.7) | 7 (6.4) | .11 |
| Myocardial infarction | 37 (12.5) | 17 (9.0) | 20 (18.3) | **.02** |
| Peripheral vascular disease | 23 (7.7) | 12 (6.4) | 11 (10.1) | .25 |
| Cerebrovascular disease | 32 (10.8) | 24 (12.8) | 8 (7.3) | .14 |
| Dementia | 18 (6.1) | 8 (4.3) | 10 (9.2) | .09 |
| Chronic pulmonary disease | 67 (22.6) | 38 (20.2) | 29 (26.6) | .18 |
| Connective tissue disease | 13 (4.4) | 10 (5.3) | 3 (2.8) | .29 |
| Peptic ulcer disease | 9 (3.0) | 7 (3.7) | 2 (1.8) | .36 |
| Mild liver disease | 19 (6.4) | 11 (5.9) | 8 (7.3) | .61 |
| Diabetes | 59 (19.9) | 31 (16.5) | 28 (25.7) | .06 |
| Moderate-severe renal disease | 39 (13.1) | 21 (11.2) | 18 (16.5) | .18 |
| Diabetes with organ damage | 24 (8.1) | 16 (8.5) | 8 (7.3) | .72 |
| Any tumour (within last 5 y) | 34 (11.4) | 26 (13.8) | 8 (7.3) | .09 |
| Lymphoma | 7 (2.4) | 5 (2.7) | 2 (1.8) | .65 |
| Moderate-severe liver disease | 5 (1.7) | 4 (2.1) | 1 (0.9) | .43 |
| Metastatic solid tumour | 18 (6 1) | 11 (5.9) | 7 (6.4) | .84 |
| AIDS | 7 (2.4) | 5 (2.7) | 2 (1.8) | .65 |
| Alcohol abuse | | | | |
| Previous | 19 (6.4) | 10 (5.3) | 9 (8.3) | .55 |
| Current | 51 (17.2) | 34 (18.1) | 17 (15.6) | |
| Tobacco use | | | | |
| Previous | 94 (31.6) | 50 (26.6) | 44 (40.4) | **.04** |
| Current | 74 (24.9) | 52 (27.7) | 22 (20.2) | |
| Drugs prescribed, mean;(SD) | 10.3 (4.5) | 10.3 (4.5) | 10.2 (4.6) | .50 |
| <5 drugs | 30 (10.1) | 21 (11.2) | 9 (8.3) | |
| 5-10 drugs | 134 (45.1) | 82 (43.6) | 52 (47.7) | |
| >10 drugs | 133 (44.8) | 85 (45.2) | 48 (44.0) | |

Bold = statistically significant value.
Results are presented as n (%), if not otherwise specified.
[a]Comparisons between the control and intervention groups determined using the chi-square and Mann-Whitney tests.

used in diabetes (n = 81), anti-infective drugs (n = 72), paracetamol (n = 58), lipid modifying agents (n = 43), nicotine replacement therapy (n = 42), antiplatelet drugs (n = 41), anticoagulants (n = 41), opioid analgesics (n = 40), and anxiolytics and hypnotics (n = 38). No significant differences were observed between the control and intervention groups regarding the drugs or therapeutic classes involved in DRPs.

## 3.3 | Secondary outcomes:

### 3.3.1 | Electronic detection of DRPs in the intervention group using the PIM-Check application

The PIM-Check application's screening function displayed 1499 alerts or a mean of 13.9 (95% CI: 12.5-15.2) per patient.

**TABLE 2** Distribution of drug-related problem (DRP) subtypes in both groups

| DRP subtypes | Control group Number (%) | Intervention group Number (%) |
|---|---|---|
| Untreated indication/non-conforming with guidelines | 158 (26.4) | 87 (28.0) |
| Overprescription—duplicate therapy | 143 (23.9) | 72 (23.2) |
| Drug-drug interactions | 83 (13.9) | 42 (13.5) |
| Adverse drug events | 51 (8.5) | 31 (10.0) |
| Inadequate dosage for physiological state | 37 (6.2) | 24 (7.7) |
| Inappropriate monitoring | 39 (6.5) | 21 (6.8) |
| Inappropriate route of administration or galenic formulation | 30 (5.0) | 13 (4.2) |
| Underdosage | 26 (4.3) | 3 (1.0) |
| Overdosage | 11 (1.8) | 7 (2.3) |
| Inappropriate time or frequency of administration | 12 (2.0) | 10 (3.2) |
| Inappropriate treatment duration | 3 (0.5) | 1 (0.3) |
| Drug prescribed unavailable | 2 (0.3) | 0 (0.0) |
| Missing patient data | 1 (0.2) | 0 (0.0) |
| Non-administered treatment | 2 (0.3) | 0 (0.0) |
| All DRPs | 598 (100.0) | 311 (100.0) |

Of the 311 DRPs identified in the intervention group, 33.4% (n = 104) had also been displayed by the electronic application, but no treatment modifications had been performed within 24 hours of the medication review.

### 3.3.2 | Usability of the electronic application

All the nine chief residents involved completed the survey. Eight of them were favourable towards the application, and seven were satisfied or totally satisfied with it and considered the application to be useful in a physician's daily practice. Seven found that the application was either easy or very easy use and rapid to use. All participants appreciated the software's ergonomic design. However, six physicians highlighted the high number of alerts displayed for each patient and regretted the lack of specificity. Regarding future use of PIM-Check, six physicians noted their willingness to use the application repeatedly during a patient's hospital stay, as a monitoring tool. Finally, eight physicians noted that they would recommend its use to colleagues or other healthcare professionals.

## 4 | DISCUSSION

This prospective study demonstrated the challenges of implementing an electronic screening tool in internal medicine wards when used by physicians at admission. The expert panel identified an average of 3 DRPs for each of the 297 patients included in the study. After physicians had used the PIM-Check application in the intervention group, no significant difference in the mean number of DRPs was observed compared to the control group. DRP subtypes and their clinical relevance were also similar in both groups, suggesting this electronic screening tool has not improved the resolution of clinically important DRPs in the intervention group. However, among the DRPs which the expert panel identified in the intervention group, one-third had been displayed by the electronic application. The chief resident physicians who were surveyed about their use of the PIM-Check application considered it accurate, useful, easy and rapid to use, as well as ergonomic. However, they also highlighted the high number of alerts displayed and the consequent lack of time available to select the most useful alerts.

As previously demonstrated, DRPs are a frequent issue for hospitalized patients.[14-17] The present study identified a mean of 3.1 DRPs per patient, and most patients had at least one DRP identified, which is consistent with previously published results.[14-18] Studies specific to general internal medicine patients found a mean number of DRPs varying between 2.1 and 3.0.[14,16,18] Therefore, patients hospitalized in general internal medicine are at just as high a risk of DRPs as geriatric patients.

Untreated indications, overprescription/duplicate therapy and DDIs were the main DRP subtypes encountered in the present study. This is in accordance with results previously published for hospitalized patients.[14,16,17]

The use of other screening tools to detect and manage PIM has been associated with improvements in pharmacotherapy. In a clinical trial conducted by Gallagher *et al*, using the STOPP-START screening tool to identify PIM was associated with a significant improvement in appropriate prescribing. This was sustained 6 months after discharge, thus reducing unnecessary polymedication, incorrect doses and potential DDIs.[19] The underuse of indicated drugs also improved

when using this screening tool.[19] Finally, decreases in the number of drugs prescribed, falls and costs have also been reported following the introduction of this specific tool in geriatric patients.[20]

Our study tried to demonstrate that an electronic screening tool, specifically aimed at internal medicine patients, could also improve pharmacotherapy. Unfortunately, our results showed no reduction in DRPs in the patients who underwent an electronic medication review using PIM-Check. Several reasons may explain the absence of a reduction in DRPs despite PIM-Check's propositions. First, the electronic medication review was time-consuming for physicians which could explain the low inclusion rate in the intervention group. Indeed, because PIM-Check is not directly linked to the patient's electronic medical record, the necessary data (comorbidities and medications) have to be transcribed, which could discourage them. Furthermore, the high number of alerts contributed significantly to the time needed for analysis. Second, some of the electronic tool's alerts do not require medication changes (17 of the 160 criteria relate to lifestyle changes, drug monitoring, treatment duration, patient education, etc.). Third, in some cases, physicians might not have felt comfortable changing medication, either because the electronic medication review took place too early in the hospital stay and thus patients' conditions were considered too unstable, or because they were reluctant to modify treatment plans established by general practitioners for chronic medical conditions. The decision to perform the electronic medication review soon after admission (first 24 hours) was dictated by organizational constraints: admission necessarily involves a specific moment dedicated to the analysis of a patient's condition, medical problems, medication and comorbidities—an analysis of the overall situation. It was therefore the best moment to ensure repeatable results.

The electronic PIM-Check screening tool can identify specific DRPs for general internal medicine patients; however, it cannot identify all of them. Indeed, some elements required for a complete medication review cannot be integrated into the PIM-Check algorithm (eg patient preferences, previously tried therapies and results obtained by the general practitioner, drug allergies and specific adverse effects). A patient-specific approach is therefore needed. Furthermore, this screening tool does not cover all the possible comorbidities and medical conditions (falls, anaemia, ascites, undernutrition, urinary incontinence, etc.) encountered in general internal medicine patients.

In several previously published articles, electronic clinical decision support systems have had a positive impact on healthcare outcomes and pharmacotherapy, enhancing prescribing quality and reducing PIM and adverse drug events.[21-23] The lack of positive impact on the number of DRPs could be related to healthcare professionals using PIM-Check (ie in the present study the chief resident physicians) and the moment of the analysis (ie during the admission process).

Medication reviews performed by clinical pharmacists and pharmacologists have been associated with reductions in the number of DRPs and improvement of the quality of pharmacotherapy.[24-26] Combining an electronic medication review integrated into the patient electronic medical record with interventions provided by specialized healthcare professionals (clinical pharmacists and pharmacologists) would seem to be an interesting strategy—one with the potential to overcome the difficulties encountered during the present study.

The results of our study need to be interpreted with regard to certain limitations. First, the retrospective analysis of DRPs limited the analysis to the data available on the medical charts. Some specific information could be missing from patients' files, and this could have influenced the results on the DRPs identified. Second, only 50% of the patients screened for the intervention group were included (thus, a PIM-Check medication review was not performed for all patients) due to time constraints from the physicians, which could have also influenced the results. However, considering the characteristics of the patients included, a selection bias seems implausible, given that both groups were almost comparable. Due to its single-centre design, the study's results would have to be observed in other general internal medicine wards before they could be generalized. Finally, the number of patients included in the present study would have not allowed us to perform a clinical outcomes analysis such as unplanned emergency consults, hospital admissions or readmissions.

## 5 | WHAT IS NEW AND CONCLUSION

In conclusion, to the best of our knowledge, this was the first study to test an electronic checklist with which general internal medicine physicians can detect PIM in order to decrease DRPs. The study showed no significant differences in the mean number of DRPs identified in the control and the intervention groups, although PIM-Check seemed to be useful for reducing DRP when used by chief resident during the admission process. Further studies are needed to identify the right healthcare professional to use the electronic tools and at which specific moment of the hospitalization.

However, to become a routinely used tool for performing medication reviews, PIM-Check will require some improvements, including its specificity, its inclusion in the electronic patient medical record and the support of specialized healthcare professionals (clinical pharmacists and pharmacologists) to prioritize interventions.

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## COMPETING INTEREST

No competing interests to declare.

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## SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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