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Predictive factors for clinically significant pharmacist interventions at hospital admission

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Abstract

Pharmaceutical care activities at hospital admission have a significant impact on patient safety. The objective of this study was to identify predictive factors for clinically significant pharmacist interventions (PIs) performed during medication reconciliation and medication review at patient hospital admission.

A 4-week prospective study was conducted in 4 medicine wards. At hospital admission, medication reconciliation and medication review were conducted and PIs were performed by the pharmaceutical team. The clinical impact of PIs was determined using the clinical economic and organizational (CLEO) tool. Clinical characteristics, laboratory results, and medication data for each patient were collected and analyzed as potential predictive factors of clinically significant PIs. Univariate and multivariate binary logistic regression were subsequently used to identify independent predictive factors for clinically relevant PIs.

Among 265 patients admitted, 150 patients were included. Among 170 PIs performed at hospital admission, 71 were related to unintentional discrepancies (41.8%) during medication reconciliation, and 99 were related to drug-related problems (DRPs) (58.8%) during medication review. Overall, 115 PIs (67.7%) were considered to have a clinical impact. By multivariate analysis, number of medications ≥ 5 ($P = .01$) based on the best possible medication history, and Charlson comorbidity index score ≥ 2 ($P < .01$) were found to be independent predictive factors of clinically significant PIs at hospital admission.

Identifying predictive factors of clinically significant PIs is valuable to optimize clinical pharmacist practices at hospital admission during both medication reconciliation and medication review. These 2 steps of the pharmaceutical care process improve medication safety at hospital admission.

Abbreviations: ATC = anatomical therapeutics classification, BPMH = best possible medication history, CKD EPI = chronic kidney disease epidemiology collaboration, CLEO = clinical economic and organizational, DRPs = drug related problems, NCC MERP = National Coordinating Council for Medication Error Reporting and Prevention, OTC = over the counter, PIs = pharmacist interventions, SFPC = French Society of Clinical Pharmacy, TdP = Torsade de Pointe.

Keywords: medication reconciliation, medication review, medication safety, patient hospital admission, pharmacist intervention, predictive factor

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1. Introduction

To optimize drug therapy and improve medication safety, clinical pharmacists have been developing many pharmaceutical care activities at different steps of the medication process, from medication reconciliation at hospital admission and medication review to medication reconciliation at hospital discharge.^[1–3] During pharmaceutical care activities, clinical pharmacists may perform pharmacist interventions (PIs), which are defined as “any action taken by a pharmacist that directly results in a change of patient management or therapy.”^[4]

Problems linked to inaccurate patient medication lists at hospital admission have emerged as a major concern for patient safety in recent years.^[5–10] Indeed, medication discrepancies—defined as differences between the best possible medication history (BPMH) and the first medication orders at hospital admission—have been reported to account for over half of medication errors^[11] and increase adverse drug events in hospital.^[12–14] Medication reconciliation at hospital admission has been endorsed by patient safety organizations in many countries as a good method to identify and correct medication discrepancies.^[15,16]

After conducting medication reconciliation, pharmacists also contribute to prevent drug related problems (DRPs) through

medication review by detecting inappropriate drug use or incorrect dose.^[17-19] PIs performed about unintentional discrepancies during medication reconciliation and DRPs during medication review both improve drug safety at hospital admission.

In France, legislation published in December 2016^[20] stipulates that clinical pharmacy activities are among one of the missions of hospital pharmacists. However, the integration of clinical pharmacists into the admission care process requires significant human resources. For example, Leguelinel-Blache et al^[10] revealed that the median time required to perform BPMH was 35 minutes (min) ($P=.0001$) for a median number of 7 ($Q25\%=5$; $Q75\%=10$) prescribed medications ($P<.05$). Moreover, the median time to achieve the medication discrepancy analysis has been reported to be 25 min and 15 min, respectively.^[10] Unfortunately, despite a nationwide willingness to extend clinical pharmacy activities, no additional human resources have been allocated to achieve this goal within the healthcare system. In order to improve the management of medications in hospitalized patients, it would appear essential to direct available resources towards activities that are most likely to yield meaningful PIs, as underscored by an evaluation of their clinical impact.

Indeed, PIs have different clinical impacts. Some PIs can prevent a theoretical or minimally adverse event, whereas others may avoid damage and even death. In a study by Cornish et al,^[21] most (61.4%) of the discrepancies detected during medication reconciliation were judged to have no potential to cause serious harm.

In our university hospital, a computerized prescription system is used for 163 beds (out of a total of 2365), spread over 5 medical wards. In these wards, at patient hospital admission, medication reconciliation is performed by a pharmacy student, and medication review is then performed by a senior qualified pharmacist with biological results, previous medical history and data collected during medication reconciliation. In usual practice, medication reconciliation and medication review are therefore not exhaustive in our institution because of insufficient human resources: about 25 medication reconciliations and reviews are performed at hospital admission every week in these wards. To enhance the efficacy of medication reconciliation and review, we tried to target patients at hospital admission in whom PIs would be likely to have a significant clinical impact.

The main objective of this study was therefore to identify predictive factors for clinically significant PIs performed during medication reconciliation and medication review at hospital admission. The prevalence and clinical impact of PIs performed during clinical pharmacy activities at hospital admission were also evaluated.

2. Materials and methods

2.1. Setting and population

A prospective study was conducted in 4 medical wards: infectious diseases (26 beds), internal medicine (54 beds), respiratory medicine (22 beds), and the endocrinology unit (24 beds) in a single French University Hospital (CHU Reims).

All consecutive patients admitted between October 22, 2015 and November 19, 2015 were screened. The medication reconciliation and medication review were performed up to 72 hours after patient hospital admission. Verbal informed consent was obtained from each patient who met the inclusion criteria. We excluded patients who could not speak French or who were unable to communicate clearly, patients transferred from another

ward, patients with fewer than 3 available sources of information for the medication reconciliation, and patients with an expected length of hospital stay less than 48 hours.

In our university hospital, clinical pharmacists are assigned to the clinical wards and involved in the provision of pharmaceutical care. They are not routinely involved in documenting patients' admission medication histories, unless specifically requested to do so. This function is primarily the responsibility of the pharmacy students (master's degree in pharmacy) following a standardized hospital-wide protocol. Each pharmacy student is assigned to a ward. In the ward, the pharmacy student is required to collect information from at least 3 sources (such as patient and family interviews, review of personal medical records, or phone calls to the patient's general practitioner, nurse, and community pharmacist) to compile the best possible medication history (BPMH). Afterward, the pharmacy student compares the BPMH with the patient's admission medication in order to detect discrepancies and clarifies directly with the medical team whether the discrepancy(ies) is(are) intentional or unintentional.

During our study, a specific process has been set up to conduct medication reconciliation and medication review in all consecutive patients admitted (Fig. 1). Firstly, the pharmacy student performed the medication reconciliation following the standardized hospital-wide protocol as described above but reported the discrepancy(ies) to the clinical pharmacist assigned to the ward. The pharmacist and the pharmacy student together clarified the discrepancy(ies) with the medical team, and the prescription was corrected by the physician or the medical resident if unintentional discrepancy(ies) was(were) detected. Right after, the pharmacist performed medication review to detect any DRP(s), taking account of the patient's admission biology results, medication and medical history, patient interview, allergies, drug doses, whether the indication is consistent with recommendations, drug interactions, and the cost of the drug (Fig. 1). This medication review corresponds to level 3 of the French Society of Clinical Pharmacy (SFPC) recommendations.^[22] DRPs were transmitted by the pharmacist (by phone or directly in the ward) to the medical team, in order to correct the medication order.

In our study, PIs included both unintentional discrepancies reported during medication reconciliation and DRPs reported during medication review at hospital admission. Discrepancies were defined as unintentional when a hospital physician or medical resident confirmed that it was indeed an error and made the appropriate correction to the prescription. Discrepancies included: omission or addition of a medication, substitution of an agent, changes in dose, frequency, or route of administration. It was the responsibility of the medical team to make changes in the inpatient medication orders when unintentional discrepancies were brought to their attention. DRPs were classified using the instrument validated by the SFPC.^[23] Any identified DRPs, as well as its description, the drug and ATC drug class involved, the outcome of the intervention were all recorded in a dedicated follow-up file for active monitoring.

The time needed to perform the BPMH was collected after each medication reconciliation by pharmacy students. The time needed to perform medication review was evaluated by the experienced pharmacists. Time spent to perform medication review per day was correlated to the number of medication review.

2.2. Data collection and outcomes

Data were collected using a structured and standardized data collection form. Administrative data included ward and length of

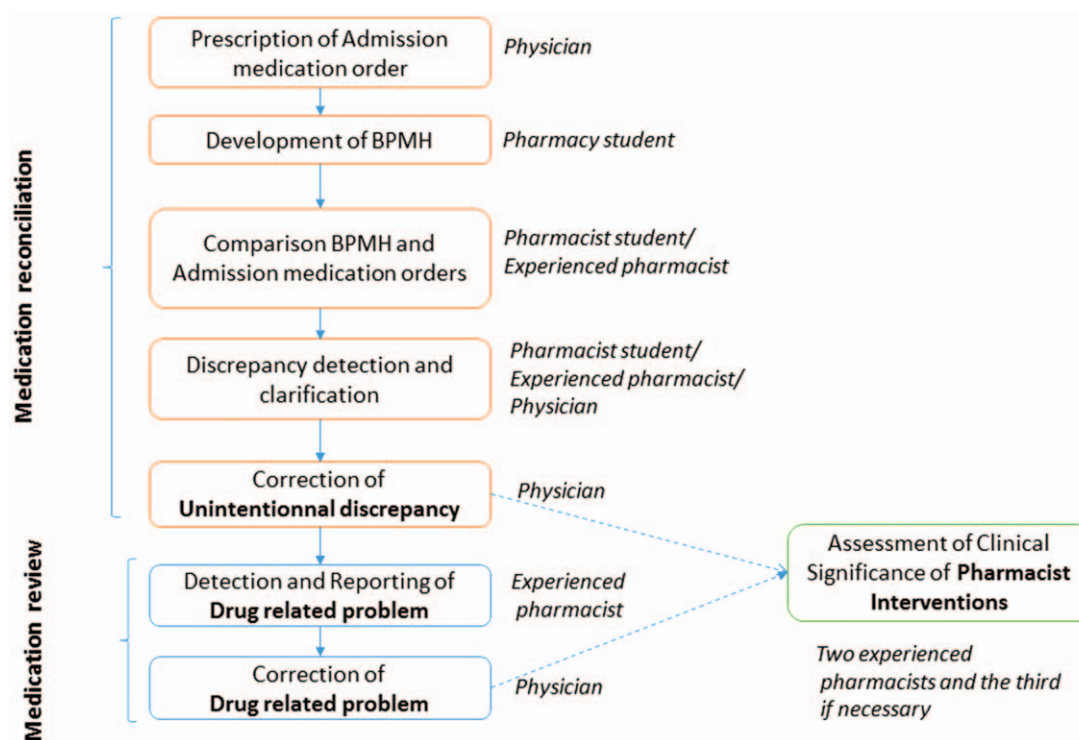


Figure 1. Study design and respective contribution of each health professional at hospital admission.

stay. Clinical characteristics included age, gender, body mass index (BMI), Charlson Comorbidity Index Score,^[24] and history of allergy. Laboratory results included estimated glomerular filtration rate (according to the Chronic Kidney Disease Epidemiology Collaboration, CKD EPI expressed per 1.73 m²) and Child Pugh score. Medication data included both over the counter (OTC) medications and prescription medications (all formulations), number of medications on the BPMH, number of unintentional discrepancies. All drugs were classified according to the ATC classification. During medication review, the type and outcome of each DRP were classified according to the stratification tool of the SFPC.^[23]

The clinical impact of all PIs, including both unintentional discrepancies and DRPs at hospital admission, was assessed by 2 independent and experienced pharmacists from outside our institution, who were not involved in the phases of medication reconciliation or review. The pharmacists rated the severity of PIs according to the Clinical, Economic and Organizational (CLEO) tool developed by the SFPC.^[25] The CLEO tool was inspired by Hatoum's tool^[26] and the National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP) index.^[27] The "Clinical impact" scale ranges from -1C (negative) to 4C (positive) (Supplementary file 1, <http://links.lww.com/MD/C142>). To illustrate this scale, a PI scored at level 2C can prevent harm that requires further monitoring/treatment, but does not lead to prolongation of hospitalization. Each rater reviewed data collection forms, pharmacy patient profiles, and medical record orders. If disagreement occurred, a consensus was reached by a third pharmacist independently. Clinically significant PIs were defined as a clinical impact $\geq 2C$ and only these PIs were considered to apply logistic regression analyses.

2.3. Ethics statements

This study was declared to the National authority for the protection of privacy and personal data (CNIL), under the number 1987678. The Research Ethics committee of the University Hospital of Reims (Groupe de Réflexion Ethique Clinique et Soins) waived the need for informed consent due to the observational nature of the study. Patient records and information were rendered anonymous prior to analysis. Oral informed consent was obtained from all participants.

2.4. Statistical analysis

Descriptive statistics were reported as number (percentage) for categorical variables; and as mean \pm standard deviation for continuous variables with normal distribution; or median and interquartile range for non-normally distributed variables. Cohen's kappa coefficient was used to assess inter-rater reliability of the clinical impact.^[28]

Bivariable and multivariable binary logistic regression modeling were conducted to identify possible variables independently associated with a clinically significant PI at hospital admission. The variables included were: administrative data, clinical characteristics, laboratory results and medication data described above. We preselected these variables that we can have in routinely practices at patient's admission. The following variables were tested by univariate analysis: number of medications on BPMH (≥ 5 drugs vs < 5 drugs); high-risk ATC drug class on BPMH (ATC B—blood and blood forming organs; C—cardiovascular system; J—general anti-infectives for systemic use; N—nervous system) (≥ 1 , nil);^[29] Charlson comorbidity index score (≥ 2 , < 2). Variables with a significant relationship ($P < .20$) by univariate analysis were included in the

multivariable model. Results were presented as odds ratios (OR) and 95% confidence intervals (CI). Statistical analyses were performed using SAS version 9.4 software (SAS Institute, Inc., Cary, NC). The significance level was $P < .05$.

3. Results

3.1. Description of study sample

During the 4-week period of this study, 265 patients were admitted (Fig. 2). Among these, 150 patients (56.6%) met the inclusion criteria. The reasons for patient exclusion were: patients transferred from another ward (28 patients), anticipated length of stay < 48 hours (40 patients) and lack of information sources for compilation of the BPMH (47 patients).

The characteristics of the 150 patients included are shown in Table 1. Over half (55.3%) was aged over 65 years, and a majority (74.5%) was taking at least five drugs. Approximately 89% had a prescription of one or more drugs belonging to high-risk ATC medication classes at hospital admission.

3.2. Types of PIs and their clinical impact at hospital admission

The number of PIs was 1.13 per patient with an overall prescriber's acceptance rate of 86.5% (71/71 PIs performed during medication reconciliation and 76/99 performed during medication review). The percentage of PIs performed during medication reconciliation (41.8%) was lower than that performed during the medication review (58.2%). Conversely, the percentage of PIs with a clinical impact was 34.7% ($n=59$) during medication reconciliation, and 32.9% ($n=56$) during medication review (Table 2). The most frequent types of PIs performed during both medication reconciliation and medication review at hospital admission were respectively those related to omissions of drugs (44 PIs/29.4%) and incorrect dose (27 PIs/19.4%). Of the 170 PIs identified, 67.7% had a clinical impact ($\geq 2C$ level according to CLEO tool). Inter-rater reliability of clinical reliability was good, with a kappa coefficient of 0.822

Table 1

Characteristics of the 150 patients included in the study.

Characteristic	Value
Age, years (mean \pm SD)	65.3 \pm 19.5
< 65 years	67 (44.7)
65–74 years	28 (18.7)
≥ 75 years	55 (36.6)
Male	62 (41.3)
Unit	
Respiratory medicine	23 (15.3)
Internal medicine	63 (42.0)
Infectious diseases	23 (15.3)
Endocrinology	41 (27.4)
Length of stay, days (mean \pm SD)	11.3 (2–39)
Allergy	39 (26)
Charlson Comorbidity Index Score (mean \pm SD)	2.6 (0–11)
Body Mass Index (mean \pm SD), kg/m ²	27.4 (13.4–57.8)
CKD EPI Clearance	
> 60 mL/min	103 (68.7)
30–60 mL/min	37 (24.7)
≤ 30 mL/min	9 (6.0)
Child Pugh score	
A	61 (40.7)
B	7 (4.7)
Missing value	82 (54.6)
Number of medications on BPMH (mean \pm SD)	7.5 (0–23)
Number of medications on BPMH ≥ 5	112 (74.5)
High-risk ATC drug class on BPMH (≥ 1)	
C: Cardiovascular organ	103 (68.7)
N: Nervous system	96 (64.0)
B: Blood and blood forming organ	73 (48.7)
J: Anti-infectious for systemic use	12 (8.0)
OTC medication use	56 (37)

ATC = anatomic therapeutic chemical, BPMH = Best Possible Medication History, CKD-EPI = Chronic Kidney Disease Epidemiology Collaboration, OTC = over the counter. Data are number (%) unless otherwise indicated.

[95%CI 0.74–0.90]. Discussion was required to reach a consensus in 19/170 (11%) cases (9 unintentional discrepancies and 10 DRPs). Estimated time to perform a BPMH was 33 min (15–60 min). Estimated time was 224 min per day (25–540 min) to perform 2.5 medication reviews (3–58) which represented about 9 min for each medication review at hospital admission.

3.3. Predictive factors of clinically significant pharmacist interventions at hospital admission

Univariate analysis identified 4 variables that were related to clinically significant PIs, namely presence of nervous system medication (class N ATC) or cardiovascular medication (class C ATC) on the BPMH, ≥ 5 number of medications on the BPMH, and a Charlson Comorbidity Index score ≥ 2 , as shown in Table 3.

By multivariable logistic regression model, 2 variables were found to be independently associated with a clinically significant PI at hospital admission, namely ≥ 5 medications on the BPMH (OR 3.03; 95% CI 1.29–7.51), and a Charlson Comorbidity index score ≥ 2 (OR 3.13; 95% CI 1.49–6.71).

There was no significant association between clinically significant PIs and other factors, such as age, estimated glomerular filtration rate or length of stay.

Among patients included, 81 patients (54%) had ≥ 5 medications on the BPMH and/or a Charlson Comorbidity index score ≥ 2 .

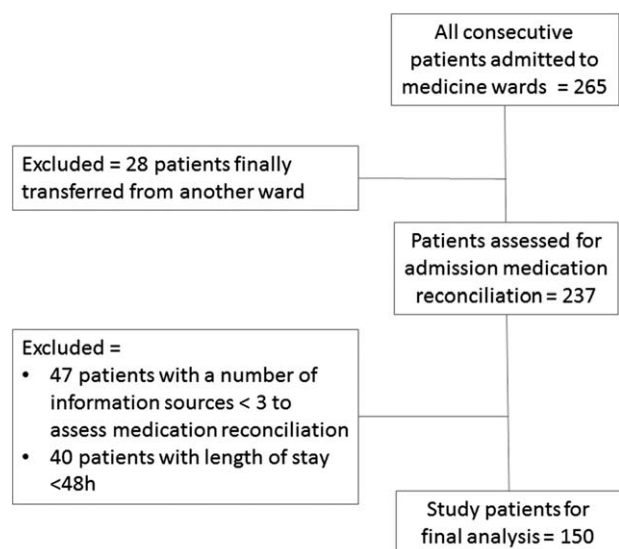


Figure 2. Flowchart of patient inclusion and exclusion at hospital admission.

Table 2

Types of pharmacist interventions (PIs) and their clinical impact performed during medication reconciliation and medication review at hospital admission.

Pharmacists interventions	Type of problems	Clinical impact of PIs
Unintentional discrepancies (71/41.8%)	Omission (50/29.4%) Wrong dose (13/7.7%) Wrong frequency of administration (8/4.7%)	-1C: Negative (0/0%) 0C: Null (0/0%) 1C: Minor (12/7.0%) 2C: Moderate (54/31.8%) 3C: Major (4/2.3%) 4C: Lethal (1/0.6%)
Drug-related problems (99/58.2%)	Nonconformity to guidelines/Contra indication (31/18.2%) Improper administration (20/11.8%) Incorrect dose (33/19.4%) Untreated indication (12/7.0%) Drug without indication (3/1.8%)	-1C: Negative (0/0%) 0C: Null (7/4.1%) 1C: Minor (36/21.2%) 2C: Moderate (44/25.9%) 3C: Major (10/5.9%) 4C: Lethal (2/1.2%)
Total (170/100%)	Nonconformity to guidelines/Contra indication (31/18.2%) Improper administration (28/16.5%) Incorrect dose (46/27.1%) Untreated indication (12/7%) Drug without indication (3/1.8%) Omission (50/29.4%)	-1C: Negative (0/0%) 0C: Null (7/4.2%) 1C: Minor (48/28.2%) 2C: Moderate (98/57.6%) 3C: Major (14/8.2%) 4C: Lethal (3/1.8%)

ATC=anatomical therapeutic chemical, PIs=pharmacist interventions, N=170 problems=170 pharmacist interventions.

4. Discussion

This study investigates the factors that predict PIs with a clinical impact during medication reconciliation and medication review activities performed at admission of a patient to hospital, which is a transition known to be particularly vulnerable to medication errors. Results of this study help us to target patients at hospital admission in whom PIs would be clinically relevant to enhance efficacy of medication reconciliation and review.

Risk factors for PIs have been analyzed in previous studies. However, to the best of our knowledge, our study is the first that included PIs performed both during medication reconciliation and medication review at hospital admission, as well as identifying predictive factors for clinically significant PIs only. In fact, at hospital admission, medication reconciliation and medication review are 2 closely related steps of the pharmaceutical care process that should not be assessed separately. Indeed, we found that PIs with a clinical impact were performed as frequently during medication reconciliation as during medication review (34.7% vs 32.9%, respectively).

This study shows that during medication reconciliation and medication review at hospital admission, we performed an average of 1.13 PIs per patient. Our results confirm the high rate of unintentional discrepancies at admission medication reconciliation (0.42 error per patient), which is consistent with findings of

other studies.^[30–32] Similarly, during medication review, we found an average of 0.40 DRP per patient, which is similar to a previous report from a French study,^[18] who also found an average of 0.4 DRP per patient, while Bates et al^[33] reported an average of 0.53 DRP per patient.

The most common types of PIs were those related to medication omission (29.4%) and use of the incorrect dose (19.4%). This is consistent with previous studies showing that the majority of unintentional discrepancies were medication omission^[30–32,34] during medication reconciliation, and that the majority of DRPs were incorrect dose during medication review at hospital admission.^[18,35]

In our study, the evaluation of the clinical impact of PIs showed that 67.7% had a clinical impact (level $\geq 2C$ according the CLEO tool), indicating that they had the potential to avoid patient harm. Previous studies demonstrated that approximately 28–91% of medication discrepancies identified during medication reconciliation were clinically significant.^[36] To the best of our knowledge, the true incidence of serious or fatal medication errors identified during medication reconciliation and medication review remains unknown during the admission care process. However, comparison to other studies appears to be difficult mainly because of differences in the definition of “severity” between the different tools, the methods used to evaluate these errors subjectively, and differences in patient populations.

Table 3

Identification of predictive factors at hospital admission for pharmacist interventions with a clinical impact. Laboratory results, clinical characteristics and medication data were analyzed with univariate and multivariable regression.

Variable	Univariate model			Multivariate model		
	OR	95%CI	P-value	OR	95%CI	P-value
Nervous system drug class on BPMH	2.33	1.17–4.64	.02			ns
Cardiovascular drug class on BPMH	2.49	1.20–5.14	.01			ns
Number of medication on BPMH ≥ 5	4.67	2.01–10.83	<.001	3.03	1.29–7.51	.01
Charlson Comorbidity index score ≥ 2	4.36	2.12–8.96	<.001	3.13	1.49–6.71	<.01

ATC=anatomic therapeutic chemical, BPMH=Best Possible Medication History, CI=confidence interval, ns=nonsignificant, OR=odds ratio.

Our study found that more than 5 medications on the BPMH was an independent predictive factor of clinically significant PIs, with an OR of 3.03 during both medication reconciliation and medication review at hospital admission. During admission medication reconciliation, Leguelinel-Blache et al^[10] also revealed that more than 7 medications on BPMH were correlated with the risk of an unintentional discrepancy. Other researchers found a correlation between unintentional discrepancies and the number of drugs at hospital admission.^[29,37–39]

We also identified a Charlson Comorbidity score ≥ 2 as a predictive factor for clinically significant PIs. Other studies have suggested that a higher number of comorbidities was independently associated with the risk of at least one DRP in hospitalized patients with advanced age.^[40] Cabello et al^[41] revealed that the presence of >4 comorbidities was an independent predictive factor of adverse drug reaction-related death. In our study, we used the Charlson Comorbidity score index to classify comorbid conditions and to assess the seriousness of comorbid disease. The Charlson index includes renal impairment and liver disease. When testing renal clearance and Child Pugh score separately and without weighting, no association between the variables was found.

Conversely, Gleason et al^[38] demonstrated that age ≥ 65 years was a risk factor for unintentional discrepancies at hospital admission. But, compared to this study,^[38] our PIs were performed during both medication reconciliation and medication review at hospital admission. Furthermore, in our study, PIs were found to be related to comorbidity-related factors rather than age itself and patients' age repartition in our study is older than Gleason et al (respectively 55% and 36% of patients < 65 years).

In our study, cardiovascular and nervous system drug classes on the BPMH were associated with a clinically significant PI at hospital admission by univariate analysis, but not by multivariable analysis. Gleason et al. showed that the cardiovascular medication class frequently resulted in errors at hospital admission.^[38] Cardiovascular and nervous drugs classes have been identified as risk factors for adverse events.^[42–44] These results could possibly be explained by the smaller number of patients included.

QTc interval prolongation or Torsades de Pointe (TdP) was not evaluated for each patient in this study. Several studies described risk factors for TdP.^[45,46] Some of these are routinely obtained (sex, smoking) during admission care process but several risks cannot be implemented in routinely clinical practices such as a baseline electrocardiogram, serum magnesium or calcium. In our study, these laboratory results could not be obtained routinely at hospital admission and then evaluated as possible variable independently associated with a clinically relevant PI. However, during our routinely practice, in case of drug interaction with a risk of drug-induced QTc interval prolongation or TdP, we perform PIs to propose electrocardiogram and serum potassium monitoring.

In this study, pharmacy students performed the BPMH, which was then verified by an experienced clinical pharmacist, like in the study by Cornish et al.^[21] Pharmacists, as drugs' experts, are expected to acquire more accurate and complete BPMH's than other health care providers such as physicians, nurses, and medical students, as shown in previous studies.^[47,48] Moreover, when there is a shortage of clinical pharmacists, integrating trained pharmacy students into the pharmaceutical care process to perform simple tasks such as patient medication history, can help to free up senior pharmacists for other tasks that require more highly developed skills.^[49]

The time needed to perform the BPMH and to perform medication review was consistent with findings of other

studies.^[10,32] These pharmaceutical care activities require a lot of human resources but they must be performed as soon as possible after patient's hospital admission. It means that specific human resources should be allocated to this practice in the wards and it explains the importance of prioritizing patients according predictive factors for clinically significant PIs. In our study, we could have prioritize 81/150 patients applying these 2 independent predictive factors to perform pharmaceutical care activities at admission care process.

This study had some limitations. First, it was conducted in general medicine wards and patients' medical conditions at admission were not collected, that is why the results may not be generalizable to other settings. Secondly, active monitoring of medication reconciliation and review in 4 wards was performed for all patients for a short study period only. This is due, in part, to the lack of human resources, to pharmacists' time constraints (about 1 pharmacist for 250 beds) and to a computerized prescription system not fully deployed (163 beds out of a total of 2365). Some studies have shown that pharmacist-led medication reconciliation is a cost effective process.^[48,50] Our clinical activity will prioritize all patients with these 2 predictive factors at hospital admission. Thirdly, statistical analyses for medication data were performed on ATC drug classes but not on individual drug. A further study on a larger panel of patients could evaluate on one or more individual drugs as predictive factor for clinically significant PIs at hospital admission. Fourth, despite excellent agreement between raters for the evaluation of the clinical impact of PIs, assessment by a physician would have provided a multidisciplinary perspective that would certainly be useful and informative. Fifth, we did not analyze the cumulative effects of multiple medication errors for a single patient, and only used the highest harm level to analyze patient-level risk factors. Hence our ratings may underestimate preventable harm. Finally, thresholds of continuous variables (example the number of medications) were performed before statistical analyses. We did not test several thresholds to avoid multiplicity of tests resulting in an increased alpha risk.

5. Conclusion

Compiling the findings from our study and prior studies emphasizes the importance of incorporating pharmacists into the whole medication reconciliation and medication review at hospital admission to perform PIs. In this study, ≥ 5 medications on the BPMH and a Charlson Comorbidity score ≥ 2 were found to be predictive factors for a clinically significant PI at hospital admission. These results are helpful for prioritization of patients during the admission care process in medical wards. Further studies are necessary to identify predictive factors specific to each medical specialty, and to assess predictive factors in other clinical medical and surgical wards.

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References

- [1] Bond CA, Raehl CL, Franke T. Clinical pharmacy services and hospital mortality rates. *Pharmacotherapy* 1999;19:556–64.
- [2] Hellström LM, Bondesson A, Höglund P, et al. Impact of the Lund Integrated Medicines Management (LIMM) model on medication appropriateness and drug-related hospital revisits. *Eur J Clin Pharmacol* 2011;67:741–52.

- [3] Kaboli PJ, Hoth AB, McClimmon BJ, et al. Clinical pharmacists and inpatient medical care: a systematic review. *Arch Intern Med* 2006;166:955–64.
- [4] Dooley MJ, Allen KM, Doecke CJ, et al. A prospective multicenter study of pharmacist initiated changes to drug therapy and patient management in acute care government funded hospitals. *Br J Clin Pharmacol* 2004;57:513–21.
- [5] Steurbaut S, Leemans L, Leysen T, et al. Medication history reconciliation by clinical pharmacists in elderly inpatients admitted from home or a nursing home. *Ann Pharmacother* 2010;44:1596–603.
- [6] Michels RD, Meisel SB. Program using pharmacy technicians to obtain medication histories. *Am J Health Syst Pharm* 2003;60:1982–6.
- [7] Rodehaver C, Fearing D. Medication reconciliation in acute care: ensuring an accurate drug regimen on admission and discharge. *Jt Comm J Qual Saf* 2005;31:406–13.
- [8] Mergenhausen KA, Blum SS, Kugler A, et al. Pharmacist- versus physician-initiated admission medication reconciliation: impact on adverse drug events. *Am J Geriatr Pharmacother* 2012;10:242–50.
- [9] Farley TM, Shelsky C, Powell S, et al. Effect of clinical pharmacist intervention on medication discrepancies following hospital discharge. *Int J Clin Pharm* 2014;36:430–7.
- [10] Leguelinel-Blache G, Arnaud F, Bouvet S, et al. Impact of admission medication reconciliation performed by clinical pharmacists on medication safety. *Eur J Intern Med* 2014;25:808–14.
- [11] Rozich JD, Howard RJ, Justeson JM, et al. Standardization as a mechanism to improve safety in health care. *Jt Comm J Qual Saf* 2004;30:5–14.
- [12] Tam VC, Knowles SR, Cornish PL, et al. Frequency, type and clinical importance of medication history errors at admission to hospital: a systematic review. *Can Med Assoc J* 2005;173:510–5.
- [13] Bates DW, Spell N, Cullen DJ, et al. The costs of adverse drug events in hospitalized patients. Adverse Drug Events Prevention Study Group. *JAMA* 1997;277:307–11.
- [14] Boockvar KS, Blum S, Kugler A, et al. Effect of admission medication reconciliation on adverse drug events from admission medication changes. *Arch Intern Med* 2011;171:860–1.
- [15] World Health Organization. 2013 Assuring medication accuracy at transitions in care. Standard operating protocol fact sheet. Available at: <http://www.who.int/patientsafety/implementation/solutions/high5s/en/>. Accessed May 23, 2017.
- [16] The Joint Commission. 2006 Sentinel event alert. January 25, 2006. Available at: http://www.jointcommission.org/assets/1/18/SEA_35.PDF. Accessed May 25, 2017.
- [17] Bedouch P, Sylvoz N, Charpiat B, et al. French Society of Clinical Pharmacy's Act-IP© Group. Trends in pharmacists' medication order review in French hospitals from 2006 to 2009: analysis of pharmacists' interventions from the Act-IP© website observatory. *J Clin Pharm Ther* 2015;40:32–40.
- [18] Bedouch P, Charpiat B, Conort O, et al. Assessment of clinical pharmacists' interventions in French hospitals: results of a multicenter study. *Ann Pharmacother* 2008;42:1095–103.
- [19] Lenssen R, Heidenreich A, Schulz JB, et al. Analysis of drug-related problems in three departments of a German University hospital. *Int J Clin Pharm* 2016;38:119–26.
- [20] Ordonnance n° (2016-1729 du 15 Décembre 2016 relative aux pharmacies à usage intérieur. Available at: <https://www.legifrance.gouv.fr/affichTexte.do?cidTexte=JORFTEXT000033616692&categorieLien=id>. Accessed February 28, 2017.
- [21] Cornish PL, Knowles SR, Marchesano R, et al. Unintended medication discrepancies at the time of hospital admission. *Arch Intern Med* 2005;165:424–9.
- [22] Bedouch P, Charpiat B, Roubille R, et al. Site internet de la Société française de pharmacie clinique pour l'analyse des interventions pharmaceutiques: finalité, mode d'emploi et perspectives. *J Pharm Clin* 2007;26:40–4.
- [23] Allenet B, Bedouch P, Rose FX, et al. Validation of an instrument for the documentation of clinical pharmacists' interventions. *Pharm World Sci* 2006;28:181–8.
- [24] Quan H, Li B, Couris CM, et al. Updating and validating the Charlson comorbidity index and score for risk adjustment in hospital discharge abstracts using data from 6 countries. *Am J Epidemiol* 2011;173:676–82.
- [25] Vo TH, Charpiat B, Juste M, et al. Development of a multidimensional scale "CLEO" for evaluation of clinical, economic, and organizational impacts of a pharmacist intervention. *Int J Clin Pharm* 2014;37:184–5.
- [26] Hatoum HT, Hutchinson RA, Witte KW, et al. Evaluation of the contribution of clinical pharmacists: inpatient care and cost reduction. *Drug Intell Clin Pharm* 1988;22:252–9.
- [27] National Coordinating Council for Medication Error Reporting and Prevention. NCC MERP index for categorizing medication errors 2011. Available at: <http://www.nccmerp.org/types-medication-errors>. Accessed July 28, 2017.
- [28] Cohen J. A coefficient of agreement for nominal scales. *Educ Psychol Meas* 1960;20:37–46.
- [29] Suggett E, Marriott J. Risk factors associated with the requirement for pharmaceutical intervention in the hospital setting: a systematic review of the literature. *Drugs Real World Outcomes* 2016;3:241–63.
- [30] Cornu P, Steurbaut S, Leysen T, et al. Effect of medication reconciliation at hospital admission on medication discrepancies during hospitalization and at discharge for geriatric patients. *Ann Pharmacother* 2012;46:484–94.
- [31] Lau HS, Florax C, Porsius AJ, et al. The completeness of medication histories in hospital medical records of patients admitted to general internal medicine wards. *Br J Clin Pharmacol* 2000;49:597–603.
- [32] Quéllennec B, Beretz L, Paya D, et al. Potential clinical impact of medication discrepancies at hospital admission. *Eur J Intern Med* 2013;24:530–5.
- [33] Bates DW, Boyle DL, VanderVliet MB, et al. Relationship between medication errors and adverse drug events. *J Gen Intern Med* 1995; 10:199–205.
- [34] Climente-Martí M, García-Mañón ER, Artero-Mora A, et al. Potential risk of medication discrepancies and reconciliation errors at admission and discharge from an inpatient medical service. *Ann Pharmacother* 2010;44:1747–54.
- [35] Blix HS, Viktil KK, Moger TA, et al. Characteristics of drug-related problems discussed by hospital pharmacists in multidisciplinary teams. *Pharm World Sci* 2006;28:152–8.
- [36] Mekonnen AB, McLachlan AJ, Brien JE. Pharmacy-led medication reconciliation programmes at hospital transitions: a systematic review and meta-analysis. *J Clin Pharm Ther* 2016;41:128–44.
- [37] Hellström LM, Bondesson Å, Höglund P, et al. Errors in medication history at -hospital admission: prevalence and predicting factors. *BMC Clin Pharmacol* 2012;12:9.
- [38] Gleason KM, McDaniel MR, Feinglass J, et al. Results of the Medications at Transitions and Clinical Handoffs (MATCH) study: an analysis of medication reconciliation errors and risk factors at hospital admission. *J Gen Intern Med* 2010;25:441–7.
- [39] Becerra-Camargo J, Martínez-Martínez F, García-Jiménez E. The effect on potential adverse drug events of a pharmacist-acquired medication history in an emergency department: a multicentre, double-blind, randomised, controlled, parallel-group study. *BMC Health Serv Res* 2015;15:337.
- [40] Urbina O, Ferrández O, Grau S, et al. Design of a score to identify hospitalized patients at risk of drug-related problems. *Pharmacoepidemiol Drug Saf* 2014;23:923–32.
- [41] Pardo Cabello AJ, Del Pozo Gavilán E, Gómez Jiménez FJ, et al. Drug-related mortality among inpatients: a retrospective observational study. *Eur J Clin Pharmacol* 2016;72:731–6.
- [42] Davies EC, Green CF, Taylor S, et al. Adverse drug reactions in hospital in-patients: a prospective analysis of 3695 patient-episodes. *PLoS One* 2009;4:e4439.
- [43] Thomsen LA, Winterstein AG, Søndergaard B, et al. Systematic review of the incidence and characteristics of preventable adverse drug events in ambulatory care. *Ann Pharmacother* 2007;41:1411–26.
- [44] Kanjanarat P, Winterstein AG, Johns TE, et al. Nature of preventable adverse drug events in hospitals: a literature review. *Am J Health Syst Pharm* 2003;60:1750–9.
- [45] Tisdale JE, Jaynes HA, Kingery JR, et al. Development and validation of a risk score to predict QT interval prolongation in hospitalized patients. *Circ Cardiovasc Qual Outcomes* 2013;6:479–87.
- [46] Vandael E, Vandenberk B, Vandenberghe J, et al. Risk factors for QTc-prolongation: systematic review of the evidence. *Int J Clin Pharm* 2017;39:16–25.
- [47] Reeder TA, Mutnick A. Pharmacist- versus physician-obtained medication histories. *Am J Health Syst Pharm* 2008;65:857–60.
- [48] Carter MK, Allin DM, Scott LA, et al. Pharmacist-acquired medication histories in a university hospital emergency department. *Am J Health Syst Pharm* 2006;63:2500–3.
- [49] Buckley MS, Harinstein LM, Clark KB, et al. Impact of a clinical pharmacy admission medication reconciliation program on medication errors in "high-risk" patients. *Ann Pharmacother* 2013;47:1599–610.
- [50] Karnon J, Campbell F, Czoski-Murray C. Model-based cost-effectiveness analysis of interventions aimed at preventing medication error at hospital admission (medicines reconciliation). *J Eval Clin Pract* 2009;15:299–306.