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Research Article

# Identification of Risk Factors for Medication Errors in Hospital Geriatric Departments

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## Abstract

**Purpose:** Given limited human resources in France's healthcare system, this study aimed to identify the predictive factors of unintentional medication discrepancies (UD) (described as unintentionally changes, adds or omits medication taken by a user prior to admission) in the elderly, in order to help prioritize which patients should undergo Medication Reconciliation (MR) upon hospital admission.

**Methods:** A single-centre ancillary observational study was conducted using data for patients who were included in ConcReHosp study between 03, 2016 and 02, 2019 and who were randomized to the arm that received MR. The risk of UD was assessed on the basis of MR patients' demographic, clinical and drug characteristics.

**Results:** 188 patients were included with a mean age of 86 years ± 6.5 years. A total of 240 UD were discovered in 104 patients (55.3%). After multivariate analysis, both hospital admission via the emergency department (OR=3.8; 95% CI 1.5-10.0) and having more than 7 medications in one's Best Possible Medication History (Exhaustive as possible list of a patient's usual prescribed treatments) (OR=2.3; 95% CI 1.1-4.9) were significantly associated with the presence of at least one UD. Conversely, renal clearance <30 mL/min (OR=0.4; 95% CI 0.2-0.8) and hospitalization for a neurological issue (excluding dementia) (OR=0.4; 95% CI 0.2-1.0) were significantly related to the absence of any UD.

**Conclusion:** The problem of targeting patients when performing MR is generalized internationally. To date, no prioritization factors have been defined. This work identifies a limited number of factors for targeting at-risk patients. Nevertheless, a medico-economic analysis in terms of efficiency is also necessary. The savings made by improving medication safety in the patient care pathway could assist in recruiting of pharmacists in order to generalize MR in the French hospital context.

**Keywords: Medication reconciliation; Medication errors; Unintentional medication discrepancies; Risk factors; Elderly patients**

## Introduction

Transitions of care in the clinical pathway constitute periods of vulnerability for patients in terms of the continuity of existing prescribed medication treatment. Medication Errors (ME), which is by definition avoidable, may occur due to incomplete or poorly communicated information. It is estimated that up to 75% of patients have at least one ME (also known as Unintentional Medication Discrepancy (UD)) in their prescribed treatments (omission of treatment, incorrect prescription, etc.) at hospital admission [1]. Saint-Germain et al. [2] recorded 316 UD in 117 patients (58.5%) among the 200 patients admitted to a geriatric ward, with an average of 2.7 UD per patient.

Similar observations have been made internationally, for example in Spain where Rodriguez et al. [3] found 359 UD in 145/206 patients (70.4%) admitted to a geriatric ward. In 2006, the World Health Organization (WHO) launched the international High 5sinitiative [4], which aimed to facilitate the development, implementation and evaluation of Standard Operating Procedures (SOPs) to tackle frequent and potentially serious patient safety problems. This initiative was built through a partnership between the Commonwealth Fund, the WHO, the Joint Commission International, and the initiative's founding countries Germany, Australia, Canada, the United States of America, New Zealand, the Netherlands and the United Kingdom.

France joined the High 5s initiative in 2009, and jointly developed the Medication Reconciliation project, which specifically focuses on the accuracy of drug prescription at transitions of care in the patient pathway (i.e., hospital admission, discharge and transfer). The results of this work highlighted that Medication Reconciliation (MR) was a means to prevent and intercept ME by ensuring that the patient medication information transmitted between healthcare professionals at transition points was complete and accurate [4]. Medication reconciliation at hospital admission entails the comparison-undertaken by a pharmacist-of an exhaustive as possible list of a patient's usual prescribed treatments (called the Best Possible Medication History (BPMH)) with the list of medications prescribed by the hospital doctor at admission (called the Admission Medication Order (AMO)).

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This comparison makes it possible to highlight Intentional Medication Discrepancies (ID)-such as deliberate treatment modifications by the prescribing hospital doctor-and UD. These UD can cause serious adverse events during hospitalization [1,5,6] which in turn can lead to complications, prolonged hospital stays, and an avoidable resulting additional cost. Medication reconciliation guarantees: i) medication continuity, with a reduction in ME; ii) a reduction in hospitalizations because of iatrogenesis, and iii) better control of health expenditure, by reducing iatrogenesis-associated costs. Furthermore, medico-pharmaceutical (i.e. joint doctor and pharmacist) collaborations lead to a stronger culture of safety in terms of prescribed medication, with the optimisation of prescriptions during discussions based on pharmaceutical analysis and therapeutic relevance.

Order No. 2016-1729 (December 15, 2016) [7] introduced the objective of clinical pharmacy in France, defined as any action in collaboration with the other members of a healthcare team which contributes to the safety, relevance and efficiency of the use of healthcare products and also contributes to the quality of care, by involving patient. This order implicates pharmacists as key players in MR. However, although MR is absolutely necessary, it is time consuming. Furthermore, no new human resources have been deployed to MR in France. Leguelinel-blache et al. [8] concluded that a median time of 35 minutes was needed to perform MR. Accordingly, not all patients in a healthcare facility can have it. The patients who were eligible to participate in the Medication Reconciliation project (see above) were over 65 years of age, had been hospitalized after admission to the emergency department, in a short-stay department. The French National Authority for Health (HAS) recommends prioritizing MR for hospitalized populations most at risk of UD. However, despite the many risk factors found (age, polypharmacy, etc.) in the literature [9], no specific patient profile has yet been identified for MR prioritization.

The French health establishments that have implemented MR to date have unanimously identified the need to combine MR with a medico-economic analysis focusing on efficiency, when targeting patients most at risk of UD, thereby optimizing the use of care. In contexts where no additional human resources are allocated to perform MR, it is essential to accurately target most-at-risk patients among the geriatric population who should be given priority when it comes to MR during their hospital stay [10]. The objective of our study was to identify profiles of patients at risk of UD in order to prioritize those who should have MR in hospitals.

## Methods

### Study design and participants

This was a single-centre ancillary observational study conducted using data from patients included in the ConcReHosp study (NCT02734017) [11], from March 2016 to February 2019 in two medical departments (a post-emergency department and a geriatric short-stay department) in Marseille, France, who benefited from retroactive MR (i.e. after the AMO) at hospital admission in line with the French HAS recommendations [10]. ConcReHosp is a randomized trial comparing care provided to persons who have MR both at hospital admission and discharge with the usual hospital care provided without MR. The objective was to assess the impact of medico-pharmaceutical-based MR on the rate of re-hospitalization and/or death 30 days after discharge. The patients included were over 65, had social security cover, were living in France and provided consent to participate. Patients who already had another hospitalization planned within 30 days of discharge were excluded. For the present ancillary study, only data from the MR arm of the ConcReHosp study were used.

Two groups of patients were defined: those for whom at least one UD was observed during MR on admission (UD ≥ 1), and those with no identified UD (UD=0).

The study's registered number is RGPD 2020-74 and was conducted according to the reference methodology MR-004 approved by France's National Commission for Informatics and Freedoms (CNIL). In accordance with French law, the approval of a Committee for Personal Protection (CPP) was not necessary as this was a non-interventional retrospective study based on the use of existing data and had no separate purpose.

### Outcomes

To meet the primary objective, the demographic and medical factors associated with the risk of UD were explored. To meet the secondary objectives, the types of UD observed were described, and the duration and cost of hospital stays depending on the presence or not of UD at hospital admission were compared.

### Data collection

The following data were collected from computerized records:

**Potential risk factors for UD:**

- Demographic data and admission procedures for hospitalization: age, sex, living place before hospitalization (home, nursing home or follow-up and rehabilitation facility and emergency department admission;

Medical and drug data:

- Medical history (cardiovascular pathology, respiratory pathology, bone fracture, bacterial or viral infection, surgical history including neurosurgery, urology, nephrology, gastrointestinal pathology, endocrine system or orthopaedics);
- Comorbidities including cardiovascular pathologies (including arterial hypertension, Atrial Fibrillation (AF), others cardiac rhythm disorders, heart failure, ischemic heart disease and thrombotic disease), respiratory pathologies (asthma, chronic obstructive pulmonary disease and respiratory failure), neurological pathologies (including epilepsy and Parkinson's disease), dementia pathologies (including Alzheimer's disease and other cognitive disorders), depression, anxiety, others psychiatric disorders, dermatological, rheumatological, osteoporosis, ophtalmologic, oto-rhino-laryngological, endocrinopathy, gastrooesopheal disorders, hemogram disorders, cancer and hematologic malignancies, autoimmune disease, alcoholism, smoking, recurrent falls, benign prostatic hyperplasia and lower-limb prostheses;
- Reason for hospitalization (Infection, cardiovascular, respiratory, hematological, metabolic pathology, delirium, non-rheumatic pain, dizziness, psychiatric pathology, deterioration of general condition (asthenia+anorexia+weight loss), neurological pathology, loss of functional autonomy, falls, rheumatic pathology, iatrogenesis).
- Weight, height and Body Mass Index (BMI). Patients with cachexia or with a BMI under 21 kg/m$^2$ were considered

undernourished. Overweightness and obesity were considered if they were mentioned in the medical file or if the BMI was between 25 and 29.9 kg/m² and ≥ 30 kg/m², respectively.

- Renal function was estimated by calculating creatinine clearance according to the Cockcroft-Gault equation. Patients with a creatinine clearance under 30 mL/min were considered to have severe renal impairment, while those with a clearance under 15 mL/min were considered to have end-stage renal disease.
- The number of drugs prescribed.

**Descriptive UD data:**

- Number of UD on admission (as highlighted by MR) and UD type (omission, different dose, wrong frequency, wrong drug, wrong galenic form, incorrect administration route and error in therapeutic follow-up (such as proportion of folate not being measured when folic acid supplement is prescribed)).
- Drug group involved in the UD (according to the Anatomical Therapeutic Chemical Classification System): A (Alimentary tract and metabolism), B (Blood and blood-forming organs), C (Cardiovascular system), D (Dermatologicals), G (Genito-urinary system and sex hormones), L (Antineoplasic and immunomodulating agents), M (Musculo-skeletal system), N (Nervous system), R (Respiratory system), S (Sensory organs), Other (Homeopathy, parapharmacy, oral nutritional supplements).

**Data related to the hospital stay:**

- Length and cost of stay, these data being collected from the hospital's medico-administrative database.

### Statistical analysis

Continuous variables were expressed as means with their standard deviation, and, where appropriate, with their extreme's values, while qualitative variables were expressed in numbers and percentages.

The qualitative parameters were compared between the two groups (UD yes/no) using a Chi-squared or Fisher's exact test, depending on the application conditions, while the quantitative parameters were compared using either the Student's t-test or the Mann-Whitney U test when the conditions for the t-test were not met.

A multivariate analysis was then performed by taking into account all the variables associated with the occurrence of at least one UD with a p <0.10 in the univariate analysis using logistic regression. The results were expressed using Odds Ratios (OR), 95% confidence intervals (95% CI) and the corresponding p-value. The significance threshold was set at 5%. All analyses were performed using IBM SPSS® Statistics software version 20.

## Results

### Characteristics of the study population

Between March 2016 and February 2019, 188 patients over 65 years of age were included in the ConcReHosp study. All had MR at hospital admission. The majorities was women (71.8%), and mean age was 86 years ± 6.5 years old (70 years - 99 years old). One hundred and eight-four (97.9%) had multiple pathologies, 159 (84.6%) had more than 5 treatments in their AMO, while 136 (72.3%) had more than 7 drugs in their BPMH. On average, the number of International Nonproprietary Name (INN) drugs per patient was 10.1 ± 4.7. The majority of the patients (84.6%) were hospitalized via the emergency department.

In total, 1907 medications were analysed, and 1653 discrepancies were identified, including 240 UD in 104 patients (55.3%), or an average of 2.31 UD per patient.

### Factors associated to the presence of at least one UD

The results of the univariate analysis are shown in Table 1.

**Demographic data and hospital admission modalities:** Among the variables studied in the univariate analysis, patients with at least one UD were significantly more likely to be women (p=0.039) and to have been admitted to hospital via the emergency department (p=0.014) than patients with no UD (Table 1).

**Medical and drug data:** With regard to medical history, no previous health problem was significantly related to the presence of at least one UD (Table 1).

In terms of comorbidities, 27 patients in the UD ≥ 1 group versus 13 patients in the UD=0 group had non-insulin-dependent (Type II) diabetes (p=0.081). The proportion of overweight or obese hospitalized patients was also higher in the UD ≥ 1 group (39/59) (p=0.058). Conversely, the number of patients with severe or end-stage renal failure was lower in the UD ≥ 1 group (p=0.073). For the 163 patients with more than 3 comorbidities, a significantly greater number belonged to the UD ≥ 1 group (p=0.037) (Table 1).

With respect to the reasons for hospitalization (Table 1), all patients (n=6) hospitalized for a blood count disorder had at least one UD (p=0.034). Conversely, the proportion of patients hospitalized for a neurological pathology was significantly lower in the UD ≥ 1 group (p=0.028).

The UD ≥ 1 group had a significantly greater number of patients with more than 7 drugs in their BPMH (p=0.001).With regard to the multivariate analysis (Table 2), after adjustment, hospital admission via the emergency department (OR=3.8; 95% CI 1.5-10.0) and strictly more than 7 drugs in the BPMH (OR=2.3; 95% CI 1.1-4.9) were both significantly associated with the presence of at least one UD. Conversely, renal failure with a clearance <30 mL/min (OR=0.4; 95% CI 0.2-0.8) and hospitalization for a neurological reason (OR=0.4; 95% CI 0.2-1.0) were both significantly related to an absence of UD.

### Descriptive data of UD

In our population, UD mostly comprised omissions (63.8%) (Table 3) and most frequently concerned drugs intended for the digestive system and various metabolic pathologies such as proton pump inhibitors and anti-diabetic drugs (23.8%) followed by cardiovascular drugs (19.2%) and drugs for the nervous system, especially all psychotropic drugs (16.3%) (Table 3).

### Data related to hospital stay

Data on the length and cost of hospital stays were also analysed. Hospitalisations were significantly longer (p=0.015) in the UD ≥ 1 group, with a mean of 13.6 ± 9.3 days compared with a mean of 11.1 ± 4.3 days in the group with UD=0. The cost of a stay was not higher (p=0.634) in the UD ≥ 1 group (mean of 5544.3 ± 2422.0 euros) than in the UD=0 group (mean of 5396.7 ± 1611.3 euros). Two missing data for each of these variables were identified during this analysis.

**Table 1:** Results of univariate analysis of factors potentially linked to the presence of at least one Unintentional medication Discrepancies (UD): demographic, medical, and drug data.

| Demographic, medical and drug data | Total | UD=0 | UD ≥ 1 | *p* |
|---|---|---|---|---|
| | n | n (%) | n (%) | |
| | | | mean ± SD | |
| Sex | | | | |
| Man | 53 | 30 (56.6) | 23 (43.4) | 0.039* |
| Woman | 135 | 54 (40.0) | 81 (60.0) | |
| Age | | | | 0.224 |
| Age >80 years old | 154 | 72 (46.8) | 82 (53.2) | |
| Admitted via Emergency department | 159 | 65 (40.9) | 94 (59.1) | 0.014* |
| Number of drugs in BPMH† >7 | 136 | 51 (37.5) | 85 (62.5) | 0.001* |
| Number of drugs in AMO‡ >5 | 159 | 21 (13.2) | 138 (86.8) | 0.004* |
| Living place before hospitalization: | | | | |
| Home | 179 | 80 (44.7) | 99 (55.3) | 0.576 |
| Follow-up care and Rehabilitation facility | 4 | 1 (25.0) | 3 (75.0) | |
| Nursing home | 5 | 3 (60.0) | 2 (40.0) | |
| Comorbidities | | | | |
| Number of comorbidities >3 | 163 | 68 (41.7) | 95 (58.3) | 0.037* |
| Cardiovascular pathologies | 176 | 78 (44.3) | 98 (55.7) | 0.702 |
| Overweightness and obesity§ | 59 | 20 (33.9) | 39 (66.1) | 0.058 |
| Severe and end-stage renal failure§ | 48 | 26 (64.0) | 22 (46.0) | 0.073 |
| Non-autoimmune arthropathy | 47 | 21 (44.7) | 26 (55.3) | 1 |
| Undernutrition | 45 | 22 (48.9) | 23 (51.1) | 0.395 |
| Non-insulin-dependent diabetes | 40 | 13 (32.5) | 27 (67.5) | 0.081 |
| Lower limb prosthesis | 37 | 17 (45.9) | 20 (54.1) | 0.863 |
| Dyslipidaemia | 36 | 15 (41.7) | 21 (58.3) | 0.686 |
| Dysthyroidism | 34 | 17 (50.0) | 17 (50.0) | 0.491 |
| Fall | 33 | 11 (33.3) | 22 (66.7) | 0.149 |
| Cancer and malignant hemopathy | 29 | 13 (44.8) | 16 (55.2) | 0.986 |
| Depression | 27 | 9 (33.3) | 18 (66.7) | 0.2 |
| Cognitive disorder | 26 | 12 (46.2) | 14 (53.8) | 0.871 |
| Asthma/COPD | 23 | 9 (39.1) | 14 (60.9) | 0.568 |
| Ophthalmologic disorder | 23 | 9 (39.1) | 14 (60.9) | 0.568 |
| Gastroesophageal disorder | 23 | 8 (34.5) | 15 (65.2) | 0.308 |
| Osteoporosis | 22 | 7 (31.8) | 15 (68.2) | 0.197 |
| Benign prostatic hypertrophy | 13 | 4 (30.8) | 9 (69.2) | 0.296 |
| Parkinson's disease | 8 | 4 (50.0) | 4 (50.0) | 1 |
| Hematologic disorder | 8 | 3 (37.5) | 5 (62.5) | 0.733 |
| Chronic alcoholism | 8 | 3 (37.5) | 5 (62.5) | 0.686 |
| Chronic smoking | 8 | 3 (37.5) | 5 (62.5) | 0.911 |
| Epilepsy | 6 | 3 (50.0) | 3 (50.0) | 1 |
| Alzheimer's disease | 5 | 3 (60.0) | 2 (40.0) | 0.658 |
| Dermatological pathology | 5 | 2 (40.0) | 3 (60.0) | 1 |
| Autoimmune disease | 4 | 2 (50.0) | 2 (50.0) | 1 |
| Non-rheumatic pain | 4 | 1 (25.0) | 3 (75.0) | 0.63 |
| Respiratory failure | 3 | 1 (33.3) | 2 (66.7) | 1 |
| Psychiatric disorder | 3 | 2 (66.7) | 1 (33.3) | 0.587 |
| Anxiety | 3 | 0 (0.0) | 3 (100.0) | 0.255 |
| Otorhinolaryngological pathology | 2 | 2 (100.0) | 0 (0.0) | 0.198 |
| **Medical data** | **Total** | **UD = 0** | **UD ≥ 1** | ***p*** |
| | **n** | **N** | **n (%)** | |
| | | | **mean ± SD** | |
| Previous health problems | | | | |
| Number of previous health problems | 188 | 0.5 ± 0.9 | 0.9 ± 0.9 | 0.741 |
| Bone fracture | 32 | 16 (50.0) | 16 (50.0) | 0.506 |
| Cardiovascular pathology | 31 | 12 (38.7) | 19 (61.3) | 0.464 |
| Bacterial infection | 23 | 12 (52.2) | 11 (47.8) | 0.44 |
| Respiratory pathology | 11 | 2 (18.1) | 9 (81.9) | 0.115 |
| Viral infection | 6 | 2 (33.3) | 4 (66.7) | 0.693 |
| Gastrointestinal surgery | 23 | 11 (47.8) | 12 (52.2) | 0.746 |
| Thyroid surgery | 15 | 7 (46.7) | 8 (53.3) | 0.872 |
| Urology surgery | 7 | 3 (42.9) | 4 (57.1) | 1 |
| Nephrology surgery | 5 | 1 (20.0) | 4 (80.0) | 0.383 |
| Neurosurgery | 3 | 2 (66.7) | 1 (33.3) | 0.587 |
| Limb surgery | 3 | 1 (33.3) | 2 (66.7) | 1 |
| Reasons for hospitalisation | | | | |
| Fall | 57 | 22 (38.6) | 35 (61.4) | 0.268 |
| Deterioration of general condition | 41 | 18 (43.9) | 23 (56.1) | 0.91 |
| Neurological pathology (excluding dementia) | 40 | 24 (60.0) | 16 (40.0) | 0.028* |

| | | | | |
|---|---|---|---|---|
| Infection pathology | 25 | 8 (32.0) | 17 (68.0) | 0.171 |
| Cardiovascular pathology | 22 | 10 (45.5) | 12 (54.5) | 0.938 |
| Metabolic disorder | 11 | 5 (45.5) | 6 (54.5) | 1 |
| Loss of functional autonomy | 11 | 3 (27.3) | 8 (72.7) | 0.351 |
| Delirium | 10 | 4 (40.0) | 6 (60.0) | 1 |
| Iatrogenesis | 9 | 3 (33.3) | 6 (66.7) | 0.733 |
| Rheumatic pathology | 8 | 3 (37.5) | 5 (62.5) | 0.733 |
| Hematologic disorder | 6 | 0 (0.0) | 6 (100.0) | 0.034* |
| Non-rheumatic pain | 4 | 3 (75.0) | 1 (25.0) | 0.326 |
| Dizziness | 2 | 1 (50.0) | 1 (50.0) | 1 |
| Psychiatric pathology | 2 | 1 (33.3) | 3 (66.7) | 1 |

†Best Possible Medication History (BPMH)
‡Admission Medication Order (AMO)
§35 missing data
*p <0.05

**Table 2:** Results of multivariate analysis on 188 patients for factors potentially linked to the presence of at least one unintentional medication discrepancies, adjusted using logistic regression.

| Factors potentially associated to the presence of at least one unintentional medication discrepancies | Odd Ratio (OR) | CI† 95% | *p* |
|---|---|---|---|
| Severe or end-stage renal failure | 0.4 | 0.2-0.8 | 0.02 |
| Neurological pathology (excluding dementia) | 0.4 | 0.2-1.0 | 0.04 |
| Admission via emergency department | 3.8 | 1.5-10.0 | 0.01 |
| Number of BPMH drugs >7 | 2.3 | 1.1-4.9 | 0.04 |

The multivariate model was adjusted for the following variables which were not significant in the multivariate analysis: Hematological disorders, Number of comorbidities >3, Overweightness and obesity, Non-insulin-dependent diabetes, Sex.
†Confidence interval

**Table 3:** Type of observed unintentional medication discrepancies and medications involved, according to their Anatomical Therapeutic Chemical group.

| Type of unintentional medication discrepancies | n (%) |
|---|---|
| Drug omission | 153 (63.8) |
| Dosage error | 29 (12.0) |
| Drug error | 22 (9.2) |
| Timing error in drug administration | 17 (7.1) |
| Dose error | 11 (4.6) |
| Therapeutic follow-up error | 4 (1.7) |
| Galenic form error | 2 (0.8) |
| Adminsitration route error | 1 (0.4) |
| Error in drug administration flow rate | 1 (0.4) |
| **Anatomical Therapeutic Chemical Classification** | **n (%)** |
| A (Alimentary tract and metabolism) | 57 (23.8) |
| C (Cardiovascular system) | 46 (19.2) |
| N (Nervous system) | 39 (16.3) |
| S (Sensory organs) | 28 (11.7) |
| Other† | 20 (8.3) |
| B (Blood and blood-forming organs) | 19 (7.9) |
| R (Respiratory system) | 9 (3.8) |
| M (Musculo-skeletal system) | 9 (3.8) |
| G (Genito-urinary system and sex hormones) | 8 (3.3) |
| D (Dermatologicals) | 4 (1.7) |
| L (Antineoplasic and immunomodulating agents) | 1 (0.4) |

†Other (Homeopathy, parapharmacy, oral nutritional supplements)

## Discussion

Aiming to help identify the patients which should be prioritized for MR at hospital admission, our study highlighted that polypharmacy and admission *via* the emergency room were factors significantly associated with the presence of UD. Conversely, hospitalization for neurological problems and severe or end-stage renal failure were both significantly associated with an absence of UD.

Polypharmacy is one of most frequently found UD risk factors in the literature [3,9,12-21]. In our study, patients with more than 5 drugs in their AMO were associated with a great risk UD, confirming this finding. This result was expected in our study.

We also studied the number of drugs in the BPMH to comprehensively establish the related risk of UD for each patient and found that patients with more than 7 drugs in their BPMH had a significantly greater risk. However, the fact that the BPMH occurs after (i.e., not before) the MR starts, together with the large proportion of patients who had more than 5 drugs in their AMO, means that polypharmacy was an irrelevant factor in the study's objective (i.e., prioritizing MR in elderly hospitalized patients).

Our study also found that patients hospitalized *via* the emergency room had a higher risk of having at least one UD. This reflects Audurier et al. [22], study in Montpellier in an internal medicine hospital department. Furthermore, those authors highlighted that hospitalization *via* the emergency room was a risk factor for severe ME. This finding can be explained by the high influx of patients and rapid treatment in emergency departments, where priority is not often given to verifying the exhaustiveness of patient treatment information. The study by Manias et al. [23] conducted in the emergency department of a principal referral hospital in Melbourne, Australia, showed that the risk of UD was 3.70 times greater when the patient was seen one hour after staff shift change. The waiting time before being seen by a doctor on the ward was also a risk factor for UD in the same study [23]. All these findings from the above-mentioned studies clearly confirm that admission to the ward after passing through the emergency department is an important factor when prioritizing patients for MR at hospital admission. In the present study, we confirm these findings for elderly patients.

In our study, patients with severe or end-stage renal failure had a significantly lower risk of UD than patients with a creatinine clearance greater than 30 mL/min. To our knowledge, this risk factor has never previously been reported in the literature. Greater attention to the treatment of patients with renal failure upon hospital admission may explain this result. Indeed, the medical profession is particularly aware of need to adjust treatment dosages when renal clearance is less than 30 mL/min according to the Cockroft-Gault equation.

Patients hospitalized for a neurological pathology (excluding dementia) were significantly less at risk of UD on admission in our study. Considering that cerebrovascular accidents represented the majority of neurological pathology-related reasons for hospitalization in our study, this decreased risk may be explained by the discontinuation of a large number of treatments during hospitalization for this type of

pathology. More specifically, treatment with anti-diabetes and anti-hypertension drugs belonging to ATC groups A and C, respectively-which are the two classes most often linked to a UD -is suspended in patients hospitalized for a neurological pathology during the acute phase of all cerebrovascular accidents. However, while the risk of UD at hospital admission is low in these patients, it is probably high upon their discharge because a large number of suspended treatments need to be resumed.

Unlike many other studies [9,12-15,22,24], age was not a determining factor of UD risk in our study. This can be explained by the high mean age of the patients, which was 86 years old, and by the age study inclusion criterion, set at over 65 years. Over 65 years, no link was found between age and the risk of presenting a UD.

In the univariate analysis, having more than three comorbidities was significantly associated with the risk of UD. This risk factor has already been reported in the literature. More specifically, Pardo et al. [25], found that having more than three comorbidities was a significant risk factor for UD. Another French study [26] investigating UD in a cardiology hospital department found that having two comorbidities was already associated with an increased risk in univariate analysis. Moreover, Mongaret et al. [16] looked at the Charlson comorbidity index [27] and found that a score greater than 1 was predictive of UD. The Charlson index comprises 12 pathologies each with a different weighting coefficient depending on their potential severity. Validated to adjust for the risk of mortality, the value of using this index when targeting patients at risk of UD should be compared to simply taking into account the type and number of comorbidities involved.

Diabetes was not a risk factor for UD in our study. This finding is consistent with another French study [28] evaluating the risk of UD in a hospital endocrinology department. That study's results highlighted that it was not the pathology that created a risk of UD but the number of prescribed drugs and their frequent changes.

In our study, the most frequent UD at hospital admission was omission. This finding reflects those of several other studies [21,29-34] and confirms the importance of relying on several sources of information to ensure an exhaustive list of the drugs being taken and/or to be taken by the patient. We found a significant association between the presence of at least one UD and longer hospital stay in patients over 65 years of age. We can hypothesize that this was because of potential care for iatrogenesis complications. This hypothesis reinforces the notion that MR must be performed proactively or as early as possible after creating the AMO [35].

Our study has limitations. First of all, it was a single-centre study, conducted in two short-stay hospital departments and therefore our study population does not represent patients hospitalized in other departments. Indeed, the two departments in our study were more likely to receive mostly elderly patients via the emergency department. Second, ATC groups could not be analysed as factors potentially related to UD (unlike the work carried out by Barbier et al. [18]) because only the ATC groups of the drugs involved in a given UD were available for data collection in the ConcReHosp study. Nevertheless, we observed that the ATC groups most often involved were groups A (Alimentary tract and metabolism), C (Cardiovascular system), N (Nervous system), and S (Sensory organs). This result reflects those in the literature [13,15,16,18,32,36-38].

This work provides the first elements of a response to the organizational challenges of developing and implementing MR. While our results need to be confirmed by a multicentre study on a larger geriatric population, the risk factors for UD which we identified could help to improve the prioritization of geriatric patients for MR, and thus an extension of this activity for this population to other medical departments. In a context where additional human resources allocated to MR are not currently available, targeting which patients to prioritize could help avoid more ME, thereby reducing potential complications and consequently, lengths of stay. The savings generated could be used as an argument to employ more pharmacists to perform MR in hospital.

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## Availability of Data and Material

The data that support the findings of this study are available from the corresponding author upon reasonable request.

## Authors' Contributions

Conception and design of the work: FC, AD, SH, PV, JB; Data collection and analysis: TDM, FC, MM, ALC, AD

Interpretation of data: TDM, FC, AD, SH, PV, AD, PA, JB; T.S. Drafting/critically revising the work for important intellectual content: TDM, FC, AD, JB; Final approval of the version to be published: All authors; Agreement to be accountable for all aspects of the work: All authors.

### Ethics approval

The study's registered number is RGPD 2020-74 and was conducted according to the reference methodology MR-

004 approved by France's National Commission for Informatics and Freedoms (CNIL). In accordance with French

Law, the approval of a Committee for Personal Protection (CPP) was not necessary as this was a non-interventional

Retrospective study based on the use of existing data and had no separate purpose.

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