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Impact of medication characteristics and adverse drug events on hospital admission after an emergency department visit: Prospective cohort study

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Abstract

Objectives: Emergency department (ED) overcrowding is a problem for the delivery of adequate and timely emergency care. To improve patient flow and the admission process, the quick prediction of a patient's need for admission is crucial. We aimed to investigate the variables associated with hospitalisation after an ED visit, with a particular focus on the variables related to medication.

Methods: This prospective study was conducted from 2011 to 2018 in subacute medical ED of a French University Hospital. Specialised EDs (paediatric, gynaecologic, head and neck and psychiatric) and the outpatient unit of the ED were not included. Participation in this study was proposed to all adult patients who underwent a medication history interview with a pharmacist. Pharmacists conducted structured interviews for the completion of the medication history and the detection of adverse drug events (ADE). Relations between patient characteristics and hospitalisation were analysed using logistic regression.

Results: Among the 14 511 included patients, 5972 (41.2%) were hospitalised including 69 deaths. In total, 7458 patients (51.4%) took more than 5 medications and 2846 patients (19.6%) had an ADE detected during the ED visit. In hospitalised patients, bleeding (32.2%) and metabolic disorders (16.8%) were the most observed ADE symptoms. Variables associated with increased hospital admission included 2 demographic variables (age, male gender), 4 clinical variables (renal and hepatic failures, alcohol addiction, ED visit for respiratory reason) and 6 medication-related variables (medications >5, use of blood, systemic anti-infective, metabolism and antineoplastic/immunomodulating medications and ADE).

Conclusion: We identified variables associated with hospitalisation including drug-related variables. These results point out the importance and the relevance of collecting medication data in a subacute medical ED (study registered on ClinicalTrials.gov, NCT03442010).

What's known

- Emergency department is a major source of urgent or unexpected hospitalisation.
- Emergency department overcrowding is a problem for the delivery of adequate and timely emergency care.
- Reliable medication data are not immediately obtainable and can be time consuming to collect in emergency department.

What's new

- More than 40% of patients admitted to subacute medical emergency department (ED) were hospitalised.
- Polymedication and occurrence of an adverse drug event were independently associated with increased hospitalisation.
- Medication-related data are worthwhile to consider in the context of ED visit.

1 | INTRODUCTION

The emergency department (ED) is a major source of urgent or unexpected hospitalisation. Besides the significant cost associated with these unscheduled hospitalisations, estimated at more than £13 billion per year in England,^{1,2} they can also expose patients to various hospitalisation-related adverse events (such as stress, nutritional issues, infections) resulting in a general vulnerability.³ Thus, the reduction in emergency hospitalisation has become a priority and a long-term ambition, notably for health systems such as the National Health Service (NHS) in England.^{1,2} One possible approach is the identification of patients at high risk of emergency hospitalisation in order to implement targeted prevention measures in primary care.⁴ Several risk prediction models or other tools have been developed for this purpose, highlighting the risk factors of emergency hospitalisation from ambulatory care.^{5,6} They use various data sources (self-reported data, administrative databases, population registries, clinical records, etc) which enable a large number of candidate variables to be analysed: demographic data, lifestyle variables, chronic diseases, prescribed medication, clinical data, laboratory test results, etc.⁵

In parallel with these ambulatory models, other emergency admission risk prediction models have been developed for emergency department use.⁷⁻¹¹ In addition to the potential aforementioned applications, they intend to quickly predict a patient's need for admission, to provide logistical support to the ED team and to improve patient flow and admission processes. Indeed, ED overcrowding is a problem for the delivery of adequate and timely emergency care.¹² It is also a factor of patient dissatisfaction, with prolonged waiting times and lower morale and productivity for physicians.^{13,14} The rapid determining of patients most at risk of hospitalisation could be a solution to partly reduce this multifactorial phenomenon in the ED. These ED models generally use routinely collected and readily available data which are demographic, administrative as well as a few clinical variables. Medication data are virtually not tested in ED models, yet they are sometimes predictor variables of admission in ambulatory care models.⁵ It is currently estimated that drug-related problems account for 5%-15% of hospitalisation.¹⁵ In a previous study, we highlighted that 15.7% of patients

admitted to the ED had an ADE, with a higher proportion of hospitalisation and death during the ED visit compared to patients without an ADE.¹⁶ Reliable medication data are not immediately obtainable and can be time consuming to collect, which may explain their low utilisation in ED models. In the ED of our hospital, a pharmacist team is routinely deployed to help the ED team by collecting the patients' medication history and detecting Adverse Drug Events (ADEs). In this study, we aimed to investigate variables associated with hospitalisation after the ED visit, using standard data collected in the ED, with a particular focus on variables related to medication.

2 | METHODS

2.1 | Design

This study is an ancillary analysis of a previously published study.¹⁶ This prospective study was conducted from November 2011 to November 2018 in the subacute medical ED of our University Hospital, France (2600-bed tertiary care centre). Paediatric, gynaecologic, head and neck and psychiatric EDs are physically separated from the medical ED and were not included in this study. The outpatient unit of the adult medical ED which treats non-urgent cases (small traumatology and benign pathologies) was also not included in the study. Our study was approved by the Hospital Institutional Review Board and registered on ClinicalTrials.gov (NCT03442010). All participants or a member of their family gave verbal consent.

2.2 | Study population

Participation in this study was proposed to all adult patients (>18 years) who underwent a medication history interview with a member of the pharmacist team, briefly after triage. Non-inclusion criteria were refusal to participate, voluntary medication poisoning or acute psychological problems. All patients were prospectively and consecutively included without any prioritisation criteria such as age

or polymedication from Monday to Friday from 8.00 to 18.00, and were followed until ED discharge.

2.3 | Interventions and measurements

Interventions have been published previously.¹⁶ Briefly, the ED staff includes a pharmacist team (1 senior pharmacist, 1 resident and 4 pharmacy students). The pharmacist team carried out a medication history and ADE detection for each included patient. The medication history was conducted following the standard operating procedures recommended by the World Health Organisation,¹⁷ as previously described.¹⁸ It was defined as the most comprehensive list of all medications taken by the patient, including prescription drugs, self-medication (over the counter medication and herbal medication) and as-needed treatments. We also collected the self-reported adherence. The medication history is based on a structured interview of the patient (and/or relatives if needed) and additional sources such as medication prescription, medical record, and contact with community pharmacy, general practitioner or nurse. The entire process (data collection, cross-checking of information and validation of the final medication history) usually required 20-30 minutes. It could be started before or after the medical consultation depending on the availability of the pharmaceutical team but was performed independently and blindly from the medical management. An ADE was defined as "any injury resulting from medical intervention related to a drug", according to the Institute of Medicine's definition.¹⁹ ADEs were attributed to a medication by the pharmacist and confirmed, in real time, by the treating senior ED physician. In the case of doubt about the diagnosis or category of an ADE during the study, the case was reviewed by an expert committee that included ED physicians, clinical pharmacists and pharmacovigilance physician. At the end of the study, ADE cases were verified by 2 expert clinical pharmacists and/or the expert committee if necessary (Figure S1). The ADE severity was assessed according to the Common Terminology Criteria for adverse events as spontaneous regression, regression after symptomatic treatment, hospitalisation with no life-threat, life-threatening risk and death.

All pharmacist team members received specific training on medication history realisation, according to the High 5s project standard operating procedures¹⁷ and on ADE detection and documentation.^{20,21}

The pharmacist team collected socio-demographic data (age, gender), the FRENCH triage scale level,²² clinical data (cause of ED visit, comorbidities), medications (number, ATC level 1 and 2), detection and characteristics of the ADE. These data were prospectively collected and recorded from the medical record and/or structured patient interview. The primary outcome was hospitalisation after the subacute medical ED visit. As already seen elsewhere,⁷ deaths in the subacute medical ED were counted as hospitalisation, because it was considered that the health condition of such patients would have led to an admission had they survived.

2.4 | Analysis

The patients' characteristics were described with percentages for categorical variables and means \pm standard deviations (SD) for quantitative variables. To assess the representativeness of our study sample, main characteristics of included patients were compared with those of the entire population of patients admitted to the medical ED (including the outpatient ED unit, which was excluded from our population). Such data were obtained retrospectively from the hospital's information systems medicalisation program.

Among the study population, the characteristics of patients with hospitalisation and without hospitalisation were compared with the Student's *t* or the Mann-Whitney *U* test for continuous variables, and with the Chi square or Fisher exact test for categorical variables.

The variables considered as candidate hospitalisation predictors included all data collected by the pharmacist team. The impact of our variables of interest on the primary outcome was analysed using logistic regression. The variables with *p*-values lower than 0.15 in univariate models were considered for a multivariable model. After a stepwise selection of variables, only the variables with *P*-values lower than .05 in the multivariable model were considered to be significantly associated with hospitalisation or death in the ED, and were kept in the final multivariate model. Missing data were not replaced and the absence of collinearity between the variables of interest has been verified. In order to assess multicollinearity in our regression models, the correlation matrix of the final parameters was executed, and both the Variance Inflation Factors and the proportion of variation using condition indices of linear combination of the parameters were analysed.

Statistical analyses were performed with SAS 9.1 (SAS Institute, France), and the statistical bilateral significance threshold was set at 5%.

3 | RESULTS

3.1 | Characteristics of the study population

Among the 210 587 patients who visited the medical ED during the study period, accounting for 338 592 admissions, 14 619 patients (6.9%) admitted to the subacute medical ED and benefiting from a medication history by pharmacists were included in the study. For 108 of them, an outcome was not available. Therefore, the study population consisted of 14 511 patients, of which 5903 (40.7%) were hospitalised after the subacute medical ED visit and 69 (0.5%) died in the subacute medical ED. Thus, the primary outcome concerned 5972 (41.2%) patients (Figure 1). Our study population had a higher mean age (64.6 ± 24.7 vs 47.5 ± 22.6 years), triage category (\leq level 3 FRENCH triage scale, 70.0% vs 45.6%) and hospitalisation or death rate (41.2% vs 20.1%) than the population admitted to the adult medical ED (including subacute medical ED but also the outpatient ED unit) during the study period (Table S1).

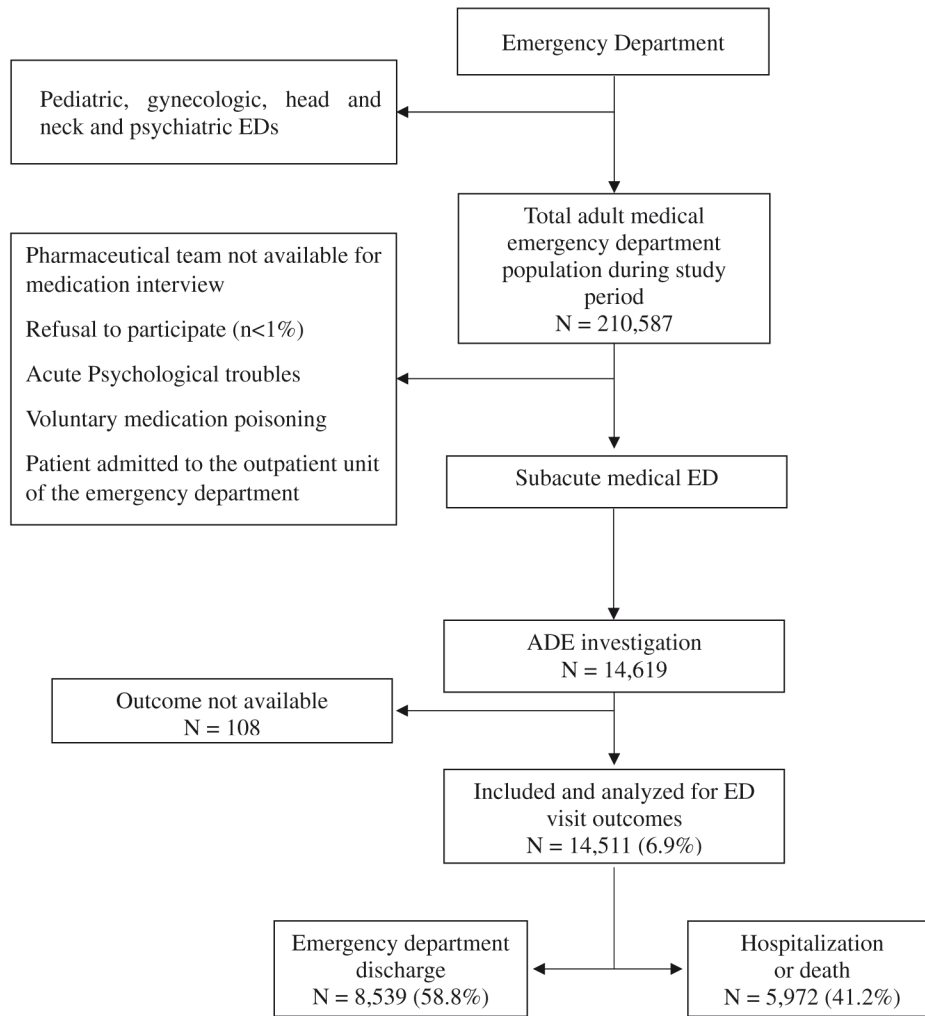


FIGURE 1 Flowchart of the study population. ADE, adverse drug event; ED, emergency department

The population baseline characteristics according to the ED visit outcome—discharge versus hospitalisation are described in Table 1. Among the hospitalised patients, age, proportion of men and proportion of patients living in an institution were higher. In both groups of patients, the main cause of the ED visit was gastroenteric, respiratory and cardiologic symptoms. Respiratory symptom was the cause of the ED visits that mostly led to hospitalisation, with 57.5% (1036/1803) of patients hospitalised. A low triage category was more frequent among discharged patients (12.4% vs 7.1% for level 5) while a high triage category was more common among hospitalised ones (4.6% vs 1.2% for level 1). In fact, the rate of hospitalisation increased with priority of care according to the triage category: 28.6% (420/1469) for level 5, 36.5% (1035/2838) for level 4, 41.9% (3241/7728) for level 3, 48.5% (949/1958) for level 2 and 72.7% (274/377) for level 1.

3.2 | Description of medication data

Concerning medication treatment, 13 600 patients (93.7%) reported taking at least 1 medicine (chronic prescribed treatment or self-medication). The majority (69.5%) were on neurological medications

and a significant proportion on drugs related to the alimentary tract and metabolism (63.2%) and to the cardiovascular system (57.6%). For all major class medications, the proportion of patients under treatment was higher in hospitalised patients than in discharged ones. Polypharmacy (number of medications greater than 5) was more frequent in hospitalised patients (63.5% vs 43.0%), while the self-management of treatment was less common (62.6% vs 76.5%).

In total, 88 856 drugs were recorded: 45 635 (51.4%) among the 8539 patients further discharged, and 43 221 (48.6%) among the 5972 hospitalised patients. The distribution of these medications by ATC class (level 1 and 2) is presented in Table 2. Row percentages allow the likelihood of being in one or the other group to be highlighted given the class of drug prescribed. For the hospitalised group, the highest probability was observed with antineoplastic and immunomodulating agents for level 1 ATC class (56.1%) and diuretics for level 2 (58.6%).

3.3 | Description of ADE symptoms

As presented in Table 1, in 2849 patients (19.6% of the total study population and 20.9% of patients taking at least one medicine), an ADE was detected during the ED visit. In total, 77.5% of them were

TABLE 1 Characteristics of the study population according to ED visit outcomes

Characteristics	Missing data	TOTAL	Discharge	Hospitalisation
N (% of patients)		14 511	8539	5972
Age (y)	0	64.6 ± 24.7	59.5 ± 23.0	71.9 ± 25.1
Gender, male	0	7003 (48.3)	3991 (46.7)	3012 (50.4)
Body mass index >30kg/m ²	2500	1624 (13.5)	917 (12.8)	707 (14.7)
FRENCH triage scale	141	14 370	8451	5919
Level 1		377 (2.6)	103 (1.2)	274 (4.6)
Level 2		1958 (13.6)	1009 (11.9)	949 (16.0)
Level 3		7728 (53.8)	4487 (53.1)	3241 (54.8)
Level 4		2838 (19.8)	1803 (21.3)	1035 (17.5)
Level 5		1469 (10.2)	1049 (12.4)	420 (7.1)
Type of ED unit	19	14 492	8526	5966
Emergency Critical Care Unit		464 (3.2)	117 (1.4)	347 (5.8)
Observation Emergency Unit		12 825 (88.5)	7901 (92.7)	4924 (82.5)
Short Stay Hospitalisation Unit		1203 (8.3)	508 (5.9)	695 (11.6)
Lifestyle	34	14 477	8516	5961
At home		12 962 (89.5)	7717 (90.6)	5245 (88.0)
In institution		1515 (10.5)	799 (9.4)	716 (12.0)
Main cause of ED visit	2	14 509	8538	5 971
Cardiovascular		1713 (11.8)	1176 (13.8)	537 (9.0)
Hepato-gastrointestinal		3080 (21.2)	2065 (24.2)	1015 (17.0)
Genitourinary		289 (2.0)	209 (2.5)	80 (1.3)
Respiratory		1803 (12.4)	767 (9.0)	1036 (17.4)
Neurologic		980 (6.8)	589 (6.9)	391 (6.6)
Self-medication	0	4013 (27.7)	2715 (31.8)	1298 (21.7)
Daily medications >5	0	7458 (51.4)	3668 (43.0)	3790 (63.5)
Daily medications	0	6.1 ± 4.2	5.4 ± 4.1	7.2 ± 4.2
Presence of ADEs	0	2849 (19.6)	1463 (17.1)	1386 (23.2)
Patient with at least 1 medication	0	13 600 (93.7)	7842 (91.8)	5758 (96.4)
Self-management of medications	941	9585 (70.6)	5981 (76.5)	3604 (62.6)
Major class medications (ATC level 1)				
Alimentary tract and metabolism		8593 (63.2)	4516 (57.6)	4077 (70.8)
Blood and blood-forming organs		6527 (45.0)	3189 (37.4)	3338 (55.9)
Cardiovascular system		8361 (57.6)	4214 (49.3)	4147 (69.4)
Nervous system		10,085 (69.5)	5720 (67.0)	4365 (73.1)
Respiratory system		2,751 (20.2)	1544 (19.7)	1207 (21.0)

Note: Data are the mean ± SD, or n (%); FRENCH triage scale level 1: Immediately life-threatening; level 2: Marked impairment of a vital organ, or imminently life-threatening, or functionally disabling traumatic lesion; level 3: Functional impairment, or organic lesions likely to deteriorate within 24h, or complex medical situation justifying the use of several hospital resources; level 4: Stable, non-complex functional impairment or organic lesions, but justifying the urgent use of at least one hospital resource; level 5: No functional impairment or organic lesion justifying the use of hospital resources;

Abbreviations: ADEs, adverse drug events; ATC, anatomical therapeutic classification; ED, emergency department.

involved in the ED visit. Patients with an ADE were hospitalised in 48.6% of the cases (1386/2849). Table 3 describes symptoms of ADE and shows differences between the 2 populations. In hospitalised patients, bleeding and metabolic disorders were the most observed ADE symptoms while, in the discharged group, it was neurologic disorders followed by bleeding. The largest differences in proportions

between the discharged and hospitalised patients were observed for bleeding (20.1% vs 32.2%), haematology and coagulation test abnormalities (4.3% vs 10.1%), gastrointestinal disorders (13.5% vs 7.2%) and neurologic disorders (22.6% vs 11.7%). Severity of ADE was classified as ADEs with spontaneous regression, regression after symptomatic treatment, hospitalisation with no life threat,

TABLE 2 Distribution of medications (anatomical therapeutic classification level 1 and 2) according to outcome after ED visit

	Discharge (n = 45 635)	Hospitalisation (n = 43 221)
A. Alimentary tract and metabolism	9293 (50.3)	9192 (49.7)
A02. Drugs for acid-related disorders	2774 (51.1)	2653 (48.9)
A03. Drugs for functional gastrointestinal disorders	956 (59.5)	650 (40.5)
A06. Laxatives	1207 (51.2)	1149 (48.8)
A10. Drugs used in diabetes	2181 (47.9)	2369 (52.1)
A12. Supplementation	720 (44.4)	900 (55.6)
Others	1455 (49.7)	1471(50.3)
B. Blood and blood forming organs	3953 (47,1)	4441 (52.9)
B01. Antithrombotic agents	3360 (47.5)	3721 (52.5)
Others	593 (45.2)	720 (54.8)
C. Cardiovascular system	9832 (48.3)	10531 (51.7)
C01. Cardiac therapy	1109 (47.1)	1244 (52.9)
C03. Diuretics	1413 (41.4)	1999 (58.6)
C07. B-blocking agents	1678 (48.4)	1791 (51.6)
C08. Calcium channel blockers	1005 (46.7)	1145 (53.3)
C09. Agents acting on the renin-angiotensin system	2440 (51.5)	2294 (48.5)
C10. Lipid-modifying agents	1857 (52.0)	1714 (48.0)
Others	330 (49.0)	344 (51.0)
D. Dermatologicals	562 (51.5)	530 (48.5)
G. Genitourinary system and sex hormones	1307 (52.9)	1164 (47.1)
G04. Urological drugs	907 (47.9)	987 (52.1)
Others	400 (69.3)	177 (30.7)
H. Systemic hormonal preparations	1358 (51.4)	1286 (48.6)
H03. Thyroid therapy	846 (54.8)	698 (45.2)
Others	512 (46.5)	588 (53.5)
J. Anti-infective drugs for systematic use	1125 (49.5)	1150 (50.5)
J01. Antibacterial drugs for systematic use	954 (49.8)	961 (50.2)
Others	171 (47.5)	189 (52.5)
L. Antineoplastic and immunomodulating agents	399 (43.9)	509 (56.1)
M. Muscular-skeletal system	1706 (58.2)	1224 (41.8)
M.01 Anti-inflammatory and antirheumatic products	1065 (65.3)	566 (34.7)
Others	641 (49.3)	658 (50.7)
N. Nervous system	12 573 (55.2)	10 213 (44.8)
N02. Analgesics	4622 (55.5)	3700 (44.5)
N03. Antiepileptic drugs	1022 (55.5)	820 (44.5)
N05. Psycholeptics	4020 (55.5)	3220 (44.5)
N06. Psychoanaleptics	2112 (53.0)	1871 (47.0)
Others	797(57.0)	602 (43.0)
R. Respiratory system.	2658 (56.0)	2089 (44.0)
R03. Antiasthmatics	1584 (52.9)	1412 (47.1)
Other	1074 (61.3)	677 (38.7)
S. Sensory organs	526 (48.1)	568 (51.9)
Others	343 (51.4)	324 (48.6)

Note: Data are presented as n (row %).

TABLE 3 Description of adverse drug event symptoms according to Emergency Department visit outcomes

	Discharge (n = 1463)	Hospitalisation (n = 1386)
Bleeding	294 (20.1)	447 (32.2)
Gastrointestinal bleeding	38	160
Haematoma	89	81
Haematuria/haemoptysis/ epistaxis	75	59
Intracranial haemorrhage	27	72
Others	65	75
Cardiovascular disorders	132 (9.0)	107 (7.7)
Hypotension	39	29
Cardiac rhythm disorders/ tachycardia/bradycardia	30	30
Hypertension	29	8
Others	34	40
Fatigue/fall	51 (3.5)	35 (2.5)
Gastrointestinal disorders	197 (13.5)	100 (7.2)
Constipation	54	34
Abdominal pain/diarrhoea	56	21
Nausea/vomiting	50	19
Gastroduodenal pain	31	10
Others	6	16
Haematology and coagulation test abnormalities	63 (4.3)	140 (10.1)
Increase of blood INR values	47	106
Others	16	34
Infections	29 (2.0)	62 (4.5)
Pneumonia	4	19
Others	25	43
Metabolic disorders	183 (12.5)	233 (16.8)
Electrolyte disorders	82	114
Hyperglycaemia/ hypoglycaemia	81	72
Others	20	47
Neurologic disorders	331 (22.6)	162 (11.7)
Altered consciousness/ confusion/discomfort	173	117
Convulsion	100	20
Others	58	25
Pulmonary disorders	28 (1.9)	31 (2.2)
Psychological disorders	24 (1.6)	13 (0.9)
Skin diseases	83 (5.7)	27 (1.9)
Allergic reactions	45	14
Urticaria	26	1
Other	12	12
Others	48 (3.3)	29 (2.1)

Note: Data are n (%).

Abbreviation: INR, International Normalised Ratio.

hospitalisation with life-threatening risk and death respectively at 6.7%, 47.4%, 38.8%, 5.7% and 1.2%, respectively.

3.4 | Variables associated with hospitalisation

The results of the univariate and multivariate analysis for the variables associated with hospitalisation are described in Table 4. In the final model, 15 variables were independent predictors of hospital admission. Variables associated with increased hospital admission included 2 demographic variables (increasing age and male gender), 4 clinical variables (renal and hepatic failure, alcohol addiction, ED visit for respiratory reason) and 6 medication-related variables: polypharmacy (number of medications greater than 5), the use of blood, systemic anti-infective, metabolism and antineoplastic/immunomodulating medications, and the occurrence of an ADE. Conversely, an ED visit without immediate need of urgent care (FRENCH triage scale level 5), and an ED visit for cardiovascular and hepato-gastrointestinal reasons were negatively associated with hospital admission.

4 | DISCUSSION

A rapid identification and management of patients at risk of hospitalisation are crucial during the ED visit. In a subacute medical ED, physicians need to quickly refer patients and anticipate hospitalisation needs in order to relieve overcrowding. In total, 41.2% of our population was hospitalised following their admission to the subacute medical ED. We highlighted some of the variables associated with hospitalisation such as age, male gender, renal and hepatic failures, polypharmacy, blood, systemic anti-infective, metabolism, antineoplastic and immunomodulating medications, and ADE.

Our hospitalisation rate from a subacute medical ED visit is very close to those found in the literature. Three retrospective studies covering 1 232 016, 1 721 294 and 100 123 visits found hospitalisation rates of 38.7%, 40.7% and 38.6%, respectively.⁸⁻¹⁰ Moreover, the populations of these studies are very close to ours in terms of age (adult with mean age around 50 years old), sex ratio (near to 1) and triage category. However, our study population is not representative of the general population of an emergency department but rather corresponds to a sub-acute emergency population with a higher age and triage level and especially a higher rate of hospitalisation.

We identified standard admission data (age, male gender, triage level), clinical data (main cause of ED visit, comorbidity) and medication data (number of drugs, medication classes, ADE) as factors influencing the outcome after an ED visit in our population. Standard admission data are the most tested variables and are commonly integrated in ED admission prediction models, notably because they are readily and rapidly available. Thus, several retrospective studies involving thousands of patients share the same candidate predictor variables, particularly demographic data (age, gender or race), administrative data (day or time of arrival, mode of arrival, previous ED admission...) and other admission data (triage score).^{7-11,23} The

TABLE 4 Univariate and multivariable analyses of variables associated with hospitalisation

	Univariate analysis		Multivariable analysis	
	Odds ratio 95% CI	P-value	Odds ratio 95% CI	P-value
Age (for 5 y)	1.14 (1.13-1.15)	<.0001	1.11 (1.09-1.12)	<.0001
Male gender	1.16 (1.09-1.24)	<.0001	1.22 (1.13-1.32)	<.0001
Body mass index ≥ 30 kg/m ² (yes vs no)	1.17 (1.06-1.31)	.003		
In institution (yes vs no)	1.32 (1.19-1.47)	<.0001		
Comorbidities				
Renal failure (GFR <60 mL/min/1.73 m ²) (yes vs no)	2.06 (1.84-2.31)	<.0001	1.30 (1.14-1.48)	.0001
Hepatic failure (yes vs no)	2.10 (1.67-2.65)	<.0001	1.69 (1.29-2.20)	.0001
Psychiatric disease (Yes Vs No)	1.08 (0.98-1.18)	.13		
Dementia (yes vs no)	1.56 (1.39-1.74)	<.0001		
Alcohol addiction (yes vs no)	1.16 (0.99-1.35)	.066	1.23 (1.03-1.47)	.024
Tobacco use (yes vs no)	0.60 (0.55-0.65)	<.0001		
Triage				
FRENCH triage scale level 5 (yes vs other levels)	0.54 (0.48-0.61)	<.0001	0.62 (0.54-0.71)	<.0001
Cause of ED visit				
Cardiovascular (vs other causes of ED visit)	0.62 (0.56-0.69)	<.0001	0.66 (0.59-0.75)	<.0001
Hepato-gastrointestinal (vs other causes of ED visit)	0.64 (0.59-0.70)	<.0001	0.51 (0.38-0.70)	<.0001
Genitourinary (vs other causes of ED visit)	0.54 (0.42-0.70)	<.0001		
Neurologic (vs other causes of ED visit)	0.95 (0.83-1.08)	.41		
Respiratory (vs other causes of ED visit)	2.13 (1.93-2.35)	<.0001	1.49 (1.32-1.68)	<.0001
Number of drugs >5 (vs ≤ 5)	2.31 (2.16-2.47)	<.0001	1.19 (1.07-1.33)	.0014
Medications (ATC Level 1)				
B. Blood and blood-forming organs (vs other medication types)	2.13 (1.99-2.27)	<.0001	1.12 (1.02-1.24)	.017
L. Antineoplastic and immunomodulating agents (vs other medication types)	1.84 (1.58-2.14)	<.0001	1.64 (1.37-1.96)	<.0001
J. Anti-infective drugs for systemic use (vs other medication types)	1.44 (1.30-1.58)	<.0001	1.31 (1.17-1.48)	<.0001
N. Nervous system (vs other medication types)	1.34 (1.25-1.44)	.0002		
C. Cardiovascular system (vs other medication types)	2.33 (2.18-2.50)	<.0001		
A. Alimentary tract and metabolism (vs other medication types)	1.92 (1.79-2.05)	<.0001	1.17 (1.06-1.29)	.0024
R. Respiratory system (vs other medication types)	1.08 (1.00-1.18)	.067		
ADE (yes vs no)	1.46 (1.34-1.59)	<.0001	1.28 (1.15-1.42)	<.0001

Abbreviations: ADE, adverse drug event; ATC, anatomical therapeutic classification; CI, confidence intervals; ED, emergency department; FRENCH, French Emergency Nurses Classification in Hospital scale (FRENCH), level 5: no functional impairment or organic lesion justifying the use of hospital resources; GFR, glomerular filtration rate.

variables most significantly associated with hospitalisation in these studies are increasing age and urgent triage level, as found in our study, as well as arrival by ambulance.

Some authors have also investigated the link between hospitalisation after the ED visit and clinical variables such as blood test request,⁹ presence of a chronic condition²³ or main cause of the ED visit.^{8,9,11} Like Dinh et al, we found a relation between reasons of ED visit and risk of hospitalisation.⁸ It is difficult to compare our results due to possible differences in categorisation of presenting symptoms. Indeed, we used the clinical categorisation system whose principal limitation overlaps between categories. Moreover, due to our smaller dataset, we evaluated 5 major causes of admission, while Dinh et al evaluated 18. However, like them, we observe

that cardiovascular causes of ED visits decrease the probability of hospitalisation. Concerning chronic diseases, none of the conditions investigated and reported by Sun et al²³—as associated with the admission risk (diabetes, hypertension or dyslipidemia)—have been tested in our study. However, we identified chronic kidney and hepatic failures as a factor associated with hospitalisation.

In our study, we finally assessed the impact of medication and the presence of an ADE on the risk of hospitalisation. This was made possible by our organisation and by the presence of a pharmaceutical team in the ED, allowing us to add these therapeutic data as routinely collected candidate predictor variables. Thus, we were able to show that a significant number of drugs (more than 5), treatment by antineoplastic and immunomodulating agents, blood, systemic

anti-infective, metabolism medications, and the presence of an ADE were significantly associated with hospitalisation in multivariate analyses. Polypharmacy and prescribed medication have already been tested and included in several models designed for primary care.⁵ However, to our knowledge, no hospitalisation prediction model designed for ED patients has ever investigated medication and ADE-related variables. We found only 1 retrospective study evaluating patient treatment through electronic health record,²⁴ but primary care databases are often incomplete or out of date.²⁵ Unavailability or poor accuracy of the patients' medication history in the ED^{26,27} may partly explain the low utilisation of medication and ADE-related data in ED admission prediction models, as well as the difficulty of detecting ADEs and the problem of their under-reporting.²⁸⁻³²

Moreover, unlike some ambulatory models, we did not focus on the presence or absence of specific medication³³ but recorded prospectively all the drugs taken by the patient. This allowed us to highlight the implication of drugs that were less investigated, or less prescribed. We were thus able to identify antineoplastic and immunomodulating agents, blood, systemic anti-infective and metabolism medications as medications associated with hospitalisation risk in the subacute medical ED. These medications have already been linked to hospital admission due to drug-related problems.^{15,34} As polypharmacy is also a well-known risk factor of ADE,³⁵ it is therefore not surprising that our third medication-related factor for admission was the occurrence of an ADE. A greater proportion of hospitalisation in ED patients with an ADE has already been found in several studies and only in univariate analyses.^{16,36-38}

To our knowledge, this is the first prospective study to have highlighted ADEs as a factor independently associated with hospitalisation following admission to a subacute medical ED. Furthermore, the integration of the clinical pharmacist team in the ED for medication history collection ensured a high level of ADE detection and a rigorous prospective data collection, in particular concerning medication. This large data collection and our large sample size are major strengths of our study.

4.1 | Study limitations

Our study also has some limitations, mainly due to its monocentric design and recruitment method. Indeed, we did not analyse some of the variables described in the literature such as previous ED visits or hospitalisation, mode of arrival at the ED, vital signs or more comorbidities which might have been of interest. The detection of ADEs was performed by the clinical pharmacist and the emergency physician and only contentious cases were reviewed by the expert committee. An evaluation of all cases would have been more robust. In our study, ADEs were detected jointly by the clinical pharmacist and the emergency physician, then reviewed by an expert committee when deemed necessary. Similar methodology has been used in several comparable studies.^{31,37,39,40} However, some studies have used external or independent expert committees for ADE verification.^{36,41} Finally, possible selection bias due to the recruitment

procedure questions the generalisation of our results. For this study, we did not include patients from the outpatient unit as their duration of care was not compatible with the study process and their probability of hospitalisation was extremely low or even null. Exclusion of specialised units and outpatient unit can account for our population being older, with more medication and more prone to hospitalisation. This may have introduced a selection bias. However, our objective was to highlight the risk factors associated with hospitalisation and improve patient flow and admission process. We therefore carried out this study in units in line with this objective, where patients' flow was difficult to manage, with long waiting times.

5 | CONCLUSION

In summary, in a large ED population (n = 14 511), we identified independent predictors for hospitalisation following the ED visit. Besides commonly tested variables, we investigated the potential implication of medication on patient disposition. Thus, in addition to standard admission and clinical data, we have identified variables associated with treatments (polypharmacy, treatment by antineoplastic or immunomodulating agents, blood, systemic anti-infective and metabolism medications and presence of an ADE). These results point out the importance and relevance of collecting medication data in the context of a subacute medical ED visit.

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