Identifying older inpatients at high risk of unintentional medication discrepancies: a classification tree analysis

Mathieu Corvaisier [1-3], Dolores Sanchez-Rodriguez [4-6], Kevin Sautret [1], Jérémie Riou [7,8], Laurence Spiesser-Robelet [2], Cédric Annweiler [1,3,8,*]

1. Department of Geriatric Medicine, Research Center on Autonomy and Longevity, Angers University Hospital, Angers, France
2. Department of Pharmacy, Angers University Hospital, Angers, France
3. Health Faculty, University of Angers, Angers, France
4. Geriatrics Department, Brugmann university hospital, Université Libre de Bruxelles, Brussels, Belgium
5. WHO Collaborating Centre for Public Health Aspects of Musculo-Skeletal Health and Ageing, Division of Public Health, Epidemiology and Health Economics, University of Liège, Liège, Belgium
6. Geriatrics Department, Rehabilitation Research Group, Hospital del Mar Medical Research Institute (IMIM), Barcelona, Spain
7. Delegation to Clinical Research and Innovation, Angers University Hospital, Angers, France
8. Robarts Research Institute, Department of Medical Biophysics, Schulich School of Medicine and Dentistry, the University of Western Ontario, London, Ontario, Canada

*** Corresponding authors**: Cedric.Annweiler@chu-angers.fr¸ Department of Geriatric Medicine, Research Center on Autonomy and Longevity, Angers University Hospital, Angers, France. Tel.: +33-241-354-725; Fax: +33 241 354 894.

ABSTRACT

Unintentional medication discrepancies at admission are differences between the best possible medication history and the prescribed treatment at admission, and are associated to adverse outcomes, particularly in older people. This study aimed to identify the clinical profiles of geriatric inpatients with unintentional medication discrepancies at hospital admission. A classification tree Chi-square Automatic Interaction Detector (CHAID) analysis was conducted to assess those patients' profiles and characteristics that were associated to a higher risk of unintentional medication discrepancies. One-hundred thirty consecutive older patients admitted to acute care (87±5-year-old; 61.8% women) were assessed. The CHAID analysis retrieved 5 clinical profiles of older inpatients with a risk of up to 94.4% for unintentional medication discrepancies. These profiles were determined based on combinations of three characteristics: Use of eye drops, frequent falls (≥1/year), and admission due to urgent hospitalization. These easily measurable clinical characteristics may be helpful as a supportive measure to improve pharmacological care.

KEY WORDS: Unintentional medication discrepancy; pharmacological care; drug management; medication reconciliation; older adults.

HIGHLIGHTS

- The study identified inpatients at a higher risk of unintentional medication discrepancies
- The patients with eye drops, frequent falls (≥1/year), and urgent hospitalization upon admission were at a higher risk of unintentional medication discrepancies
- Taking into consideration these characteristics may be helpful as a supportive measure to improve pharmacological care

INTRODUCTION

Unintentional medication discrepancies at admission are defined as "differences between the best possible medication history and the prescribed treatment at admission" [1], they endanger patients' safety, and are associated to adverse health outcomes [2]. Advancing age, polypharmacy, and transitions of care from home to the hospital or among different healthcare settings are among the most frequent and relevant risk factors for unintentional medication discrepancies [3]. These factors highlight older inpatients who have recently been admitted to acute care units as a population particularly at high risk for unintentional medication discrepancies [2], which points out this population as an adequate target for pharmacological interventions aimed at improving the quality of care [4].

The European Union Geriatric Medicine Society (EuGMS) launched the Special Interest Group on Pharmacology and the EuGMS Task and Finish group on Fall-Risk-Increasing Drugs (FRIDs), aimed at improving pharmacological care for older people in Europe. Several strategies have been shown to enhance pharmacological care, including clinical medication review, active patient and caregiver counseling, and medication reconciliation [5,6]. These strategies have been shown to be effective in preventing such discrepancies [5,7] and in improving adverse health outcomes, particularly when combined [8,9]. Among the potential actions to be taken, the EuGMS Task and Finish group on Fall-Risk-Increasing Drugs (FRIDs) encourages the identification of unintentional medication discrepancies, for the sake of patient safety [10]. Moreover, updated clinical practice guidelines recommend paying particular attention to adequate pharmacological care for populations at higher risk, such as older persons with multimorbidity and polypharmacy [11].

We hypothesized that identifying the clinical profiles of the older inpatients at higher risk of unintentional medication discrepancies may be helpful as an additional supportive measure for enhancing pharmacological care. The objective of this study was to identify the clinical profiles of older inpatients at higher risk of unintentional medications discrepancies at admission in an acute care geriatric unit.

METHODS

Cross-sectional study with a prospective data collection conducted in the acute care geriatric unit of a university hospital in France (February-May 2019). The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement was followed [12]. Procedures and data collection have been published in detail elsewhere [13].

Eligibility criteria

The study included all the consecutive patients ≥75-year-old admitted to the acute care unit in the study period who agreed to participate and signed the informed consent. No specific exclusion criteria were applied.

Procedures and variables

Study participants received standardized clinical evaluation, medical examination and comprehensive geriatric assessment consisting of structured validated questionnaires, at admission. The following variables were recorded and used as confounders: Age, sex, BMI, marital status (i.e., cohabiting with partner), place of living (i.e. home or institution), type of hospitalization (i.e. scheduled or non-scheduled, urgent), Instrumental Activities of Daily Living (IADL) score, Mini-Mental State Examination (MMSE) score, Cumulative Illness Rating Scale-Geriatric (CIRS-G) score**,** history of ≥1 falls in the previous 6 months, prior fragility fractures, and diagnosis on admission.

A clinician pharmacist, as part of the interdisciplinary team in the acute care unit [13], systematically assessed each study participant at admission and registered the number of drugs, presence of polypharmacy (≥5 drugs per day), and the class of the drugs taken, which were categorized according to the Anatomical Therapeutic Chemical (ATC) classification system.

Outcome measure

The outcome measure was the presence of unintentional medication discrepancy at admission in the acute care unit, registered as a categorical variable by the clinician pharmacist. Each patient was considered to have unintentional medication discrepancy in presence of at least one of the following: Drug omission (deletion of a drug used before admission), drug commission (addition of a drug not used before admission), or drug partially matched (discrepancy in the name of the drug, in the strength and/or frequency and/or number of units of dosage, in the dosage form/route of administration, in the time of drug administration, or in the duration of

therapy) [13,14]. The volitional therapeutic adjustments made by the hospital physician (a member of the medical staff, frequently a geriatritian, but not exclusively) to patients' usual treatment upon admission to the acute care unit were not considered unintentional medication discrepancies. Queries were resolved through consensus among the above mentioned hospital physician and the clinician pharmacist [13].

Statistical analysis

The study sample was categorized into patients with or without at least one unintentional medication discrepancy at admission in the acute care geriatric unit. Chi² test or exact Fisher tests for qualitative variables, and Student t-test or Mann-Whitney Wilcoxon tests for quantitative variables were conducted.

As unintentional medication discrepancies are multifactorial, a classification tree analysis, using the Chi-square Automatic Interaction Detector (CHAID) algorithm and adjusted for age, was performed with all available data [15]. CHAID analysis is an algorithm used to discover relationships between a categorical response variable (the outcome measure, i.e., the presence of at least one unintentional medication discrepancy) and other predictor variables. It divides a parent group into two subgroups ('nodes') in which covariates are homogenous, and the outcome is distinct. The probability of unintentional medication discrepancies was calculated for each end node as a relative risk (RR) with a 95% confidence interval (CI). The end node with the lowest prevalence of unintentional medication discrepancies served as the reference (Node 3). CHAID analysis thus made it possible to define several groups with different risks of unintentional medication discrepancies. P-values <0.05 were considered statistically significant. Statistics were performed using SPSS version 19.0, Inc., Chicago, IL, USA).

Ethics

The study was approved by the Ethics Board of Angers University Hospital (2018). The study was conducted in accordance with the Good Clinical Practice (CGP) guidelines, the ethical standards of the Helsinki Declaration (1975), and its subsequent amendments (Fortaleza 2013). Informed consent was obtained from all participants, their caregivers, or their legal representants. Data were processed and treated in compliance with the EU Regulation 2016/679.

Results

From the 173 patients admitted to the acute care unit in the study period, 130 patients meet the eligibility criteria and were included (n= 130, 87 ± 5-year-old [74 to 99-year-old]; 61.8% women). From the 130 patients, 57 (43.8%) had at least one unintentional medication discrepancies at admission. **Table 1** shows the clinical characteristics of the participants based on the presence of unintentional medication discrepancies at admission. The characteristics of the patients with or without unintentional medication discrepancies at admission were similar, except that those patients with unintentional medication discrepancies used more drugs per day (9[6-11] vs. 8[6-10]; P=0.036), were more frequently under treatment with eye drops [22 (38.6) vs. 6 (8.2); P<0.001], and were less often hospitalized on a scheduled basis [12 (21.1%) vs. 27 (37%); P= 0.049].

The CHAID analysis identified 5 end-nodes, with the use of eye drops as the first split (Figure 1). Among patients not using eye drops, those who did not report frequent falls formed the end node with the lowest prevalence of unintentional medication discrepancies (12.5%) and the lowest odds ratio for unintentional medication discrepancies [OR= 0.24 (95%CI 0.07-0.78)] (Node 3, reference node). Compared to the reference node (Node 3), the probability of unintentional medication discrepancies was 1.74-fold higher in those without eye drops but reporting frequent falls and scheduled hospitalization (21.7% unintentional medication discrepancies)(Node 7); 3.93-fold higher in those without eye drops but with frequent falls and urgent hospitalization (49.1% unintentional medication discrepancies) (Node 8); 4-fold higher in those using eye drops and with scheduled hospitalization (50.0% unintentional medication discrepancies) (Node 5); and finally, 7.56-fold higher in those using eye drops and with non-scheduled, urgent hospitalization (94.4% unintentional medication discrepancies) (Node 6).

DISCUSSION

The study identified 5 clinical profiles of older inpatients with different risks of unintentional medication discrepancies based on the combinations of 3 characteristics: Use of eye drops, frequent falls (≥1/year), and non-scheduled, urgent hospitalization. The profile of patients who combined the use of eye drops and a non-scheduled, urgent hospitalization presented 7.56-fold higher risk of unintentional medication discrepancies (94.4%).

The study identified three unexpensive, objective, and easily measurable clinical characteristics that were helpful in early identifying those inpatients at higher risk of unintentional medication discrepancies. These characteristics may serve as a supportive information to be considered as part of the comprehensive geriatric assessment. Several consideration could be discussed. First, the increased risk due to the use of eye drops may be explained by the way this type of medication is issued in the French health system. Eye drops are usually prescribed by specialists in Ophthalmology and may not be included in the prescription issued by the Primary Care physician. It is also possible that the hospital physician may have overlooked or neglected the treatment with eye drops upon admission to acute care, possibly due to a lack of reliable information about them or considering the admission in acute care as a life-threatening situation. Second, the increased risk associated to frequent falls was aligned with the international guidelines and recommendations by the EuGMS Special Interest group on Pharmacology and the EuGMS Task and Finish group on fall-risk-increasing drugs [10]. Third, the unintentional medication discrepancies observed in the non-scheduled, urgent hospitalizations may be explained by the higher risk of cumulative medication errors due to the involvement of multiple prescribers or the challenge of exchanging high-quality, reliable information about medication with acutely ill older patients and their caregivers in the context of the emergency room during an urgent hospitalization [16].

Furthermore, some studies have described specific risk factors associated with unintentional medication discrepancies, such as age, polypharmacy, autonomous medication management, or living at home [1,17]. These factors were not found in our study, possibly because our population is significantly older. As a possible explanation, older adults living at home often receive more support with medication management than younger individuals, potentially reducing the risk of discrepancies. Including this last factor in our study could have been informative, and we would like to highlight it as a topic for further research. The study did not show associations between central nervous system agents and unintentional medication

discrepancies, which had been previously described as a source of potential medication errors in other populations and settings [18], and which may also require further research. Inhalers and patches may be sources of unintentional medication discrepancies in clinical practice in Geriatric Medicine, but they were not found to be among the main therapeutic classes associated with discrepancies in our study. For inhaled medications, these clinical findings have also been reported in the scientific literature [17], however, data about patches are still scarce, and further studies are needed to fill this knowledge gap.

Three limitations should be acknowledged. First, the cross-sectional design of the study does not allow us to stablish cause-effects associations. The potential impact of unintentional medication discrepancies on adverse outcomes was not assessed and this may require further longitudinal research. Second, the study was conducted in a single university hospital, with a relatively limited sample size, which might hinder the external generalizability of the findings. It would be interesting to continue exploring this hypothesis and test these findings in larger populations. Finally, the study included a relatively limited number of confounders, and the lack of available data for some of the variables should be acknoledged as a limitation. It would be important for further studies to take into consideration a larger number of confounders and other patients' characteristics, such as multimorbidity, geriatric syndromes, or frailty, which have been shown to be relevant in medication management [6,11].

Three strengths of the study should be highlighted. First, the study utilized a high-quality and innovative statistical model. The CHAID analysis is a relatively new statistical technique primarily used in market research. It is particularly helpful when searching for patterns in datasets with a large number of categorical variables, and is considered as a convenient way to summarize data as relationships can be easily visualized. Second, despite the relatively limited number of variables assessed, the study included most of the confounders commonly used in the literature and validates scales frequently administered in acute care in clinical practice. Finally, the findings are clinically meaningful, as these characteristics are part of the comprehensive geriatric assessment and may serve as supportive measures for early identification of high-risk inpatients in clinical practice. This should not imply rationing or restricting medication reconciliation to those at higher risk but rather emphasizes the interest of these findings as valuable, supportive information.

Conclusions

The study identified clinical profiles of older inpatients at the highest risk of unintentional medication discrepancies at hospital admission. Older inpatients under treatment with eye drops, experiencing frequent falls, and urdergoing non-scheduled, urgent hospitalization faced the highest risk of unintentional medication discrepancies.

The findings of the study were clinically meaningful. Considering these three inexpensive, objective, and easily measurable characteristics may be helpful as a supportive measure for the early identification of inpatients at higher risk of unintentional medication discrepancies in clinical practice and ultimately, improve the quality of care of hospitalized older adults.

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REFERENCES

1. Moges TA, Akalu TY, Sema FD. Unintended medication discrepancies and associated factors upon patient admission to the internal medicine wards: identified through medication reconciliation. BMC Health Serv Res. 2022;22.

2. Picone DM, Titler MG, Dochterman J, Shever L, Kim T, Abramowitz P, et al. Predictors of Medication Errors Among Elderly Hospitalized Patients. American Journal of Medical Quality. 2008;23:115–27.

3. Tam VC, Knowles SR, Cornish PL, Fine N, Marchesano R, Etchells EE. Frequency, type and clinical importance of medication history errors at admission to hospital: a systematic review. CMAJ. 2005;173:510–5.

4. Tobiano G, Chaboyer W, Dornan G, Teasdale T, Manias E. Older patients' engagement in hospital medication safety behaviours. Aging Clin Exp Res. 2021;33:3353–61.

5. Ensing HT, Stuijt CCM, Van Den Bemt BJF, Van Dooren AA, Karapinar-Çarkit F, Koster ES, et al. Identifying the Optimal Role for Pharmacists in Care Transitions: A Systematic Review. J Manag Care Spec Pharm. 2015;21:614–38.

6. Liau SJ, Lalic S, Sluggett JK, Cesari M, Onder G, Vetrano DL, et al. Medication Management in Frail Older People: Consensus Principles for Clinical Practice, Research, and Education. J Am Med Dir Assoc. 2021;22:43–9.

7. Quélennec B, Beretz L, Paya D, Blicklé JF, Gourieux B, Andrès E, et al. Potential clinical impact of medication discrepancies at hospital admission. 2013;24:530–5.

8. Tomlinson J, Cheong V-L, Fylan B, Silcock J, Smith H, Karban K, et al. Successful care transitions for older people: a systematic review and meta-analysis of the effects of interventions that support medication continuity. Age Ageing. 2020;49:558–69.

9. Van Den Bemt PMLA, Van Der Schrieck-De Loos EM, Van Der Linden C, Theeuwes AMLJ, Pol AG. Effect of medication reconciliation on unintentional medication discrepancies in acute hospital admissions of elderly adults: A multicenter study. J Am Geriatr Soc. 2013;61:1262–8.

10. Seppala LJ, van der Velde N, Masud T, Blain H, Petrovic M, van der Cammen TJ, et al. EuGMS Task and Finish group on Fall-Risk-Increasing Drugs (FRIDs): Position on Knowledge Dissemination, Management, and Future Research [Internet]. Eur Geriatr Med. Eur Geriatr Med; 2019; 275–83.

11. Onder G, Vetrano DL, Palmer K, Trevisan C, Amato L, Berti F, et al. Italian guidelines on management of persons with multimorbidity and polypharmacy. Aging Clin Exp Res. 2022;34:989.

12. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. Lancet. 2007;370:1453–7.

13. Chappe M, Corvaisier M, Brangier A, Annweiler C, Spiesser-Robelet L. Impact of the COVID-19 pandemic on drug-related problems and pharmacist interventions in geriatric acute care units. Ann Pharm Fr. 2022;80:669–77.

14. Almanasreh E, Moles R, Chen TF. The medication discrepancy taxonomy (MedTax): The development and validation of a classification system for medication discrepancies identified through medication reconciliation. Res Social Adm Pharm. 2020;16:142–8.

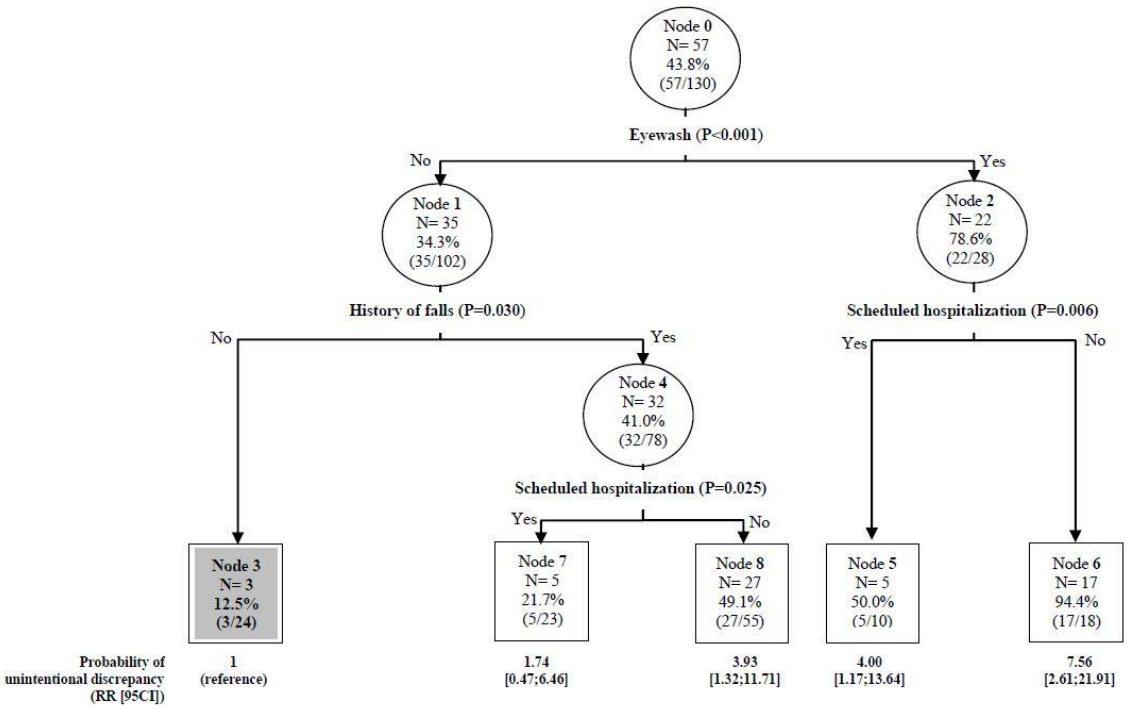
15. Magidson J. The CHAID approach to segmentation modeling: chi-squared automatic interaction detection. In: Bagozzi RP, ed. Advanced Methods of Marketing Research. Blackwell, Oxford; 1994. p. 118–59.

16. Cabilan CJ, Hughes JA, Shannon C. The use of a contextual, modal and psychological classification of medication errors in the emergency department: a retrospective descriptive study. J Clin Nurs. 2017;26:4335–43.

17. Masse M, Yelnik C, Labreuche J, André L, Bakhache E, Décaudin B, et al. Risk factors associated with unintentional medication discrepancies at admission in an internal medicine department. Intern Emerg Med. 2021;16:2213–20.

18. Renom-Guiteras A, Thürmann PA, Miralles R, Klaaßen-Mielke R, Thiem U, Stephan A, et al. Potentially inappropriate medication among people with dementia in eight European countries. Age Ageing. 2018;47:68–74.

Figure 1. Classification tree (Chi-square Automatic Interaction Detector, CHAID) analysis for the identification of older inpatients at higher risk of unintentional medication discrepancies at admission in acute care (n = 130).



For each node: node number; N with unintentional discrepancy within node; proportion of participants with unintentional discrepancy within node (N with unintentional discrepancy / N node). RR: Relative risk; 95CI: 95% confidence interval. The Anatomical Therapeutic Chemical (ATC) classification system was followed for S01 Eye drops.

Table 1. Clinical characteristics of study participants according to the presence of at least one unintentional medication discrepancy at admission in the acute care unit (n = 130).

Variables	Total sample (n = 130)	Unintentional medication discrepancies (n = 57)	No unintentional medication discrepancies (n = 73)	P-value <0.005 *
Age (years), mean ± SD	87.0 ± 5.2	86.7 ± 5.1	87.2 ± 5.3	0.531
Female sex, n (%)	80 (61.5)	35 (61.4)	45 (61.6)	0.978
BMI (kg/m²), mean ± SD	25.9 ± 5.1	25.7 ± 5.4	26.1 ± 4.8	0.728
Marital status, n (%) (n = 120†)	57 (47.5)	28/51 (54.9)	29/69 (42.0)	0.163
Living at home, n (%) (n = 83†)	69 (83.1)	30/34 (88.2)	39/49 (79.6)	0.301
Scheduled hospitalization, n (%)	39 (30.0)	12 (21.1)	27 (37.0)	**0.049**
IADL score, med [IQ]	1 [0-2]	1 [1-3]	1 [0-2]	0.155
MMSE score, /30, mean ± SD	17.9 ± 6.0	17.8 ± 6.3	18.0 ± 5.7	0.864
CIRS-G score, med [IQ]	15 [12-18]	14 [11-18]	15 [12-19]	0.622
Frequent falls in past 6 months, n (%) (n = 79†)	42 (53.2)	18/32 (56.3)	24/47 (51.1)	0.650
Prior fragility fractures, n (%) (n = 83†)	11 (13.3)	4/34 (11.8)	7/49 (14.3)	1.000
Drugs/day, med [IQ]	8 [6-10]	9 [6-11]	8 [6-10]	**0.036**
Polypharmacy, n (%) (n = 94†) **	84 (90.3)	36/38 (94.7)	46/53 (86.8)	0.509
N05B anxiolytics, n (%)	55 (42.3)	23 (40.4)	32 (43.8)	0.690
N06A Antidepressants, n (%)	45 (34.6)	20 (35.1)	25 (34.3)	0.920
N03 Antiepileptics, n (%)	10 (7.7)	5 (8.8)	5 (6.9)	0.748
N05A Antipsychotics, n (%)	9 (6.9)	2 (3.5)	7 (9.6)	0.297
C02 Antihypertensives, n (%)	96 (73.9)	41 (71.9)	55 (75.3)	0.660
A10 Antidiabetics, n (%)	25 (19.2)	7 (12.3)	18 (24.7)	0.076
B01 Antithrombotic agents (exclude platelet aggregation inhibitors), n (%)	43 (33.1)	21 (36.8)	22 (30.1)	0.420
A02 Drugs for acid related disorders, n (%)	47 (36.2)	21 (36.8)	26 (35.6)	0.885
S01 Eye drops, n (%)	28 (21.5)	22 (38.6)	6 (8.2)	**<0.001**
Main diagnosis on admission (n = 111†)				1.000
- Locomotion disorders	20 (24.3)	10/48 (20.8)	10/64 (15.6)	
- Organic failure	57 (27.9)	25/48 (52.1)	32/64 (50.0)	
- Neuropsychiatric disorders	31 (18.9)	11/48 (22.3)	20/64 (31.2)	
- Others	4 (20.7)	2/48 (4.2)	2/64 (3.1)	

BMI: Body mass index; CIRS-G: Cumulative Illness Rating Scale-Geriatric; IADL: Instrumental activities of daily living; IQR: Inter quartile range; MMSE: Mini-Mental State Examination; SD: standard deviation. The study sample was categorized into patients with or without at least one unintentional medication discrepancy at admission in the acute care unit. ***** Chi² test or de exact Fisher test for qualitative variables, and T-Student or Mann-Whitney Wilcoxon tests for quantitative variables were conducted; ****** Polypharmacy (≥5 drugs per day). † Number of patients with available data. The drugs were classified according according to the Anatomical Therapeutic Chemical (ATC) classification system (e.g., N05B anxiolytics, etc.)