

Iatrogenic risk factors associated with hospital readmission of elderly patients: A matched case-control study using a clinical data warehouse

C. Schwab, JB. Escudie, V. Savoldelli, C. Fernandez, P. Durieux, O. Saint-Jean, B. Sabatier

▶ To cite this version:

C. Schwab, JB. Escudie, V. Savoldelli, C. Fernandez, P. Durieux, et al.. Iatrogenic risk factors associated with hospital readmission of elderly patients: A matched case-control study using a clinical data warehouse. Journal of Clinical Pharmacy and Therapeutics, 2018, 43 (3), pp.393-400. 10.1111/jcpt.12670. hal-03837412

HAL Id: hal-03837412

https://hal.science/hal-03837412

Submitted on 30 Jan 2023

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

IATROGENIC RISK FACTORS ASSOCIATED WITH HOSPITAL READMISSION OF ELDERLY PATIENTS: A MATCHED CASE CONTROL STUDY USING A CLINICAL DATA WAREHOUSE

- Iatrogenic risk factors for readmission of elderly: a case control study -

C. Schwab^{1,2} and JB. Escudie^{1,3}, V. Savoldelli^{2,4}, C. Fernandez^{4,5,6}, P. Durieux^{1,3}, O. Saint-Jean⁷ and B. Sabatier^{1,2}

<u>Author information:</u> ¹INSERM UMR 1138, Equipe 22, Centre de Recherche des Cordeliers, Universités Paris 5 et 6, 75006 Paris, France

²Service Pharmacie, Hôpital Européen Georges Pompidou, Assistance Publique – Hôpitaux de Paris, 75015 Paris, France

³Département de Santé Publique et Informatique Médicale, Hôpital Européen Georges Pompidou, Assistance Publique – Hôpitaux de Paris, 75015 Paris, France

⁴Université Paris-Sud, Faculté de Pharmacie, 92296, Châtenay-Malabry, France

⁵Service de Pharmacie, Hôpital Saint-Antoine, Assistance Publique – Hôpitaux de Paris, 75012 Paris, France

⁶Sorbonne Universités, UPMC Univ Paris 06, UMR-S 1136, Institut Pierre Louis D'Epidémiologie et de Santé Publique, Paris, France

⁷Faculté de Médecine, Université Paris-Descartes, 75006 Paris, France

⁸Service de Gériatrie, Hôpital Européen Georges Pompidou, Assistance Publique – Hôpitaux de Paris, 75015 Paris, France

Corresponding Author:

Camille Schwab
Hôpital Européen Georges Pompidou
Pharmacie,
20-40, rue Leblanc
75015 Paris, France
Tel: +331 56093154

Fax: +331 56092559 camille.schwab@aphp.fr

Key Words: aged, patient readmission, risk factors, data warehouse

No conflicts of interest have been declared.

ABSTRACT

What is known: Hospital readmission within 30 days of patient discharge has become a standard to judge the quality of hospitalizations. It is estimated that 14% of the elderly, people over 75 years old or those over 65 with comorbidities, are at risk of readmission, of which 23% are avoidable. It may be possible to identify elderly patients at risk of readmission and implement steps to reduce avoidable readmissions.

Objective: The aim of this study was to identify iatrogenic risk factors of readmission. The secondary objective was to evaluate the rate of Drug Relative Readmissions (DRRs) among all readmissions and compare it to the rate of readmissions for other reasons.

Methods: We conducted a retrospective, matched, case-control study to identify non-demographic risk factors of avoidable readmission, specifically DRRs.

The study included patients hospitalized between September 1, 2014 and October 31, 2015 in an 800-bed university hospital.

We included patients aged 75 and over. Cases consisted of patients readmitted to the emergency department within 30 days of initial discharge. Controls did not return to the emergency department within 30 days. Cases and controls were matched on sex and age because they are known as readmissions risk factors.

After comparison, of the mean or percentage between cases and controls for each variable, we conducted a conditional logistic regression.

Results: The risk factors identified were an emergency admission at the index hospitalization, returning home after discharge, a history of unplanned readmissions, and prescription of nervous system drugs. Otherwise, 11.4% of the readmissions were DRRs, of which 30% were caused by an overdose of antihypertensive. The number of drugs at readmission was higher and potentially inappropriate medications were more widely prescribed for DRRs than for readmissions for other reasons.

What is new and conclusion: In this matched case-control retrospective study, after controlling for gender and age, we identified the typical profile of elderly patients at risk of readmission. These patients had an unplanned admission at the index hospitalization and prescribed nervous system drugs at discharge from the index admission, they have a history of unplanned readmission within 30 days and return home after discharge.

WHAT IS KNOWN

Hospital readmission within 30 days of patient discharge has become a standard to judge the quality of hospitalizations. Among these readmissions, unscheduled hospitalizations directly related to the index hospital stay are considered to be avoidable¹.

The elderly are defined as people over 75 years of age or those over 65 with comorbidities². They show a progressive loss of reserve and adaptive capacity and an overall deterioration in health that can result in disability or loss of independence³. Hospitalizations may be particularly deleterious for these patients, making them even more dependent⁴. It has been estimated that 14% of elderly are at risk for readmission, of which 23% are avoidable¹.

Readmission results from decompensated comorbidities, resulting in overcrowded emergency departments (EDs) and increased hospital expenses⁵. Since 2013, the French Ministry of Health has warned health professionals about the high risk of readmission for the elderly and has made the reduction of readmissions a priority¹. Various interventions have been tested to reduce readmission rates: discharge planning protocols, comprehensive geriatric assessments, discharge support arrangements, and education⁶. However, the "Haute Autorité de Santé" (HAS) advocates identifying frail patients who need these interventions. Indeed, the identification of such patients is essential, as it is not "necessary nor efficient to intervene for every patient"¹.

Prescribed drug-related readmissions (DRRs) represent between $4.2\%^7$ and $24.3\%^8$ of readmissions. They may be due to adverse reactions of drugs prescribed at discharge, suboptimal therapy, or medication nonadherence⁹. Some drugs are known to be generally associated with poor health outcomes and are listed as potentially inappropriate medications (PIMs)^{10,11}. The American Geriatrics Society has assembled the latest PIMs list: The American Geriatrics Society Beers Criteria for Potentially Inappropriate Medication Use in Older Adults¹². However, the results of studies on PIMs and readmissions are conflicting. Hagstrom *et al.* showed that the prescription of PIMS had no effect on the readmission rate¹³, whereas Pavon *et al.* showed that the prescription of benzodiazepines, which are listed as PIMs, was associated with a higher readmission risk $(OR = 1.23)^{14}$.

The DRRs should be mostly avoidable, with appropriate intervention on the management of the elderly at risk of readmission. It may be possible to identify elderly patients at risk of readmission, particularly DRRs, and implement to reduce avoidable readmissions.

We identified patients at risk of readmission using a clinical data warehouse (CDW). The CDW allows the performance of complex queries while achieving reliable and high-quality results.

OBJECTIVE

The aim of this study was to identify iatrogenic risk factors of readmission.

The secondary objective was to evaluate the rate of DRR among all readmissions and compare it to the rate of readmissions for other reasons.

METHODS

We conducted a retrospective, matched, case-control study to identify non-demographic risk factors of avoidable readmission, specifically DRR.

• Data source:

The hospital is a teaching hospital of 795 beds with 24 clinical departments (15 medical wards and nine surgical units). The clinical information system has been associated with a CDW since 2009, making it possible to reuse healthcare data and clinical research.

All medical records and prescriptions are computerized. The data needed for the study were stored in the CDW and extracted using Oracle® software, or manually by reading the electronic medical record.

An ethics committee approved the study protocol (CERHUPO, CDW_2015_0023).

• Study participants:

Patients were at least 75 years old and admitted to the university hospital from October 1st, 2014 to September 30th, 2015.

Cases consisted of elderly patients who experienced an unscheduled readmission within 30 days after the index admission. Readmissions had to originate at the ED to be considered unscheduled. All patients who were readmitted without a prior ED visit were excluded. Readmission included simple ED visits.

Controls consisted of elderly patients who had not had any unscheduled readmissions during the 30 days after the index admission. All controls that died during the index hospitalization were excluded.

Cases and controls were randomly matched.

• Study variables:

We identified readmission risk factors by literature review (Table 1). For each risk factor, we listed the category, the odds ratio (or hazard ratio or relative risk), the reference, and the variables to be used in our study. Many readmission risk factors appeared to be already known in the literature, but few were related to the medications prescribed at discharge of the index hospitalization. **Age and sex** are known to be readmission risk factors^{15–17}. Thus, controls were matched to cases (1:1), based on their sex and index age (within 5 years), to control for these two risk factors, to have similar populations between cases and controls and to keep patient characteristics, admission characteristics and therapeutic characteristics in the multivariate analysis.

The study variables were:

- **Patient characteristics:** Marital status, level of social support (living alone or accompanied, nursing home residents or elderly living at home), socio-professional category, comorbidity (Charlson index), presence of depression, dependence in activities of daily living, and malnutrition.
- **Admission characteristics:** Programmed admission or emergency admission, medical or surgical pattern, primary diagnosis and history of readmission (any hospitalizations followed by an emergency readmission within 30 days describe in the medical record) and length of stay.
- **Therapeutic characteristics**: Each drug listed on the discharge prescriptions was classified according to the ATC (*Anatomical Therapeutic Chemical*) Classification, whether it was a PIM, and the number of drugs.
- Study outcomes:

The primary outcome of the study was to identify iatrogenic risk factors of readmission for elderly patients to identify those who require interventions.

The secondary outcomes were to evaluate the rate of DRR among all readmissions and to describe the drug-related problems.

• Statistical analysis:

All statistical analyses were conducted using R software (R Version 3.3.3; 2017-03-06).

Univariate analysis: We compared the mean (quantitative variables) or percentage (qualitative variables) between cases and controls for each variable to select those for the logistic regression. We used t-tests for the quantitative variables and chi-square tests compare the percentages of qualitative variables.

The selected variables for the multivariate analysis were those that were significant following comparison (p < 0.05) or those with a p-value < 0.10 for risk factors largely described in the literature.

Multivariate analysis: After generating a diagram of eigenvalues and a performing a factor analysis, we conducted a principal component analysis to determine the correlations between selected variables. Knowledge of the correlations allowed removing variables from the logistic regression. We retained the variable with the smallest *p-value* when two were correlated. The variables were removed from the logistic regression until most had a significant *p-value* (<0.05) and a low Akaike criterion (AIC).

Secondary objective: The secondary outcome was to compare DRR with readmissions for other reasons. We used t-tests and chi-square tests for quantitative and qualitative variables, respectively.

RESULTS

From September 1, 2014 to October 31, 2015, 6,574 elderly patients meeting our criteria were admitted to the hospital. Within 30 days after discharge of the index hospitalization, 422 patients (6.4%) were readmitted, whereas 6,096 were not. These 422 patients were randomly matched with 422 controls among the 6,096 patients, creating 422 case-control pairs. Among the 422 unplanned readmissions, 137 (32.5%) were ED visits, without hospital admission.

• Bivariate analysis:

Bivariate analysis allowed the comparison of cases and controls to select the variables used for multivariate analysis (Table 2).

The patient characteristics of cases significantly differed from controls for the Charlson index and depression, as indicated in the medical record (p = 0.00681 and 0.0281, respectively). The place of residence had a p-value < 0.1 (p = 0.053). There were no statistical differences between the case and control groups for all other variables (marital status, residence, social support, depression, feeding, continence, hygiene, and mobility). The socio-professional category and nutritional status were removed from statistical analysis because of too much missing data (41% and 59%, respectively).

We then compared the index admission characteristics between cases and controls. By univariate analysis, an unplanned index admission, a medical index admission, a return to home at discharge, and a history of avoidable readmissions were significantly higher for the case than control group ($p = 7.43 \times 10^{-5}$, 0.00313, 0.00346, and 6.79×10⁻⁵, respectively). There were no statistical differences between the case and control groups for all other variables (length of stay and primary diagnosis).

Finally, we compared the treatment characteristics at discharge of the index hospitalization. Cases significantly differed from controls for the number of drugs (p = 0.00230), polypharmacy (p = 0.0131), PIM (p = 0.00637), systemic hormonal preparations (p = 0.0377) and nervous system drugs (p = 0.000556) (ATC Classes H and N). The prescription of drugs of the alimentary tract and metabolism had p-value < 0.1 (p = 0.0672). There was no statistical difference between the case and control groups for the other ATC classes.

• Multivariate analysis:

Selected variables for the multivariate logistic regression analysis were social support (living alone or not), the residence (private home or retirement home), presence of depression or dementia, Charlson index, type of index admission (planned or emergency *vs* medical or surgical), history of readmission, number of prescribed drugs at discharge of the index hospitalization and polypharmacy, number of PIMs, number of drugs in classes A, H, and N (metabolism, hormonal preparations, and nervous system drugs), and type of discharge (return home or transfer to another health institution). These variables were statistically significant by univariate analysis or highly described in the literature. Following factor analysis and principal component analysis, we observed that planned or unplanned admission and medical or surgical admission were correlated, as well as the number of prescribed drugs and polypharmacy. These correlations helped to construct the logistic regression model (Table 3).

The starting logistic regression model (with all selected variables) had an AIC of 547.813. The conditional logistic regression (Table 3) had an AIC of 537.916. In this model, an index admission in emergency, a return home at discharge, a history of readmissions, and the prescription of nervous system drugs were still significantly associated with the risk of readmission after adjustment for the Charlson index. Thus, an emergency admission at the index hospitalization increased the readmission risk (OR = 1.96, 95%CI = 1.41-2.71). Returning at home after discharge and having history of unplanned readmissions also increased the risk of readmission (OR = 1.84 and 1.66, respectively), as well as the prescription of nervous system drugs (OR = 1.81, 95% IC: 1.30-2.52). Among all the 844 subjects, 43 (5.1%) who had an index admission in emergency, a return to home at discharge, a history of readmissions, and the prescription of nervous system drugs were readmitted. On the contrary, 8 (0.95%) patients had none of these characteristics.

• Secondary objective:

In this study, 11.4% of the readmissions were DRRs, of which 30% were caused by an overdose of antihypertensive drugs, leading to falls and hypotension (6.4% and 8.5% of the reasons for DRR, respectively).

The number of drugs at readmission was higher and PIMs were more widely prescribed for DRRs than for readmissions for other reasons ($p = 6.688 \times 10^{-5}$, and 0.00837, respectively).

WHAT IS NEW AND DISCUSSION

In our study, after controlling for gender and age, patients at risk of readmission had an unplanned admission at the index hospitalization and prescribed nervous system drugs at discharge from the index admission. Furthermore, they had a history of unplanned readmission at 30 days and returned home after discharge.

Unplanned admissions were mostly related to a medical pattern. This correlation can be explained by comorbidities that lead to decompensation of a chronic condition and thus unplanned admission. Moreover, comorbidities^{16,24} and medical admissions²⁵ are known factors of readmission. Thus, these two readmission risk factors show that an unplanned admission is also a risk factor for readmission. Indeed, in 2012, Van Walraven *et al.* had already found that unplanned admission was a readmission risk factor, as it is one of the variables of the clinical LACE index²⁷.

We also found that the prescription of nervous system drugs at discharge, including antidepressants, increases readmission risk. Although patient and admission characteristics are well known readmission risk factors, therapeutic risk factors have only recently been studied. The link between psychotropic drugs and readmission has been previously shown¹⁴, especially for DRR²⁸. Indeed, psychotropic drugs (class ATC N) are highly responsible for adverse drug reactions²⁹.

A history of admissions or ED visits is known to be a risk factor for readmissions. Indeed, in a systematic review, Garcia-Perez *et al.* found that patients admitted in the previous three or six months had an increased risk of readmission on Furthermore, these variables are part of two existing clinical scores for predicting readmission risk: previous hospital admission for the HOSPITAL score on and ED use in the previous 30 days or hospitalization in the previous 90 days for the Triage Risk Screening Tool (TRST). However, we demonstrate here that patients with a history of unplanned readmission within 30 days, i.e., any hospitalization followed by an unplanned readmission within 30 days, were more likely to be readmitted. This may be because readmitted patients have chronic comorbidities at high risk of decompensation: a comorbidity that decompensates once can certainly decompensate again.

The secondary outcome of this study was to describe DRRs in cases. Patients with a DRR had more PIM's prescribed than those readmitted for reasons other than an adverse drug reaction. To our knowledge, no previous study has investigated the impact of PIMs on DRRs. However, JM. Pavon $et\ al.^{14}$ and H. Chayé $et\ al.^{28}$ showed a link between psychotropic and cardiological drugs and readmission (including DRR).

This study had several limitations and strengths. The main limitation was that we did not consider readmission to another facility as the electronic health records were limited to readmissions in the same hospital. There was also a misclassification bias: we did not consider unscheduled readmissions which didn't originate from an ED visit, because the distinction from scheduled admissions was not possible using the CDW. Thus, we may have underestimated the readmission rate, since controls might have been readmitted to another health institution or died after the index hospitalization. A matched case-control study design prevents this limitation. Finally, only readmissions annotated as iatrogenic were considered for be DRRs, which may have led to an underestimation of the DRR rate. The strength of this study is its focus on iatrogenic risk factors. These risk factors are modifiable by actions taken at discharge, unlike patient and admissions characteristics.

In conclusion, this study identified several readmission risk factors: emergency admission at the index hospitalization, the prescription of nervous system drugs, and a history of unplanned readmissions. We will be able to use these factors to identify patients at risk of readmission during their hospitalization, and offer them a program at discharge to reduce this risk, such as a comprehensive chronic treatment review with education on the self-management of the disease and transition-of-care communication. Indeed, thanks to the computerized medical records, patients presenting at least one of the identified risk factors will be selected to have the discharge program. A clinical score including the identifying risk factors will also be researched. Multimodal geriatric discharge planning intervention has already shown its efficacity³². Identifying patients at risk will help to select those for whom such planning intervention would be efficient.

REFERENCES

- (1) Haute Autorité de Santé. (2013) Comment réduire le risque de réhospitalisations évitables des personnes âgées ?
- (2) Professeur Sylvie Legrain. (2005) Consommation médicamenteuse chez le Sujet Agé : Consommation, Prescription, Iatrogénie et Observance. Haute Autorité de Santé.
- (3) Diez-Ruiz, A., Bueno-Errandonea, A., Nuñez-Barrio, J., Sanchez-Martín, I., Vrotsou, K., and Vergara, I. (2016) Factors associated with frailty in primary care: a prospective cohort study. BMC Geriatr. 16, 91.
- (4) Sager, M. A., Franke, T., Inouye, S. K., Landefeld, C. S., Morgan, T. M., Rudberg, M. A., Sebens, H., and Winograd, C. H. (1996) Functional outcomes of acute medical illness and hospitalization in older persons. Arch. Intern. Med. 156, 645–652.
- (5) Lanièce, I., Couturier, P., Dramé, M., Gavazzi, G., Lehman, S., Jolly, D., Voisin, T., Lang, P. O., Jovenin, N., Gauvain, J. B., Novella, J.-L., Saint-Jean, O., and Blanchard, F. (2008) Incidence and main factors associated with early unplanned hospital readmission among French medical inpatients aged 75 and over admitted through emergency units. Age Ageing 37, 416–422.
- (6) Hansen, L. O., Young, R. S., Hinami, K., Leung, A., and Williams, M. V. (2011) Interventions to reduce 30-day rehospitalization: a systematic review. Ann. Intern. Med. 155, 520–528.
- (7) Teymoorian, S. S., Dutcher, D., and Woods, M. (2011) Association between postdischarge adverse drug reactions and 30-day hospital readmission in patients aged 80 and older. J. Am. Geriatr. Soc. 59, 948–949.
- (8) Bonnet-Zamponi, D., d'Arailh, L., Konrat, C., Delpierre, S., Lieberherr, D., Lemaire, A., Tubach, F., Lacaille, S., Legrain, S., and Optimization of Medication in AGEd study group. (2013) Drug-related readmissions to medical units of older adults discharged from acute geriatric units: results of the Optimization of Medication in AGEd multicenter randomized controlled trial. J. Am. Geriatr. Soc. 61, 113–121.
- (9) Dormann, H., Neubert, A., Criegee-Rieck, M., Egger, T., Radespiel-Tröger, M., Azaz-Livshits, T., Levy, M., Brune, K., and Hahn, E. G. (2004) Readmissions and adverse drug reactions in internal medicine: the economic impact. J. Intern. Med. 255, 653–663.

- (10) Laroche, M.-L., Bouthier, F., Merle, L., and Charmes, J.-P. (2009) Médicaments potentiellement inappropriés aux personnes âgées: intérêt d'une liste adaptée à la pratique médicale française. Rev. Médecine Interne 30, 592–601.
- (11) Pohl-Dernick, K., Meier, F., Maas, R., Schöffski, O., and Emmert, M. (2016) Potentially inappropriate medication in the elderly in Germany: an economic appraisal of the PRISCUS list, BMC Health Serv. Res. 16.
- (12) By the American Geriatrics Society 2015 Beers Criteria Update Expert Panel. (2015) American Geriatrics Society 2015 Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults. J. Am. Geriatr. Soc. 63, 2227–2246.
- (13) Hagstrom, K., Nailor, M., Lindberg, M., Hobbs, L., and Sobieraj, D. M. (2015) Association Between Potentially Inappropriate Medication Use in Elderly Adults and Hospital-Related Outcomes. J. Am. Geriatr. Soc. 63, 185–186.
- (14) Pavon, J. M., Zhao, Y., McConnell, E., and Hastings, S. N. (2014) Identifying risk of readmission in hospitalized elderly adults through inpatient medication exposure. J. Am. Geriatr. Soc. 62, 1116–1121.
- (15) Preyde, M., and Brassard, K. (2011) Evidence-based risk factors for adverse health outcomes in older patients after discharge home and assessment tools: a systematic review. J. Evid.-Based Soc. Work 8, 445–468.
- (16) García-Pérez, L., Linertová, R., Lorenzo-Riera, A., Vázquez-Díaz, J. R., Duque-González, B., and Sarría-Santamera, A. (2011) Risk factors for hospital readmissions in elderly patients: a systematic review. QJM Mon. J. Assoc. Physicians 104, 639–651.
- (17) Mathew, S. A., Gane, E., Heesch, K. C., and McPhail, S. M. (2016) Risk factors for hospital re-presentation among older adults following fragility fractures: a systematic review and meta-analysis. BMC Med. 14.
- (18) Fethke, C. C., Smith, I. M., and Johnson, N. (1986) "Risk" factors affecting readmission of the elderly into the health care system. Med. Care 24, 429–437.
- (19) Marcantonio, E. R., McKean, S., Goldfinger, M., Kleefield, S., Yurkofsky, M., and Brennan, T. A. (1999) Factors associated with unplanned hospital readmission among patients 65 years of age and older in a Medicare managed care plan. Am. J. Med. 107, 13–17.

- (20) Morrissey, E. F., McElnay, J. C., Scott, M., and McConnell, B. J. (2003) Influence of Drugs, Demographics and Medical History on Hospital Readmission of Elderly Patients: A Predictive Model. Clin. Drug Investig. 23, 119–128.
- (21) Alassaad, A., Melhus, H., Hammarlund-Udenaes, M., Bertilsson, M., Gillespie, U., and Sundström, J. (2015) A tool for prediction of risk of rehospitalisation and mortality in the hospitalised elderly: secondary analysis of clinical trial data. BMJ Open 5, e007259.
- (22) Zanocchi, M., Maero, B., Martinelli, E., Cerrato, F., Corsinovi, L., Gonella, M., Ponte, E., Luppino, A., Margolicci, A., and Molaschi, M. (2006) Early re-hospitalization of elderly people discharged from a geriatric ward. Aging Clin. Exp. Res. 18, 63–69.
- (23) Kwok, T., Lau, E., Woo, J., Luk, J. K., Wong, E., Sham, A., and Lee, S. H. (1999) Hospital readmission among older medical patients in Hong Kong. J. R. Coll. Physicians Lond. 33, 153–156.
- (24) Franchi, C., Nobili, A., Mari, D., Tettamanti, M., Djade, C. D., Pasina, L., Salerno, F., Corrao, S., Marengoni, A., Iorio, A., Marcucci, M., Mannucci, P. M., and REPOSI Investigators. (2013) Risk factors for hospital readmission of elderly patients. Eur. J. Intern. Med. 24, 45–51.
- (25) Davies, E. C., Green, C. F., Mottram, D. R., Rowe, P. H., and Pirmohamed, M. (2010) Emergency re-admissions to hospital due to adverse drug reactions within 1 year of the index admission. Br. J. Clin. Pharmacol. 70, 749–755.
- (26) Bogaisky, M., and Dezieck, L. (2015) Early hospital readmission of nursing home residents and community-dwelling elderly adults discharged from the geriatrics service of an urban teaching hospital: patterns and risk factors. J. Am. Geriatr. Soc. 63, 548–552.
- (27) van Walraven, C., Dhalla, I. A., Bell, C., Etchells, E., Stiell, I. G., Zarnke, K., Austin, P. C., and Forster, A. J. (2010) Derivation and validation of an index to predict early death or unplanned readmission after discharge from hospital to the community. CMAJ Can. Med. Assoc. J. J. Assoc. Medicale Can. 182, 551–557.
- (28) Chayé, H., Bernard, M., Tubéry, M., Rousseau, V., Ecoiffier, M., Montastruc, J.-L., and Bagheri, H. (2015) [Hospital readmission induced by adverse drug reaction: a pilot study in a post-emergency unit of a French university hospital]. Rev. Med. Interne 36, 450–456.
- (29) Jolivot, P.-A., Hindlet, P., Pichereau, C., Fernandez, C., Maury, E., Guidet, B., and Hejblum, G. (2014) A systematic review of adult admissions to ICUs related to adverse drug events. Crit. Care Lond. Engl. 18, 643.

- (30) Donzé, J., Aujesky, D., Williams, D., and Schnipper, J. L. (2013) Potentially avoidable 30-day hospital readmissions in medical patients: derivation and validation of a prediction model. JAMA Intern. Med. 173, 632–638.
- (31) Meldon, S. W., Mion, L. C., Palmer, R. M., Drew, B. L., Connor, J. T., Lewicki, L. J., Bass, D. M., and Emerman, C. L. (2003) A brief risk-stratification tool to predict repeat emergency department visits and hospitalizations in older patients discharged from the emergency department. Acad. Emerg. Med. Off. J. Soc. Acad. Emerg. Med. 10, 224–232.
- (32) Legrain, S., Tubach, F., Bonnet-Zamponi, D., Lemaire, A., Aquino, J.-P., Paillaud, E., Taillandier-Heriche, E., Thomas, C., Verny, M., Pasquet, B., Moutet, A. L., Lieberherr, D., and Lacaille, S. (2011) A new multimodal geriatric discharge-planning intervention to prevent emergency visits and rehospitalizations of older adults: the optimization of medication in AGEd multicenter randomized controlled trial. J. Am. Geriatr. Soc. 59, 2017–2028.

Table 1: Risk Factors Described in The Literature

Risk factors		OR (or HR or RR) [95%CI]	References	Variables selected for our study	
Patient characteristics					
Sex	Women	OR = -1.539	Fethke <i>et al</i> . ¹⁸	Matching for sex and age	
Age	Age > 80 years	OR = 1.8 [1.02 - 3.2]	Marcantonio et al.19		
	Widow	OR = 1.745	Fethke <i>et al</i> . ¹⁸	Single = divorced, single or	
Marital status	Single	OR = 2.195 [0.979 - 4.919]	Morrissey et al. ²⁰	widow Maried = maried or living together	
Residence	Living in a home for the elderly	HR = 1.617 [1.176 - 2.224]	Alassaad et al. ²¹	Private home or Home for the	
Residence	Living in a convalescent home	RR = 1.9 [1.1 - 3.3]	Zanocchi et al. ²²	elderly	
Social support	Poor familial support according to patient	RR = 2.7 [1.2 - 6.1]	Kwok et al. ²³	Living alone or not	
Education level	Medium-High education level	RR = 1.8 [1.1 - 3.6]	Zanocchi <i>et al.</i> ²²	Socio-professional category	
	Pulmonary disease	HR = 1.834 [1.296 – 2.595]	Alagged et al 21	Charlson Index, depression,	
	Cancer	HR = 1.659 [1.198 – 2.297]	Alassaad <i>et al.</i> ²¹		
	CIRS Score	OR = 2.24 [1.25 – 4.03]	Franchi <i>et al.</i> ²⁴		
Comorbidities	Liver disease	OR = 2.32 [1.42 – 3.77]		prescription of antidepressant	
	Cardio-vascular disease	OR = 1.48 [1.0 – 2.17]		drugs	
	Charlson index > 2	RR = 1.8 [1.1-3.6]	Zanocchi et al. ²²		
	Antidepressant prescription	HR = 0.573 [0.410 - 0.799]	Alassaad <i>et al.</i> ²¹		
Activity of daily living	Becoming dependent for feeding (ADL-Katz scale)	OR = 1.9 [1.2 – 2.9]	Lanièce <i>et al</i> . ⁵	Dependence for feeding, continence, mobility, and hygiene	

OR = Odd-ratio, HR = Hazard Ratio, RR = Relative Risk

Table 1: Risk Factors Described in The Literature - Continued

Risk factors		OR (<i>or HR or RR</i>) [95%CI]	Reference	Variables of our study	
Admission characteristics					
Type of admission	78.4% of medical readmitted patients <i>vs</i> 65.8% medical non-readmitted patients (p < 0.0001)		Davis <i>et al.</i> ²⁵	Planned admission or emergency, medical, or surgical admission	
Length of stay (LOS)	LOS (days)	RR = 3.2 [1.5-7.3]	Zanocchi et al.22	LOS (days)	
Primary diagnosis	See comorbidities			Primary diagnosis	
Discharge	Elderly adults discharged to nursing homes after a hospitalization had a 41% higher chance of 30-day hospital readmission than those discharged to the community.		Bogaisky <i>et al.</i> ²⁶	Return home or transfer	
History of readmission Previous hospital admission (6 months before index admission)		2.09 [1.44-3.03]	Franchi <i>et al</i> . ²⁴	30-day readmission history	
Therapeutic characteristics					
Polymedication	> 4 drugs at discharge	OR = 1.757 [0.999 – 3.090]	Morrissey et al. ²⁰	Number of prescribed drugs at discharge	
Potentially Inappropriate Medication (PIM)	Benzodiazepine prescriptions	OR = 1.23 [1.04-1.44]	Pavon <i>et al</i> . ¹⁴	Number of PIMs	
	Antacid prescriptions Opioid prescriptions	HR = 1.436 [1.101 – 1.872] HR = 2.063 [1.517 – 2.806]	Alassaad <i>et al</i> . ²¹	Number of Films	

OR = Odd-ratio, HR = Hazard Ratio, RR = Relative Risk

Table 2: Univariate analysis

Variables	Cases N = 422	Controls N = 422	p-value
Marital status: n (%)			0.534
Single	230 (56.1%)	210 (53.7%)	
Residence: n (%)	,		0.053
Private home	382 (90.5%)	397 (94.1%)	
Home for elderly	40 (9.5%)	25 (5.9%)	
Social support: n (%)			0.174
Living alone	159 (39.2%)	164 (44%)	
Living with someone	247 (60.8%)	25 (5.9%)	
Comorbidities: n (%)	,		
History of myocardial infarction: n (%)	39 (9.2%)	35 (8.3%)	0.626
Congestive heart failure: n (%)	240 (56.9%)	22 (52.6%)	0.213
Chronic arterial occlusive disease of the lower extremities: n (%)	49 (11.6%)	43 (10.2%)	0.508
History of stroke: n (%)	36 (8.5%)	40 (9.5%)	0.631
Dementia: n (%)	103 (24.4%)	77 (18.2%)	0.029
Chronic pulmonary disease: n (%)	67 (15.9%)	69 (16.4%)	0.852
Connective tissue diseases: n (%)	27 (6.4%)	26 (6.2%)	0.887
Gastroduodenal ulcer: n (%)	42 (10%)	38 (9.0%)	0.638
Diabetes: n (%)	72 (17.1%)	66 (15.6%)	0.577
Kidney disease: n (%)	72 (17.1%)	58 (13.7%)	0.182
Malignant disease: n (%)	160 (37.9%)	146 (34.6%)	0.316
Charlson Index: m (sd)	6.82 (1.94)	6.45 (1.99)	0.00681**
Depression (notified in medical record): n (%)	51 (12.1%)	32 (7.6%)	0.0281*
Feeding: n (%)			0.818
Dependent	23 (5.5%)	27 (6.4%)	
Partial dependence	92 (21.8%)	94 (22.3%)	
Independent	307 (72.7%)	301 (71.3%)	
Continence: n (%)	302 (71.6%)	311 (73.7%)	0.487
Hygiene			0.571
Dependent	63 (14.9%)	61 (14.5%)	
Partial dependence	178 (42.2%)	165 (39.1%)	
Independent	181 (49.9%)	196 (46.4%)	
Mobility: n (%)			0.568
Bedridden	57 (13.5%)	60 (14.2%)	
Partial dependence	168 (39.8%)	153 (36.3%)	
Independent	197 (46.7%)	209 (49.5%)	
Admission planned or emergency: n (%)		7	.43x10 ^{-5***}

E	211 (72 70/)	257 ((0,00/)	
Emergency	311 (73.7%)	257 (60.9%)	
Medical or surgical admission: n (%)			0.00313**
Medical	294 (69.7%)	253 (60%)	
Length of stay (≥ 5 days): n (%)	216 (51.2%)	195 (46.2%)	0.148
Discharge: n (%)			0.00346**
Return home	314 (74.4%)	275 (65.2%)	
Transfer	108 (25.6%)	147 (34.8%)	
History of avoidable readmission: n (%)	106 (25.1%)	60 (14.2%)	6.79x10 ⁻ 5***
Number of drugs: m (sd)	7.51 (3.59)	6.75 (3.66)	0.00230**
Polypharmacy (> 5 drugs): n (%)	298 (70.6%)	264 (62.6%)	0.0131*
Potentially inappropriate Medication (>1): n	268 (63.5%)	229 (54.3%)	0.00637**
(%)			
Drugs according to Anatomical Therapeutic			
Chemical (ATC) Classification			
Class A drugs (>1): n (%)	327 (77.5%)	303 (71.8%)	0.0576
Class B drugs (>1): n (%)	299 (70.9%)	315 (74.6%)	0.216
Class C drugs: (>1): n (%)	343 (81.3%)	335 (79.4%)	0.489
Class G drugs (>1): n (%)	57 (13.5%)	49 (11.6%)	0.406
Class H drugs (>1): n (%)	95 (22.5%)	71 (16.8%)	0.0377*
Class J drugs (>1): n (%)	65 (15.4%)	57 (13.5%)	0.434
Class L drugs (>1): n (%)	28 (6.6%)	19 (4.5%)	0.177
Class M drugs (>1): n (%)	46 (10.9%)	49 (11.6%)	0.744
Class N drugs: (>1): n (%)	318 (75.4%)	272 (64.5%)	0.000556***
Class R drugs (>1): n (%)	57 (13.5%)	63 (14.9%)	0.554
C' 'C' *** 0 004 **0 04 0 05 0 4 D ' I'	. 1 101	D 40 40 D 6	

Significance: *** 0.001, **0.01, 0.05, 0.1. Primary diagnosis according to ICD-10: A&B = Certain infectious and parasitic disease, C&D = Neoplasms, diseases of the blood and blood-forming organs, and certain disorders involving the immune mechanism, E = Endocrine, nutritional and metabolic disease, F = Mental and behavioral disorders, G = Diseases of the nervous system, H = Diseases of the eye and adnexa, diseases of the ear and mastoid process, I = Diseases of the circulatory system, J = Diseases of respiratory system, K = Diseases of digestive system, L = Diseases of the musculoskeletal system and connective tissue, M = Diseases of the genitourinary system, R = Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified, S&T = Injury, poisoning and certain other consequences of external causes, Z = Factors influencing health status and contact with health services. ATC Classification: Class A = Alimentary tract and metabolism, Class B = Blood and blood forming organs, Class C = Cardiovascular system, Class G = Genitourinary system and sex hormones, Class H = System hormonal preparations, excluding sex hormones and insulin, Class J = Anti-infectives for systemic use, Class L = Antineoplastic and immunomodulating agents, Class M = Musculo-skeletal system, Class N = Nervous system, Class R = Respiratory system.

Table 3: Conditional logistic regression

Variable	Coefficient	Exp (coef) = OR	95% CI	p-value
Charlson index	0.069	1.07	0.99-1.16	0.09*
Emergency admission	0.67	1.96	1.41-2.71	5.22x10 ^{-5***}
Return home at discharge	0.61	1.84	1.32-2.59	0.00038***
History of readmissions	0.51	1.66	1.14-2.43	0.0086**
Prescription of nervous system drugs	0.59	1.81	1.30-2.52	0.00049***

Significance: ***0.00,1 **0.01, *0.05, •0.1