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Identifying Risk of Readmission in Hospitalized Elders through Inpatient Medication Exposure

Juliessa M. Pavon, MD[1,2], **Yanfang Zhao, MA**[4], **Eleanor McConnell, PhD, RN**[1,2,4], and **S. Nicole Hastings, MD, MHS**[1,2,3]

[1]Duke University Medical Center, Division of Geriatrics, Durham, NC Duke University Medical Center Box 3003 Durham, NC 27710 Fax: 919-668-0453

[2]Durham VAMC GRECC, Durham, NC Durham VA Medical Center 508 Fulton St. Durham, NC 27705 Fax: 919-286-6823

Corresponding author: Juliessa M. Pavon, MD Duke University Medical Center Box 3003 Durham, NC 27710 (P) 919-684-8111 (F) 919-668-0453 Juliessa.pavon@duke.edu. **Alternate corresponding author:** S. Nicole Hastings, MD, MHS 411 W. Chapel Hill St. Durham, NC 27701 (P) 919-286-0411 ext 6183 (F) 919-416-5836 Susan.hastings@duke.edu.

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*Authors can be listed by abbreviations of their names.

[3] Center for Health Services Research in Primary Care, Durham VAMC 411 W. Chapel Hill St. Durham, NC 27701

[4]Duke University, Duke Translational Nursing Institute, Durham, NC Duke University Medical Center Box 3322 Durham, NC 27710

Abstract

OBJECTIVE—To use electronic health record (EHR) data to examine the association between inpatient medication exposure and risk of hospital readmissions.

DESIGN—Retrospective, observational study

SETTING—Tertiary and quaternary care academic health system in Durham, NC

PARTICIPANTS—All patients aged 60 or older, residents of Durham Co., NC who were hospitalized and discharged alive from Duke University Hospital between 2007 and 2009 (N= 4,627).

MEASUREMENTS—Independent variables were inpatient exposure to individual medication classes. Primary outcome was readmission (to a Duke Health System hospital) within 30 days.

RESULTS—Readmission rate was 21% (n=955). In adjusted models, exposures to anticonvulsants (OR 1.26, 1.08 −1.48), benzodiazepines (OR 1.23, 1.04 - 1.44), corticosteroids (OR 1.26, 1.07 −1.50), and opioids (OR 1.25, 1.06 −1.47) were associated with increased odds of readmission. Exposure to antidepressants (OR 1.85, 1.16-2.96), and opioids on Cardiology (OR 1.76, 1.01-3.07) and exposure to opioids on Medicine (OR 1.94, 1.17-3.22) were associated with higher odds of readmission, compared to surgery patients.

CONCLUSION—Among hospitalized elders, inpatient exposure to certain medication classes was associated with increased readmissions. Incorporating medication data from EHRs may improve the performance of hospital readmission prediction models.

Keywords

Readmissions; Medications; Electronic health record

INTRODUCTION

Reducing hospital readmissions is a major goal of the Center of Medicare and Medicaid Services [1], because they are frequent, costly, and life-threatening for many Medicare beneficiaries [2]. This focus on reducing readmissions has led to a proliferation of prediction models aimed at identifying those at highest risk of readmission so that interventions can be targeted to those who need them most. However complex interactions of multiple clinical, operational and sociodemographic risk factors have made it difficult to create tools that successfully predict which patients will be readmitted [3-7]. Many readmission prediction models lack useful real-time clinical data related to the inpatient stay, and this may partially explain why they perform moderately at best [5, 8-10]. Information about inpatient medications is an example of real time clinical data that is often available in electronic health records (EHRs), which may add useful information to prediction models.

Inpatient medication exposure and risk of readmission has not been extensively studied in the literature. Inpatient medication exposure is of particular interest as many medications serve as proxies for conditions that are otherwise not diagnosed or captured in the medication record, such as delirium [11-13]. Furthermore, inpatient medication exposure is associated with high incidence of adverse drug events [14]. Medication exposure is also easily captured in the EHR. EHR use is increasing exponentially in the U.S. and it is imperative to learn how to use the vast information within these systems in a meaningful way.

Thus, the primary goal of this study was to use EHR data to examine the associations between exposure to individual medication classes during an index admission and risk of readmission to the hospital within 30 days. A secondary objective was to examine whether these associations differed by inpatient service type.

METHODS

Design and Data Source

This retrospective cohort study was conducted using a dataset constructed for the Durham's Health Innovation's Project, one of ten planning projects sponsored by the Duke Clinical Translational Science Award to improve health outcomes among residents of Durham County [15]. All study data were drawn from electronic health records of Duke University Health System (DUHS) via the Duke Enterprise for Data Unified Content Explorer (DEDUCE) data portal. DEDUCE is a Duke designed research tool that provides investigators access to patient level clinical information. Medication data were collected from Duke Hospital's MedsManager pharmacy system. The Duke University institutional review board approved this study.

Study Population and Setting

Patient sample consisted of residents of Durham County, NC, aged 60 or older, who were hospitalized at Duke University Hospital between Jan, 1, 2007 to April, 1, 2009 and discharged alive. Duke University Hospital is a 924-bed academic tertiary and quaternary care facility located in Durham, North Carolina, with approximately 40,000 admissions per year. In 2008, an estimated 34,984 adults aged 60 years and older resided in Durham County, over 40-percent of this population is non-white, and Durham County seniors accounted for 13,000 unique visits per month to DUHS clinics [15].

Primary outcome variable: Hospital Readmission

Hospital readmission was defined as admission to any hospital in the Duke University Health System (Duke University Hospital, Duke Regional Hospital, and Duke Health Raleigh Hospital) within 30 days of discharge from the index admission. Readmissions can be measured at various time points, but Medicare is most interested in the 30 day readmission, which is the timeframe used in our study.

Primary independent variable: Medication exposure

Candidate medication classes were selected based on previously documented associations with readmission risk and/or adverse drug events and clinical judgment [6,16,17]. The medication classes examined were: procholinergics and anticholinergics, anticoagulants, anticonvulsants, antidepressants, antineoplastics, antipsychotics, benzodiazepines, corticosteroids, and opioids. We grouped medications according to their American Hospital Formulary Service (AHFS) therapeutic drug classifications, which is how they are organized in MedsManager. Of the medication classes selected for our study, we included all medication names listed under each AHFS therapeutic classification, and also all routes of administration. Medication exposure was defined as medication ordered in the system. Of note, MedsManager does not capture medication exposure in the surgical operating rooms, however, does capture medication exposure in the Duke Post-Anesthesia Care Unit (PACU) areas.

Covariates

Demographic data included age, gender, and race. Admission characteristics included health insurance coverage, admissions source (direct admission, admission through the emergency department, or admission from the emergency department via observation status), type of inpatient medical service (Medicine, Cardiology, Surgery), and length of stay (LOS). Health insurance coverage was categorized as private or government insurance (Medicaid, Medicaid Pending, Medicare, State Agency Insurance, or State Employee Health Plan).

Statistical Analysis

Descriptive statistics were calculated for all study variables. For each medication class, the differences in percentages of medication exposure among those readmitted and not readmitted were examined using chi-square tests. Multivariate logistic regression models were used to determine the relationship between each medication exposure and hospital readmission, controlling for age, gender, race, length of stay and service type. Covariates with significance of $P< 0.05$ in univariate analysis (LOS and service type) and age and race were included in the final model. Significance for all analyses was set at $P< 0.05$. Results were reported as odds ratios (OR) with a 95% confidence interval (CI). There were no missing data for any of the variables in our final sample.

Finally, interactions between each medication class and service type were examined, with Surgery as the reference group in these models. First we tested interactions between each medication class and service type. Interactions that were significant ($P<0.05$) were examined in multivariate models, controlling for the same factors as the main analysis. All analyses were performed using SAS Version 9.3 (SAS Institute, Cary, NC).

RESULTS

Sample Characteristics

Of 4,637 subjects meeting initial eligibility criteria, 10 were missing inpatient medication data, and thus were excluded from our study, leaving 4,627 patients for the final analysis. Characteristics of the entire sample are shown in Table 1. Mean age was 74 years old

(±standard deviation (SD) 9.5), 43% were male and 58% were Caucasian. The percentage admitted to Medicine, Cardiology, or Surgery was 48%, 23%, and 29% respectively. Mean length of stay was 5 days (± SD 6.3), and overall readmission rate was 21% (n=955).

Medication Exposures

Exposure to each medication class during the inpatient stay is shown in Table 2. Hospitalized elderly in this cohort were commonly exposed to procholinergics and anticholinergics (48%), anticoagulants (63%), benzodiazepines (43%), and opioids (60%). Among these medication classes, the most common medications were diphenhydramine and ranitidine (procholinergics and anticholinergic group), enoxaparin and heparin (anticoagulant group), midazolam and lorazepam (benzodiazepine group), and fentanyl and oxycodone (opiate group) (Table 2).

Relationships between Medication Exposures and Readmission

With the exception of anticoagulants and antidepressants, exposure to all other medication classes was higher among patients readmitted compared to those who were not readmitted, ($P < 0.05$) (Table 3). After adjusting for age, gender, race, LOS, and service type, exposure to anticonvulsants (OR 1.26, 1.08 −1.48), benzodiazepines (OR 1.23, 1.04 - 1.44), corticosteroids (OR 1.26, 1.07 −1.50), and opioids (OR 1.25, 1.06 −1.47) remained significantly associated with increased odds of readmission (Table 3). No association was detected between exposure to procholinergics and anticholinergics, anticoagulants, antidepressants, antineoplastics, antipsychotics and hospital readmission, in adjusted models.

Interactions between medication class and service type were significant for antidepressants ($P = 0.02$) and opioids ($P = 0.04$). Exposure to antidepressants (OR 1.85, 1.16-2.96), and opioids (OR 1.76, 1.01-3.07) on Cardiology and exposure to opioids on Medicine (OR 1.94, 1.17-3.22) were associated with higher odds of readmission, compared to Surgery patients

DISCUSSION

This study used EHR data to examine the association between inpatient medication exposure and risk of 30-day hospital readmission in a group of older adults admitted to an academic medical center. We found that inpatient exposures to anticonvulsants, benzodiazepines, corticosteroids and opioids were significantly associated with increased odds of readmission. We also found clinically important differences in readmission risk based on the service type at the time of the exposure. Odds of readmission were higher for those exposed to opioids on medicine or cardiology services compared to those with opiate exposures on the surgery service. Inpatient medication exposure is an example of real time clinical data that can be obtained from EHRs, and may serve as proxies for diagnoses that may not be easily captured in the medical record. These results encourage further utilization and exploration of existing health service data, with emphasis on using electronic health data to leverage our ability to make more refined predictions of readmission and better target interventions.

Whereas prior studies have examined which pre-admission or clinical risk factors at discharge increase risk of readmission [18,19], the impact of inpatient medication exposure

on readmission risk is not well known. Consistent with our findings, Allaudeen et al. [6] found similar odds of readmission when exposed to corticosteroids [OR 1.24, 1.09–1.42] and narcotics [OR 1.33, 1.16–1.53]), at least 48 hours prior to hospital discharge. Furthermore, in another study, adverse drug events at discharge were highest for corticosteroids and also analgesics [20]. Post-discharge adverse drug events may be one potential explanation for the increased 30-day readmission risk associated with inpatient exposure to these medication classes observed in the current study.

At variance with the Allaudeen study [6], our study found an association between inpatient anticonvulsant and benzodiazepine exposure and readmission. Anticonvulsants and benzodiazepines are among the medication classes commonly associated with ADEs [21,22]. Although the medication classes associated with increased readmission risk may differ among studies, possibly due to differences in how medications are classified within each study, the current results and other's work suggests that inpatient medication exposure may be useful for targeting early those at higher risk for readmission.

Similar to Allaudeen et al. [6], we did not find an association between anticoagulant exposure and readmission risk even though it is also a medication class commonly associated with ADEs [17,20,22]. A possible explanation is that the anticoagulant medication class included a variety of anticoagulants, including intravenous heparin flushes, which may have diluted the effect of exposure to high risk anticoagulants, such as warfarin and enoxaparin, on readmission outcome. We elected to keep the medication class in its native form as we wanted to use the medication classes as they already existed in the EHR to make a pragmatic examination of their utility.

Baseline readmission risk is well-known to vary between surgical and medical patients [2], so it is important to consider how medication exposure may also differentially affect risk in these groups. Compared to exposure on the surgery service, exposure to opioids on the medicine and cardiology service, and exposure to antidepressants on the cardiology service, was associated with increased risk of readmission. This study provides important evidence that inpatient medication exposure and readmission risk may vary by service type, and that depending on the location of exposure, not all high risk medication classes are associated with bad outcomes.

Our study only focused on determining whether associations exist between inpatient medication exposure and readmission risk. The associations between inpatient medication exposure and readmissions observed in this study do not prove causality. Indeed, the rationale for examining certain medication classes was that medication exposure may serve as markers for under-recognized or under-coded conditions associated with readmissions. For example, psychoactive medications such as benzodiazepines may be a marker for the presence of delirium, a common condition among older inpatients that is frequently under-recognized and under-coded [12,13]. The purpose of readmission prediction models is to identify those at highest risk of readmission so that interventions can be targeted to those who need it most. Therefore, adding inpatient medication exposure to existing risk prediction models is valuable even without a documented causal link. Medication data is

readily available in many electronic health records, and does not require additional staff time to collect.

Implications

The results of this study offer a new lens through which we can examine readmission risk. The findings extend our ability to identify high risk medications, and in doing so, it offers a novel way for identifying high risk individuals. Future studies are needed to determine whether prospective identification of risk is helpful in improving care outcomes. For example, health systems with electronic medical records could develop automated searches to identify and flag those who are being exposed to high risk medications in the inpatient setting. Such systemwide interventions may be particularly attractive to hospitals aiming to target high risk individuals and to reduce readmissions. Our findings also extend what is known about the value and limitations of using the electronic health record to identify high risk medications. Specific EHR design and medication classification coding need to be examined closely within each health system. In future studies, examining individual high risk medications from within a medication class code (i.e. anticoagulants), and distinguishing between medications continued and not continued during discharge, may provide additional insights into the relationship between medication exposure and readmissions. Finally, our study provides a more sharpened approach for identifying who is at risk for readmissions by focusing on risk factors occurring during the inpatient hospitalization. Incorporating real-time inpatient medication data would support earlier identification of high risk individuals who would benefit from timelier implementation of interventions prior to discharge.

Limitations

These data came from a single hospital system, reducing overall generalizability of the findings. However, limiting the study to one site enabled us to look at specific patient level data that typically is not available through larger databases. Readmissions to hospitals outside the Duke Health System were not captured in our database, which may result in an underestimation of the readmission rate in our study; deaths outside the system were also not recorded. Comorbidity data were unavailable, and it is possible that an underlying medical condition, as opposed to the medication exposure itself is associated with risk of readmission. However, as described above our study focused only on determining whether associations exist between inpatient medication exposure and readmission risk. Other unmeasured confounders may explain this association as well, including a suboptimal understanding of how to take a new medication or how to recognize potential side effects of a new medication, or inability to purchase a new medication at discharge. Similarly, loss of a chronic medications therapeutic effect may explain readmission risk. In our study it is not known whether the inpatient medication exposure represented a new start, a continuation of chronic medications, or whether the medication was continued at discharge, and clarifying these relationships is an important area for future study. Although a definitive causal link cannot be reached due to the retrospective design in this study, this study indicates a significant association between inpatient medication exposure and readmission risk. The evidence of this association needs to be supported with future prospective observational studies.

Conclusions

Inpatient exposure to several medication classes was associated with increased risk of readmission to the hospital within 30 days. Administrative data from the electronic health record can be used to capture real time clinical data, such as inpatient medication exposure, to help predict readmission risk. In an era where electronic health records will soon become universal, real-time data holds great potential to improve our ability to identify and target those with high readmission risk so that interventions can be offered to those most likely to benefit.

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Table 1

Demographic and Admission Characteristics of Total Sample, N=4,627

Characteristic	Value
Demographics	
Age, mean years (± SD)	74 (± 9.5)
Men, n (%)	2010 (43)
Caucasian, n (%)	2694 (58)
Insurance	
Government/Medicare and Medicaid, n (%)	3385 (73)
Private Insurance/Managed Care, n (%)	1242 (27)
Admissions Characteristics	
Admission Type	
ED ->Inpatient, n (%)	3033 (65)
ED-> Observation, n (%)	224 (5)
Direct Inpatient, n (%)	1370 (30)
Service Location	
Medicine Service, n (%)	2206 (48)
Cardiology, n (%)	1091 (23)
Surgery, n (%)	1330 (29)
Length of Stay, mean days (± SD)	5 (± 6.3)
Readmissions, n (%)	955 (21)

Abbreviation: SD, standard deviation. ED, Emergency Department.

No missing values for any variable

Table 2

Medication Exposure of Total Sample, N=4,627

Drug class[a], n (%)[b]	Frequency, n	% of Medication Class
Procholinergics and anticholinergics, n (%)[b]	**2213**	**48**
Diphenhydramine	781	35
Ranitidine	540	24
Neostigmine	215	10
Promethazine	204	9
Nizatidine	114	5
Anticoagulants, n (%)[b]	**2940**	**63**
Enoxaparin	2003	68
Heparin	569	19
Warfarin	336	11
Bivalirudin	18	0.6
Fondaparinux	14	0.5
Anticonvulsants, n (%)[b]	**1572**	**34**
Magnesium	813	51
Pregabalin	293	19
Gabapentin	197	13
Levetiracetam	83	5
Phenytoin	74	5
Antidepressants, n (%)[b]	**1155**	**25**
Sertraline	222	19
Citalopram	160	14
Escitalopram	109	9
Mirtazapine	107	9
Paroxetine	93	8
Antineoplastics, n (%)[b]	**150**	**3**
Megestrol	25	17
Anastrozole	23	15
Methotrexate	14	9
Bicalutamide	12	8
Hydroxyurea	9	6
Antipsychotics , n (%)[b]	**481**	**10**
Risperidone	172	36
Haloperidol	145	30
Quetiapine	71	15
Olanzapine	43	9
Aripiprazole	19	4
Benzodiazepines, n (%)[b]	**2002**	**43**

Drug class[a], n (%)[b]	**Frequency, n**	**% of Medication Class**
Midazolam	1041	52
Lorazepam	489	24
Clonazepam	157	8
Alprazolam	88	4
Diazepam	74	4
Corticosteriods, n (%)[b]	**1008**	**22**
Prednisone	350	35
Dexamethasone	293	29
Methylprednisolone	202	20
Fluticasone	62	6
Hydrocortisone	35	3
Opioids, n (%)[b]	**2627**	**60**
Fentanyl	700	25
Oxycodone	667	24
Morphine	528	19
Hydromorphone	453	16
Percocet	135	5

[a] Data of top5 medications in each group, patients could be represented in multiple groups. Thus, data in each class will not sum up to 100%, because we are just showing top 5 medications, and because one person may have been exposed to more than one drug.

[b] Percent of total sample with medication exposure.

Table 3

Medication Exposure and Odds Ratio of Readmission

Medication class	Patients with readmission within 30 days, n = 955	Patients who were not readmitted, n = 3,672	Adjusted[a] OR (95% CI)
Procholinergics and anticholinergics	51*	47	1.14 (0.98 -1.32)
Anticoagulants	64	63	1.02 (0.97 -1.18)
Anticonvulsants	38*	33	1.26 (1.07 -1.48)
Antidepressants	27	24	1.13 (0.96 -1.34)
Antineoplastics	4*	3	1.42 (0.99 -2.06)
Antipsychotics	12*	10	1.16 (0.93 -1.47)
Benzodiazepines	46*	42	1.23 (1.04 -1.44)
Corticosteroids	25*	21	1.26 (1.06- 1.50)
Opioids	63*	59	1.25 (1.06- 1.47)

*P < 0.05 for unadjusted models.

[a]Models adjusted for age, gender, race, length of stay, and service location. Only length of stay and service location had significance of P< 0.05 in univariate analysis and thus were included in our univariate model. Each medication class was examined in a separate model.