

# High Prevalence of Medication Errors in a Secondary-level Lithuanian Hospital: A Prospective Cross-sectional Observational Study

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## Abstract

**Abstract Aim** As the population continues to age, the occurrence of chronic illnesses and comorbidities that often necessitate the use of polypharmacy has been on the rise. Polypharmacy, among other factors that tend to coincide with chronic diseases such as obesity, impaired kidney and liver function, and older age, can increase the risk of medication errors (MEs). Our study aims to evaluate the prevalence of MEs in the Internal medicine, Cardiology, and Neurology departments at the secondary level university hospital. **Methods** We conducted a prospective observational study of 145 patients electronic or paper-based data of inpatient prescriptions and patients' pharmacokinetic risk factors, such as an impairment of renal and/or hepatic function, weight, and age. **Results** All included patients collectively received 1252 prescribed drugs. The median (Q1; Q3) number of drugs per patient was 8 (7;10). At least one ME was identified in 133 out of the 145 patients, indicating a significantly higher prevalence than hypothesized (91.7% vs. 50%;  $p < 0.001$ ). There was moderate, positive correlation between the quantity of prescribed drugs and the number of MEs, meaning that the more drugs are prescribed, the higher the number of identified MEs (Spearman's  $\rho = 0.428$ ;  $p < 0.001$ ). **Conclusion** These findings suggest that there is a need of continuous medication education activity for prescribing physicians, continuous evaluation of prescription appropriateness to objectively identify the MEs, and to contribute to more rational patient treatment.

## High Prevalence of Medication Errors in a Secondary-level Lithuanian Hospital: A Prospective Cross-sectional Observational Study

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## What is known about this subject?

Irrational prescribing has a negative impact on patients and public health.

Medication errors (ME) that occur during prescription can be related to patients' pharmacokinetic factors, such as weight, impaired renal and/or hepatic function, gender, and age.

## What this study adds?

- In this study the drug prescription data of hospitalized patients was analysed using rationality criteria, such as effectiveness, safety, monitoring and cost-effectiveness, and pharmacokinetic risk factors of the patients to evaluate the prevalence of MEs.
- This study found that the number of MEs correlated with the quantity of prescribed drugs, meaning that the prescription as itself is the risk factor for ME to occur.
- These findings show that there is a need to develop a system which allows to monitor the rationality of prescriptions in a hospital.

## Abstract

### *Aim*

As the population continues to age, the occurrence of chronic illnesses and comorbidities that often necessitate the use of polypharmacy has been on the rise. Polypharmacy, among other factors that tend to coincide with chronic diseases such as obesity, impaired kidney and liver function, and older age, can increase the risk of medication errors (MEs). Our study aims to evaluate the prevalence of MEs in the Internal medicine, Cardiology, and Neurology departments at the secondary level university hospital.

### *Methods*

We conducted a prospective observational study of 145 patients electronic or paper-based data of inpatient prescriptions and patients' pharmacokinetic risk factors, such as an impairment of renal and/or hepatic function, weight, and age.

### *Results*

All included patients collectively received 1252 prescribed drugs. The median (Q1; Q3) number of drugs per patient was 8 (7;10). At least one ME was identified in 133 out of the 145 patients, indicating a significantly higher prevalence than hypothesized (91.7% vs. 50%;  $p < 0.001$ ). There was moderate, positive correlation between the quantity of prescribed drugs and the number of MEs, meaning that the more drugs are prescribed, the higher the number of identified MEs (Spearman's  $\rho = 0.428$ ;  $p < 0.001$ ).

### *Conclusion*

These findings suggest that there is a need of continuous medication education activity for prescribing physicians, continuous evaluation of prescription appropriateness to objectively identify the MEs, and to contribute to more rational patient treatment.

## 1. Introduction

As the population continues to age, the occurrence of chronic illnesses and comorbidities that often necessitate the use of polypharmacy has been on the rise [1-2]. Polypharmacy, among other factors that tend to coincide with chronic diseases such as obesity, impaired kidney and liver function, and older age, can increase the risk of medication errors (MEs). The US National Coordinating Council for Medication Error Reporting and Prevention proposes the following definition for MEs: "A medication error is any preventable

event that might result in inappropriate medication use or patient harm while the medication is under the control of healthcare professionals, patients, or consumers. These events can be associated with various aspects of professional practice, healthcare products, procedures, and systems, encompassing prescribing, order communication, product labelling, packaging, and nomenclature, compounding, dispensing, distribution, administration, education, monitoring, and use ” [3]. Examples of MEs recorded in our study included, but were not limited to, off-label use, deviations from recommended dosage, disregard of contraindications, clinically significant drug-drug interactions, and adverse drug reactions requiring treatment or monitoring. The prevalence of MEs varies from 18 percent to more than 40 percent across different healthcare settings [4]. Although some studies suggest that the prevalence of MEs may even reach as high as 79 percent [5].

In Lithuania, research on MEs has been conducted in tertiary care medical wards. A study published in 2017 revealed staggering rates of MEs – prescription errors were observed in 49 percent of cases analysed [6]. Furthermore, a small sample size cross-sectional pilot study conducted at the department of Psychiatry in Lithuanian University of Health Sciences (LUHS) Hospital Kaunas Clinics in 2019 analysed the data of 33 patients, 29 (87.9 percent) of whom presented with at least one case of MEs [7]. Previous studies also show a lack of knowledge on over-the-counter medications amongst patients [8]. Our study aims to evaluate the prevalence of MEs in the internal medicine, cardiology, and neurology departments at the secondary level university hospital. We hope the results help create strategies to provide safe and efficient treatment to patients and reduce medication-related spending for hospitals.

## 2. Methods

### 2.1 Design, Setting, and Population

The study was approved by the Kaunas Regional Biomedical Research Ethics Committee (No. BE-2-84). This was a prospective cross-sectional observational study carried out between 1st June 2021 and 31st May 2023 at the departments of neurology, cardiology, and internal medicine at secondary level university hospital. Patient population and sample size were calculated using official numbers of discharged patients published by these departments in 2019-2020. The number of admitted patients dropped in 2020 due to COVID-19 restrictions, however, considering a likely increase over the course of the study, patient population and sample size were calculated using averages from 2019 and 2020: 6027 patients in 2019, and 3883 patients in 2020, bringing the average to 4955. For the study to reach 95 percent statistical significance with an alpha value of 0,05 and a population of 4955, sample size should be no smaller than 135.

Study subjects were chosen using the following inclusion criteria:

- Consent to participate in the study
- Admission to one of the medical wards (internal medicine, cardiology, or neurology)
- Adult patients ([?]18 years of age)
- Patients receiving two or more medications

And withdrawn using the following exclusion criteria:

- Refusal to participate
- Receiving one medication only
- Receiving no medications

### 2.2 Data Collection

Patient data was collected using paper-based and electronic medical records throughout inpatient treatment. The following data were collected during the study: patient age, gender, weight, height, lean body mass (LBM), adjusted body mass, body mass index (BMI), plasma creatinine levels, main reason for hospital admission, other illnesses, monitored, indications with indications, dosage, start and end dates (if available) of administration, information on whether medication safety and efficacy were monitored; related laboratory and instrumental test data, outcomes.

### 2.3 Screening for potential medication errors

When reviewing a patient's prescriptions, the following were considered: conformity to indications/contraindications, dosage, contraindications listed in summary of product characteristics (SmPC) or official treatment guidelines, national/international drug databases, such as Micromedex or UpToDate. Kidney function was evaluated by calculating creatinine clearance with the Cockcroft-Gault formula, unless otherwise stated in the SmPC. For obese patients, lean body mass was used in these calculations, unless otherwise stated. Creatinine clearance was calculated using LBM when BMI was  $\geq 30$  kg/m<sup>2</sup>. For patients with hepatic impairment hepatic function was evaluated by calculating Child-Pugh score. A prescription was considered safe in the absence of contraindications or adverse effects, if the necessary tests were conducted to ensure drug safety, and the dosage was adjusted based on patient-specific factors such as age, weight, and kidney and liver function. Effectiveness of a drug was determined by adherence to registered indications and dosage guidelines, coupled with the achievement of the desired clinical effect, which could include the reduction or disappearance of symptoms and positive changes in biomarkers. Moreover, cost-effectiveness was established if a drug was prescribed in an appropriate dose and proved to be the least costly among pharmaceutical alternatives meeting the same standards of effectiveness and safety. Appropriate monitoring was defined as continuous safety and efficacy assessments through relevant testing. Finally, prescription rationality was evaluated by considering all the characteristics, including safety, efficacy, monitoring, and cost-effectiveness. Prescriptions were evaluated by two independent investigators, if there were disagreements regarding the evaluation the final decision was made by the third investigator.

## 2.4 Statistical analysis

Descriptive statistics were employed to characterize the both the included patient sample and their respective prescriptions. Nominal and categorical variables were presented using frequency tables. Interval variables (such as age, creatinine clearance, and weight) underwent normality testing. Normally distributed variables were summarized using mean and standard deviation, while non-normally distributed variables were described using median, Q1, Q3, and, where necessary, minimum, and maximum values.

Binominal test was used to evaluate the observed prevalence of MEs compared to the hypothesized 90%. Spearman's correlation was run to determine the relationship between the number of MEs and interval variables, including weight, creatinine clearance, age, and the number of drugs prescribed. To investigate the relationship between ME (none vs. at least one) and categorical variables such as gender (female vs. male), renal function (normal/mild vs. moderate to severe vs. hyperfiltration), hepatic function (normal vs. impaired), and BMI categories (under 25 vs. 25 and more), the chi-square test was utilized. For assessing the influence of potential factors on the presence of at least one ME, binomial logistic regression was initially planned. However, due to the exceptionally high prevalence of at least one ME, the regression model did not fit the data and could not be validly used.

The significance level ( $\alpha$ ) for hypothesis tests was set at 0.05. Statistical analyses were performed using SPSS v29.0.1.0 software.

## Results

One hundred forty-five patients were enrolled in the study, and they collectively received 1252 prescribed drugs. The median (Q1; Q3) number of drugs per patient was 8 (7;10). Notably, at least one ME was identified in 133 out of the 145 patients, indicating a significantly higher prevalence than hypothesized (91.7% vs. 50%;  $p < 0.001$ ). It is worth mentioning that six patients (4.1%) exhibited at least one ME across all assessed categories. Table 1 outlines the characteristics of the patients.

The assessment of various MEs revealed noteworthy findings. The median number of any ME was 11 (Q1: 4.5; Q3: 16.5), ranging from 0 to 35. Predominant among the identified ME were lack of cost-effectiveness. A comprehensive breakdown of all ME categories, along with their respective medians (Q1; Q3) per patient, is provided in the Table 2.

There was moderate, positive correlation between the quantity of prescribed drugs and the number of MEs, meaning that the more drugs are prescribed, the higher the number of identified MEs (Spearman's  $\rho =$

0.428;  $p < 0.001$ ) (Figure 1). However, there was no correlation observed between the number of MEs and age, weight, or creatinine clearance ( $p > 0.05$ ). Moreover, there was no significant relationship between the presence of MEs and gender, renal function, hepatic function, or BMI ( $p > 0.05$ ).

Additionally, drug-level analysis was undertaken, encompassing a total of 1252 prescribed drugs for 145 patients, as previously mentioned. The assessment of overall rationality revealed that 35.8% (448 drugs) were classified as not meeting rationality criteria. Notably, contraindications were identified in 2.3% (29 drugs). Regarding efficacy monitoring, a substantial 83.9% (1051 drugs) adhered to monitoring practices, whereas 12.3% (154 drugs) did not, and 3.8% (47 drugs) were considered unclear due to lack of data. Variability in dosing adequacy was observed, with 3.4% (43 drugs) being underdosed, 71.5% (895 drugs) correctly dosed, 5.1% (64 drugs) exhibiting overdose, 19.0% (238 drugs) remaining unclear, and 3.4% (12 drugs) displaying an incorrect dosing regimen (Figure 2). These findings, along with results from other rationality domains, are presented in the Table 3.

#### 4. Discussion

This study, involving 145 patients and encompassing the prescription analysis of 1252 drugs, revealed several significant insights into MEs and rationality issues in pharmacotherapy. Remarkably, 91.7% of patients were exposed to at least one ME, exceeding both the hypothesized 50% and ME prevalence rates reported in other studies [4-5].

The median number of drugs per patient per day was 8, a well-established factor associated with an increased likelihood of encountering MEs [4]. Confirming this, a moderate positive correlation was identified between the quantity of prescribed drugs and the occurrence of MEs. However, despite this correlation, no significant relationships were observed between the presence of MEs and patient-specific factors such as age, weight, sex, renal function, hepatic function, or BMI. This suggests that MEs are more influenced by the complexity and volume of the drug regimen than specific patient characteristics.

The detailed assessment of MEs highlighted cost-effectiveness issues as particularly prevalent, underscoring the need to consider economic factors to enhance resource utilization. Further drug-level analysis revealed that a substantial proportion (35.8%) of prescribed drugs did not meet rationality criteria, with 2.3% being contraindicated. Additionally, 8.5% of drugs had inadequate dosing, including 5.1% being overdosed. While efficacy and safety monitoring were satisfactory in 83.9% and 74.7% of cases, respectively, 12.3% and 10.7% lacked adequate monitoring, emphasizing the necessity for consistent oversight to ensure therapeutic effectiveness.

These findings emphasize the importance of comprehensive medication management strategies, including thorough prescription reviews, continuous monitoring, and adherence to rational prescribing practices. Implementing interventions targeting ME reduction, enhancing cost-effectiveness, and ensuring dosing adequacy could significantly enhance the quality of patient care and resource management.

#### 5. Conclusions

The primary strength of this study lies in its execution across diverse hospital departments, providing a varied patient population that enhances the applicability of the findings. However, the observational design, while suitable for determining prevalences, suggests that this study serves as preliminary groundwork for more substantial investigations, particularly in the light of the noteworthy results it has yielded.

Our findings show that there is a lot of MEs at the therapeutic departments of a secondary hospital: the quantity of medications correlated with the quantity of MEs identified. These findings suggest that there is a need of continuous medication education activity for prescribing physicians, continuous evaluation of prescription appropriateness to objectively identify the MEs and to contribute to more rational patient treatment.

#### 6. Author's contributions

- EK and LA planned the study – developed a protocol and other documentation mandatory to get the permission from the Bioethics committee to start the study.
- JB, AZ and EK collected the informed consent forms and if the patient was eligible for inclusion in the study collected paper-based and electronic medical records.
- LA, EK, JP assessed all the drug prescriptions and summarized findings.
- SZ carried out the statistical analysis.
- All authors contributed to the writing of the paper.

## 7. Funding

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