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# How an electronic prescription tool enables better prescription quality for patients

## *Como uma ferramenta de prescrição eletrônica possibilita uma melhor qualidade na prescrição para os pacientes*

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**Keywords**
drug prescriptions, drug interactions, clinical decision support systems

## ABSTRACT

**Objective:** Medication-related errors in patients are among the leading causes of preventable health damage and harm worldwide. In the United States, these errors cause at least one death a day and damage approximately 1.3 million people annually. According to the World Health Organization, the global expenditure on medication-related errors is estimated to be U$ 42 billion per year. In Brazil, the rate of potential drug interactions varies between 28% and 63.6% for primary care patients. The prevalence of drug interactions has increased following an aging population, increased chronic conditions, combined use of different drugs, and increased prescription drugs per patient. **Methods**: The data used for this study were obtained through the database from Nexodata do Brasil S.A a private health technology company with an electronic prescription system and a data intelligence area. **Results:** 65,867 electronic prescriptions were evaluated during 2019. Of these, 4,828 prescriptions had an average of 2.5 interactions. These interactive prescriptions were generated by 197 different doctors, totaling 24.5 prescriptions with interaction per doctor over 12 months. A total of 12,005 interactions were identified, 15.6% classified as mild, 70.9% as moderate, and 13.5% as severe. **Conclusion**: By implementing an electronic prescription tool, a reduction of 32.9% in the number of prescriptions with drug interaction was observed.

**Palavras-chave:**
prescrições de medicamentos, interações de medicamentos, sistemas de apoio a decisões clínicas

## RESUMO

**Objetivo**: Os erros relacionados à medicação de pacientes estão entre as maiores causas de danos e prejuízos evitáveis à saúde em todo o mundo. Nos Estados Unidos, esses erros causam pelo menos uma morte por dia e causam danos a aproximadamente 1,3 milhão de pessoas anualmente. Segundo a Organização Mundial da Saúde, estima-se que o gasto global com erros relacionados à medicação seja de US$ 42 bilhões por ano. No Brasil, a taxa de interações medicamentosas potenciais varia entre 28% e 63,6% em pacientes de serviços de atenção primária. A prevalência de interações medicamentosas tem aumentado, seguindo o envelhecimento populacional, aumento de condições crônicas, uso combinado de diferentes medicamentos e aumento na quantidade de medicamentos prescritos. **Métodos**: Os dados utilizados para o presente estudo foram obtidos por meio da base de dados da Nexodata do Brasil S.A., que é uma empresa privada de tecnologia em saúde que possui um sistema de prescrição eletrônica e uma área de inteligência de dados. **Resultados**: Foram avaliadas 65.867 prescrições eletrônicas durante o ano de 2019; dessas, 4.828 prescrições apresentaram em média 2,5 interações. Essas prescrições com interação foram geradas por 197 médicos diferentes, totalizando um total de 24,5 receitas com interação por médico ao longo de 12 meses. Foi identificado um total de 12.005 interações, sendo 15,6% classificadas como leves, 70,9% como moderadas e 13,5% como graves. **Conclusão**: Por meio da implementação de uma ferramenta de prescrição eletrônica, foi observada uma redução de 32,9% na quantidade de receitas com interação medicamentosa.

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## Introduction

Medication-related errors to patients are among the biggest causes of avoidable harm and damage to health worldwide. In the United States, these errors cause at least one death a day and harm approximately 1.3 million people annually. In addition, adverse drug reactions can increase the length of hospital stay by two days, twice the risk of death, and more than $2,000 in hospital costs. According to the World Health Organization, the global expenditure on medication-related errors is estimated to be US$42 billion per year (WHO, n.d.).

Among these errors are drug interactions (DIs), described as the phenomenon that occurs when the effects of a drug are modified by the previous or simultaneous administration of another drug. The final result of a DI can increase or reduce the effects of one or two active ingredients or can promote the appearance of a new effect that did not occur with one of the active ingredients alone. Interactions can occur between active ingredient-active ingredient, active ingredient-food, active ingredient-laboratory tests, and active ingredient-chemical substances (Tatro, 2011; Anvisa, 2002).

In clinical terms, DIs can lead to reduced treatment efficacy or the occurrence of adverse events of different severities. Mild DIs can cause discomfort to the patient with no need to change the treatment or medical intervention. Moderate DIs may require treatment modification, and severe DIs can cause permanent damage or worsen the patient's clinical condition, leading to hospitalization, increased length of stay, physical disability, and even death (Zwart-van Rijkom *et al.*, 2009).

In Brazil, the rate of potential DIs varies between 28% and 63.6% in primary care patients (Sousa *et al.*, 2014; Leão *et al.*, 2014; Santos *et al.*, 2019). The prevalence of DIs has increased following the population aging, increased chronic conditions, and the combined use of different drugs. The probability of occurrence increases with the number of medications prescribed (Coombes *et al.*, 2001; Johnell & Klarin, 2007; Baysari *et al.*, 2012). Among outpatients, the prevalence of potential DIs is approximately 50% and may reach over 80% (Tragni *et al.*, 2013; Kennedy-Dixon *et al.*, 2015).

Several interventions to reduce the frequency and impact of medication errors have already been developed; one of them is implementing electronic prescription in health services as a clinical decision support tool. Because the reported number of potential DIs is high, research shows that physicians have difficulty identifying them (Ko *et al.*, 2008). In this way, electronic prescribing systems can be beneficial for reducing medication errors by displaying alerts of potential DIs on the screen as the prescription is dispensed.

Many doctors do not adhere to alerts – this rate can vary from 49% to 96%. However, evidence shows that such alerts can positively affect prescriptive behavior when well designed and for a specific target audience (van der Sijs et al., 2006; Schedlbauer et al., 2009; Baysari *et al.*, 2011; Bright *et al.*, 2012).

This study aims to quantify and characterize the potential DIs in electronic prescriptions generated from care in Brazilian institutions that adhere to the technology.

## Methods

The data used for this study were obtained from the database from Nexodata do Brasil S.A., a private health technology company with an electronic prescription system and a data intelligence area.

The collected data for prescriptions analysis considered the entire year of 2019 and establishments using Nexodata's software instead of the API [Application Programming Interface]. Such data contain information regarding the dispensed prescriptions, containing the physician and their characteristics, patients and their characteristics, and the drugs and possible interactions for each case.

For the analysis, medical establishments from which at least one DI alert was originated during prescription were included. The DIs considered were only between drug-drug. These DIs are classified as severe, moderate, and mild according to the events that those interactions could generate.

Data were analyzed using descriptive statistics to show the current scenario of DIs in prescribing institutions.

## Results

Sixty-five thousand eight hundred sixty-seven electronic prescriptions were evaluated during 2019. Of these, 4,828 prescriptions had an average of 2.5 interactions. These interaction prescriptions were generated by 197 different physicians, totaling 24.5 interaction prescriptions per physician over 12 months. A total of 12,005 interactions were identified, with 15.6% classified as mild, 70.9% as moderate, and 13.5% as severe (Figure 1).

When we consider the number of DIs per prescription, we have an average of 2.5 interactions, ranging from 1 interaction to 23 interactions per prescription. More than half of the prescriptions (51.9%) have only one DI, while 17.3% have two DIs and 9.7% have three DIs; 21.1% are distributed between 4 and 23 DIs (Figure 2).

Table 1 shows the metrics (minimum, mean, maximum, and median) pooled by DI severity. The severity that appears the most per prescription is moderate, and DIs classified as mild and severe have remarkably similar metrics.

The distribution of the number of DIs over time shows an average of 1,000 DIs per month. Pooled by severity, we have a monthly mean of 156, 710, and 135 for mild, moderate, and severe, respectively. When analyzed by the number of prescriptions that had at least one DI, we have an average of 402 prescriptions per month and 114, 314, and 112 prescriptions per month for mild, moderate, and severe, respectively.

When comparing the number of DIs from January to December, we reduce 26.7% in overall DIs, 37.6% for mild DIs,

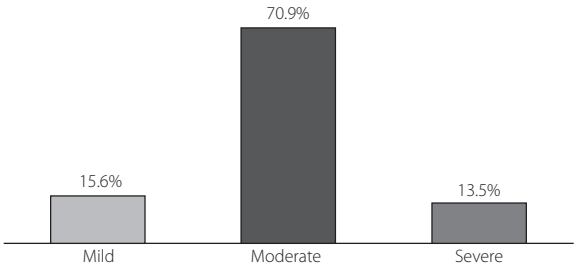


**Figure 1.** Distribution of DIs according to the interaction severity recorded in 2019 (n = 12.005).

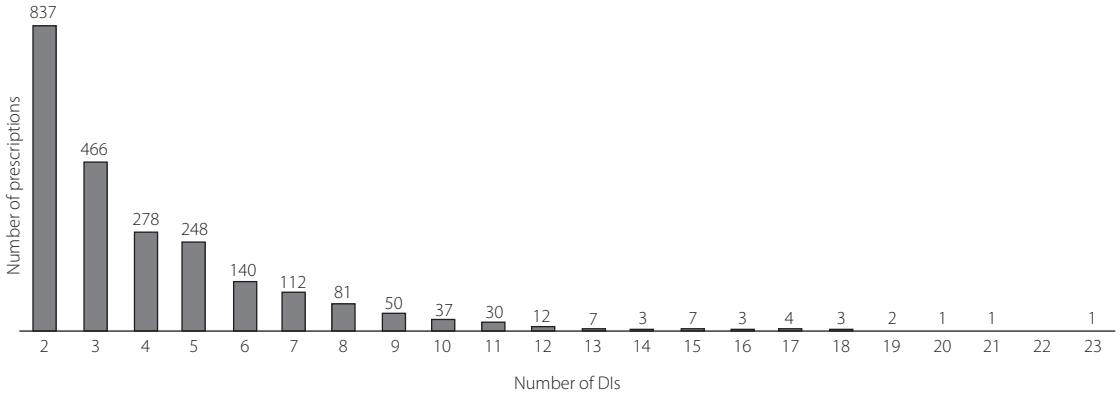


**Figure 2.** Number of prescriptions by number of DIs shown by each one.

26.3% for moderate, and 12.0% for severe. In Figure 3, we can see the variations in the number of DIs and the number of prescriptions dispensed with DIs.

Over the period, we can observe a reduction from the first to the second month of 27.8%; the following months show a variation of less than two percentage points (Figure 3).

Of the 562 prescribing physicians, 197 (35.1%) dispensed at least one prescription that had a DI. On average, physicians prescribe 24.5 prescriptions with at least one DI, with a minimum of one and a maximum of 806 prescriptions over the period; the 197 physicians have a median of four prescriptions with at least one DI.

When considering the prescription percentage with at least one prescription concerning the total of prescriptions dispensed, there is an average of 15.59% of prescriptions with DI, with a minimum of 0.02% and a maximum of 100.0% (Table 2). When only physicians with more than one prescription were considered, we have 12.48%, 0.02%, and 80.0% for average, minimum and maximum, respectively.

The monthly average proportion of prescriptions with interaction per physician is 9.7%. When analyzing physicians who dispensed at least one prescription per month over the entire period, which totals 48 physicians, we have an average prescription rate with interaction per month of 10.0%.

**Table 1.** Assessment of DIs according to the severity

| | Mild | Moderate | Severe | Total |
|---|---|---|---|---|
| Minimum | 1 | 1 | 1 | 1 |
| Mean | 1.4 | 2.3 | 1.2 | 2.5 |
| Maximum | 6 | 19 | 6 | 23 |
| Median | 1 | 2 | 1 | 1 |

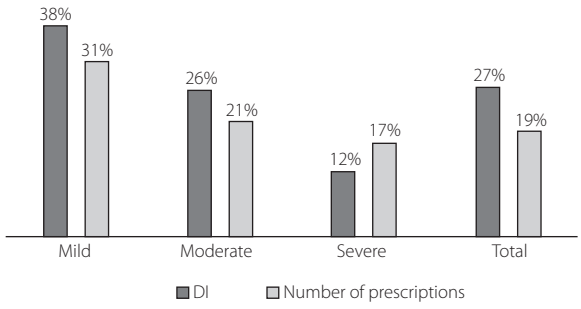


**Figure 3.** Reduction in the number of DIs and prescriptions with at least one DI between January and December 2019.

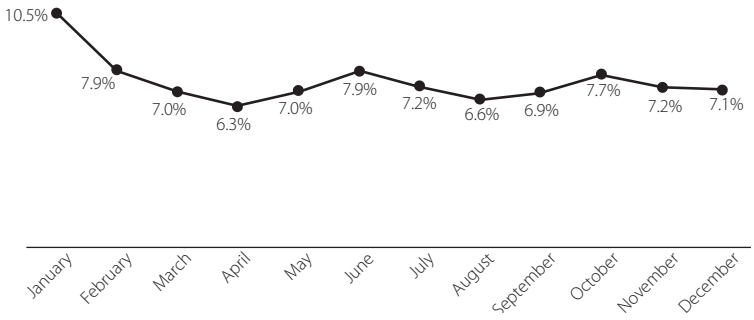


**Figure 4.** Time evolution of the number of prescriptions with at least one drug interaction.

When comparing December with January, of the doctors who dispensed at least one prescription per month in the period, we have an average of 5% reduction. The minimum is an increase of 272%, and the maximum is a reduction of 100% of prescriptions with at least one DI.

Of the total of 42 physicians who prescribed at least one prescription per month and presented at least one prescription with interaction in the period, 10 (23.8%) increased the number of prescriptions with DI, 16 (38.1%) maintained the same percentage of prescriptions with DI and 16 (38.1%) reduced the number of prescriptions with DI.

When compared by the classification of the anatomical group of the ATC code, it was observed that 37% of the interactions correspond to the same anatomical group, and 63% correspond to different anatomical groups. In the same anatomical group interactions, drugs classified in the Cardiovascular system group represent 72.3% of these interactions (Table 3).

In drug interactions from different anatomical groups, the primary interaction is between the Blood and hematopoietic organs and the Cardiovascular system group, corresponding to 33.1%. Secondly, between the groups Digestive system and metabolism and the Cardiovascular system, corresponding to 21.1% (Table 4).

**Table 2.** Proportion (%) of prescriptions with interaction to total prescriptions

| | Physicians with at least one DI | Physicians with at least one interaction and more than one prescription |
|---|---|---|
| Minimum | 0.02 | 0.02 |
| Mean | 15.59 | 12.48 |
| Maximum | 100.00 | 80.00 |
| Median | 7.27 | 6.9 |

## Discussion

The main benefits of electronic prescription include improved readability and prescription availability (without the need to carry the paper document) and allowing for adequate continued care, as the health professional has quick and easy access to medications prescribed to the patient at different times. However, no doubt, the most significant benefit of electronic prescription is its potential to reduce medication errors (Baysari & Raban, 2019).

Medication errors are a global attention priority. A recent meta-analysis concluded that, since 2007, electronic prescribing strategies have reduced medication, dosing, and adverse event errors. The studies included DIs, incomplete prescriptions, prescription correction, dosage errors, and dispensing and administration errors (Roumeliotis *et al.*, 2019).

Although not all medication errors cause direct harm or damage to a patient's health, they can create additional work for health professionals and reduce patient confidence in the care they are receiving (Franklin & Puaar, 2020).

A limitation of the current study is that it is only possible to identify interactions dispensed with a prescription. If the physician has received the alert in the software and

**Table 3.** The proportion of DIs among drugs from the same anatomical group (ATC code)

| ATC ANATOMICAL Group | NUMBER OF INTERACTIONS | |
|---|---|---|
| Cardiovascular system | 3213 | 72.27% |
| Nervous system | 572 | 12.87% |
| Blood and hematopoietic organs | 339 | 7.62% |
| Digestive system and metabolism | 126 | 2.83% |
| Anti-infectives for systemic use | 99 | 2.23% |
| Genitourinary system and sex hormones | 35 | 0.79% |
| Sense organs | 23 | 0.52% |
| Respiratory system | 22 | 0.49% |
| Dermatological | 16 | 0.36% |

**Table 4.** The proportion of DIs among drugs from different anatomical groups (ATC code) – 10 major ones

| ATC ANATOMICAL Group | ATC ANATOMICAL Group | NUMBER OF INTERACTIONS | |
|---|---|---|---|
| Blood and hematopoietic organs | Cardiovascular system | 2,501 | 33.1% |
| Digestive system and metabolism | Cardiovascular system | 1,592 | 21.1% |
| Cardiovascular system | Hormonal system preparations, excl. sex hormones | 440 | 5.8% |
| Digestive system and metabolism | Hormonal system preparations, excl. sex hormones | 327 | 4.3% |
| Hormonal system preparations, excl. sex hormones | Anti-infectives for systemic use | 322 | 4.3% |
| Cardiovascular system | Nervous system | 221 | 2.9% |
| Digestive system and metabolism | Blood and hematopoietic organs | 136 | 1.8% |
| Musculoskeletal system | Nervous system | 123 | 1.6% |

has changed the medication, it is impossible to identify this change. Another limitation is that the same drug can have more than one active ingredient, and drug interactions are determined by active ingredient and not by medication. In this case, even if the prescription has only two drugs, there is the possibility that the prescription has more than one interaction.

The main interactions are among drugs from different groups. This fact corroborates the information previously presented that a patient who needs to treat more than one disease has a higher risk of having a prescription with DI. The most significant number of drug interactions was identified between drugs from the "Blood and hematopoietic organs" groups interacting with medicines from the "Cardiovascular system" group; followed by drugs from the "Digestive system and metabolism" group interacting with those from the "Cardiovascular system" both interactions present medications for the treatment of diseases of the cardiovascular system.

Prescriptions with DIs were also identified for the same anatomical group. It corroborates the issue that a more significant number of drugs prescribed in the same prescription, even for the same anatomical group, increases the possibility of DIs. For our sample, drugs that presented the highest number of DIs belong to the anatomical groups "Cardiovascular system" and "Nervous system".

Over the period, the sample shows a reduction of 32.9% in the number of interactions compared with the total prescriptions, with at least one interaction to the total prescriptions. This may indicate that a DI alert tool helps reduce the number of prescriptions with drugs that interact with each other.

The most significant reduction was observed in DIs classified as mild (31%), followed by DIs classified as moderate (21%). The group of DIs ranked as severe had the most negligible reduction (17%). This result may indicate that physicians prefer to risk treating the patient with medications, even if they present an interaction, instead of changing the drug that could reduce the severity of the interaction and the effectiveness of the treatment.

Regarding physicians' behavior, when analyzing only those who had prescribed over the entire period, it was noticed that 38.1% of them had a decrease in dispensed prescriptions with DI.

## Conclusion

When analyzing the number of interactions just by prescription, a reduction and a change in the prescription pattern can be seen. It indicates that a tool that assists the physician during prescription time helps him make the best decision and know the risks.

Such information to support decision-making and change the prescription pattern helps reduce events caused by administering medications with DIs, ranging from treatment of adverse events to hospitalizations and deaths.

An electronic prescribing tool enables several other benefits that are not just related to DI alerts. A tool with an up-to-date database of drugs (active or not in the regulatory agency - Anvisa) and their characteristics such as dosage form and available dosage provide support to prescribing physicians and assistance through current information to make the best decision when prescribing.

In addition, a tool can also help the physician with the legal issue of dispensing, e.g., in the case of antibiotics for which two prescription copies are required, or even in the case of controlled medications that need the completion of specific forms.

With all this decision support, the biggest beneficiary is the patient, who leaves with all the necessary information and documents to purchase the medicine and, consequently, their treatment. In addition, a digital prescription means readable information, which enables correct dispensing in pharmacies. The patient feels safer and sure about the prescribed and dispensed drugs besides being assured the doctor knows any DIs.

As a next step, we suggest an analysis of clinical data in conjunction with electronic prescribing data. It can help us understand at what point doctors risk prescribing drugs, even if they have DIs.

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