



## BRIEF REPORT

# Evaluation of negative outcomes associated with medication (NOM) by pharmacists at a home assistance programme in a Brazilian teaching hospital

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## KEYWORDS

Negative outcomes associated with medication (NOM);  
Pharmaceutical care;  
Home assistance programme;  
Medicines;  
Pharmacist

## Abstract

**Background:** The concept of pharmaceutical care (PC) specifically refers to the pharmacist being able to identify, prevent and resolve negative outcomes associated with medication (NOM). According to the Third Consensus of Granada, these are patient health-related outcomes not consistent with pharmacotherapy objectives, and are associated with the proper or erroneous use of medicines. In this way, pharmacists might provide the pharmacist to provide the correct use of medicines to patients who are attended at home.

**Objective:** This study aimed to detect, classify and quantify NOM, according to the Third Consensus of Granada, in patients treated at home, who were assisted by the Home Assistance Programme of the University Hospital of University of Paulo, Brazil.

**Method:** A descriptive, observational and cross-sectional study was conducted. The pharmacotherapy plan was filled during the interview with the patient or caregiver.

**Results:** The study included 87 patients with a mean age of 66 years old, adults (89%), children (11%), female (58%) and retired (62%). A total of 62% patients presented NOM, with an average of 1.13 NOM per patient. The NOM included untreated health problems (20.6%), effects from unnecessary medicines (9.1%), non-quantitative ineffectiveness (34.5%), quantitative ineffectiveness (3.4%), non-quantitative safety problems (11.4%) and quantitative safety problems (3.4%). Patients with the following characteristics were more prevalent than expected in the NOM effectiveness group: those aged between 65 and 74 years ( $p = 0.0199$ ), those with a low education level ( $p = 0.0266$ ), those with increased comorbidity ( $p = 0.0461$ ), those using medicine for the digestive tract and metabolism ( $p = 0.0475$ ) and those using medicine for blood and blood-forming organs ( $p = 0.0466$ ). For the NOM necessity group, patients with endocrine, nutritional and metabolic diseases ( $p = 0.0587$ ) were in greater numbers than expected; and for the NOM safety group, only patients aged over 74 years ( $p = 0.01809$ ) were in greater numbers.

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**PALABRAS CLAVE**

Resultados negativos  
asociados a la  
medicación (RNM);  
Atención  
Farmacéutica;  
Programa de  
Asistencia  
Domiciliaria;  
Medicamentos;  
Farmacéutico

**Conclusion:** For this population, it was concluded that there were several factors related to the occurrence of NOM: age, education, number of comorbidities, use of medicines for the digestive tract and the metabolism and medicines for blood and blood-forming organs. The use of the Third Consensus of Granada classification was very important for the recognition and measurement of NOM.

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## **Evaluación de los resultados negativos asociados a la medicación (RNM) realizada por farmacéuticos en un programa de asistencia domiciliaria de un hospital universitario de Brasil**

**Resumen**

**Introducción:** Para utilizar el concepto de de Atención Farmacéutica (AF) en su más amplio significado, el farmacéutico debe haber podido identificar, prevenir y resolver los resultados negativos asociados a la medicación (RNM). Según el Tercer Consenso de Granada, estos RNM están relacionados con los resultados en la salud del paciente no adecuados al objetivo de la farmacoterapia y asociados al uso o fallo en el uso de medicamentos. Así pues, el farmacéutico puede facilitar el uso correcto de los medicamentos a los pacientes en régimen domiciliario.

**Objetivo:** El objetivo de este estudio es detectar, clasificar y cuantificar los RNM, según el Tercer Consenso de Granada, en pacientes tratados en régimen domiciliario que fueron atendidos a través del Programa de Asistencia Domiciliaria del Hospital Universitario de São Paulo en Brasil.

**Método:** Estudio descriptivo y observacional de corte transversal. La planificación del tratamiento farmacológico se completó durante la entrevista con el paciente o el cuidador.

**Resultados:** El estudio contó con 87 pacientes con una edad media de 66 años, del cual el 89% eran adultos, el 11% niños, el 58% mujeres y el 62% jubilados. El sesenta y dos por ciento de los pacientes presentó RNM, con una media de 1,13 RNM por paciente. La prevalencia de RNM fue: problemas de salud no tratados (20,62%), efecto de medicamentos innecesarios (9,1%), ineficacia no cuantitativa (34,5%), ineficacia cuantitativa (3,4%), problemas de salud no cuantitativos (11,4%) y problemas de salud cuantitativos (3,4%). La probabilidad de ocurrencia de RNM de eficacia aumentaba en pacientes con: edades de entre 65 y 74 años ( $p = 0,0199$ ), nivel de educación bajo ( $p = 0,0266$ ), más comorbilidades ( $p = 0,0461$ ), uso de medicamentos para el aparato digestivo y el metabolismo ( $p = 0,0475$ ) y medicamentos para la sangre y los órganos hematopoyéticos ( $p = 0,0466$ ). La probabilidad de ocurrencia de RNM de necesidad aumentaba en pacientes con enfermedades endocrinas, nutricionales y metabólicas ( $p = 0,0587$ ), y la de los RNM de seguridad solo aumentaba en pacientes mayores de 74 años ( $p = 0,01809$ ).

**Conclusión:** En la población estudiada se dieron diversos factores relacionados con la ocurrencia de RNM: la edad, el nivel educacional, el número de comorbilidades, el uso de medicamentos para el aparato digestivo y el metabolismo, y los medicamentos para la sangre y los órganos hematopoyéticos. El uso de la clasificación del Tercer Consenso de Granada fue muy importante para el reconocimiento y la medida de los RNM.

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**Introduction**

In recent decades, the pharmacy experienced profound changes, especially in relation to the increasing of industrial products and processes which are more efficient not only for diagnosis, but also for treatment of diseases.<sup>1,2</sup> Even with these advances, the absence of pharmaceutical care to patients contributes to the increase in inappropriate use of drugs.<sup>3</sup> The incorrect use of pharmacotherapy is the main cause, because medications that should cure health problems, in fact might produce a deficiency in clinical results.<sup>4</sup> The aging of the world's population, the prevalence of chronic diseases and the vast range of products are other factors that have a direct impact on the success of pharmacotherapy.<sup>5</sup> In a survey conducted in 2006, the hospitals from U.S.A. that participated in the National Electronic Injury Surveillance System-All Injury Program,

reported that 1,754,210 patients admitted to emergency services were due to the negative effects caused by medications use.<sup>6</sup> Another study found that a total of 77.3% of negative results associated with pharmacotherapy could have been in the emergency services, with an estimated expense of 14,666 euros incurred due to the treatment of these negative results.<sup>7</sup>

However, when properly used, the medicine is the most cost-effectiveness therapeutic resource.<sup>8</sup> Based on these facts, the World Health Organization recognises that the pharmacist is the professional with the best profile to administer medications through Pharmaceutical Services. Several authors reinforce or complement the concept of the need for implementation of pharmaceutical care, a practice which is not only limited to hospitalised patients but extends to those who use outpatient services, home health, drugstore and home care.<sup>9</sup> However, it is necessary that pharmacists

demonstrate their works, because patients may not know enough about pharmaceutical care and they do not know the health benefits that can be achieved through the monitoring of pharmaceutical care, especially in undeveloped countries such as Brazil.

One of the tools to measure the impact of pharmaceutical care is the classification of the Third Consensus of Granada.<sup>10</sup> With this classification the pharmacist can detect the negative outcomes associated with medication (NOM), defined as "health outcomes not appropriate to the objective of pharmacotherapy associated with the use or failure of the medications" (Appendix I).<sup>11</sup> Thus, a patient with suspected NOM may run the risk of suffering a health problem associated with the use of medications. In this way, the pharmacist can make decisions with health teams using this tool.<sup>10</sup>

Some studies have successfully detected the presence of NOM in patients admitted to emergency services.<sup>7,12,13</sup> However, they have not found any evidence that suggests the presence of NOM in chronic patients treated at home care. Thus, this study aims to detect, classify and quantify the NOM, according to the Third Consensus of Granada, in patients treated at home, who are assisted by the Home Assistance Program of the University Hospital, Brazil. This department has an interdisciplinary team that performs a set of activities that are offered to patients at their homes. Its objective is to prevent readmissions by guiding patients and caregivers with regard to their illness and pharmacotherapy.

## Methods

### Setting and population

A descriptive, observational and cross-sectional study was conducted from January to August 2008, in which patients were treated at home by the Home Assistance Program developed (PAD) by the University Hospital (secondary level) of the University of São Paulo, São Paulo City, Brazil.

The patients included in the study met the following criteria: (a) registered under Home Assistance Program from January to August of 2008, (b) eligible for the Home Assistance Program, (c) accept the Informed and Free Consenting Terms approved by the Research Ethics Committee from the University Hospital and Faculty of Pharmaceutical Sciences, University of São Paulo, (d) take at least one medicine.

The patients were chosen at random regardless of age, sex or medical diagnosis. The pharmacist visited with the scheduled Home Assistance Program team. Each patient was identified with the initials of his/her name to ensure confidentiality and privacy, image protection and non-stigmatization. The exclusion criteria were for those patients who did not receive any medications at the beginning of the present study and for those who gave up to participate in it.

### Interview

A pharmacist (P.S.K.T.) followed the Home Assistance Program team for three days a week during eight months and gathered information in the Pharmacotherapy Plan Sheet

**Table 1** Questionnaire used by the pharmacist during the visit to patients at their homes.

- (1) What medications do you currently take?
- (2) At what time do you take these medications throughout the day, from the moment that you wake up until the moment that you go to sleep?
- (3) Do you wake up during the night to take medications?
- (4) What is the amount of each drug that you take?
- (5) Do you know about the usage of this medicine?
- (6) How are they administered: during or before fasting/during or after meals?
- (7) Is the medicine taken orally or by nasogastric tube?
- (8) Do you have to crush or dissolve the medications before taking them?
- (9) Have you been crushing them in order to be administered by taking these medications?
- (10) Did you notice any different reaction after taking the medications?
- (11) Have you got any health complaints?
- (12) Have you got any questions about the medicine's usage? Do you want to make any additional comments?
- (13) I fill out a Pharmacotherapy Plan sheet that will help you in the administration of medications. I will leave a copy at your home. But I have a few comments. Mr (s)..... do you accept any suggestions that may help you?

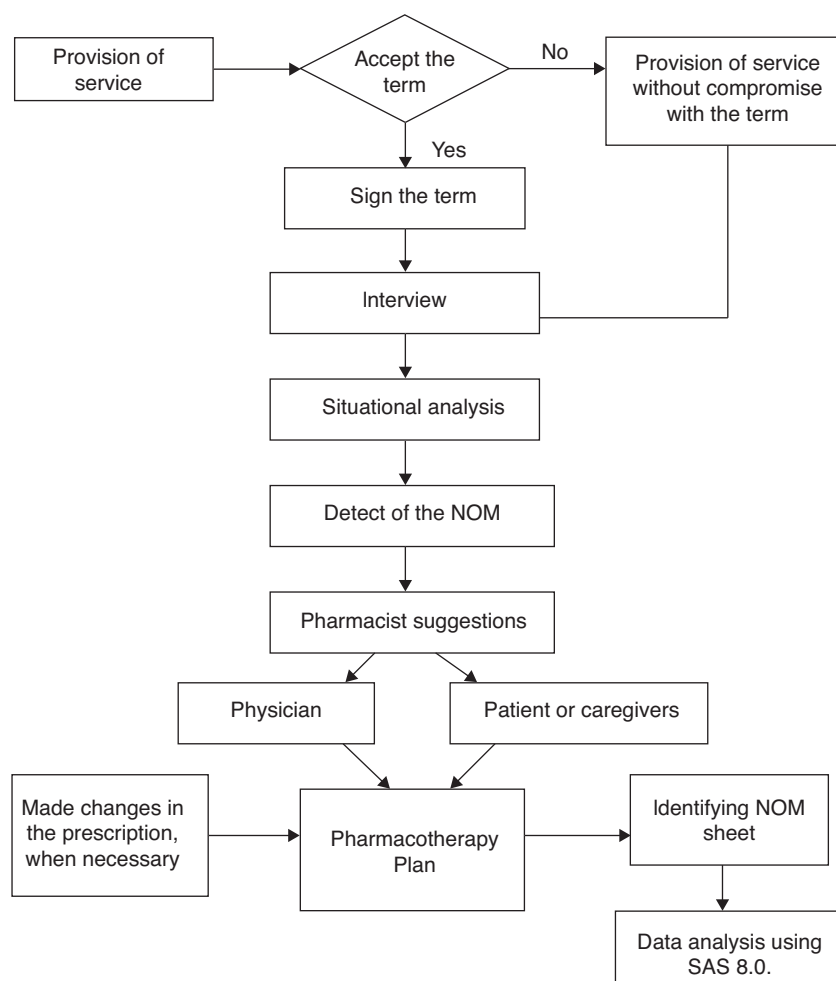
with the patient data (age, sex, weight, marital status and schooling level), the comorbidities (type of disease and duration of therapy) and pharmacotherapy (medications, dose, frequency, time and route of administration, need for crushing and dissolution of the medications and storage condition). The issues related to the pharmacotherapy were conducted according to Table 1.

The pharmacist made a situational analysis, and then the NOM detected were discussed with a physician who made changes in the prescription as necessary. All interventions were communicated to patients, families and caregivers who received a copy of the Pharmacotherapy Plan. The workflow can be observed in Fig. 1.

To improve the understanding of Pharmacotherapy Plan sheet, the pharmacist used uppercase letters, painted the lines with coloured pens, recorded signals to highlight the need to either split pills, use more than one unit of medicine or drip drop ear, eye, nose and oral administration. To differentiate drugs with similar packaging, it was supplied in plastic boxes of different colours, with the adhesives containing the name of the medicine and dosage. Some patients also received tablet cutters and oral doser to facilitate the administration of medications. The pharmacist assessed the place where the medications were stored and this place was either changed or adjusted when appropriate.

### Classification of data

The NOM detected were classified to the Third Consensus of Granada: necessity, effectiveness and safety.<sup>10</sup> The comorbidities were grouped according to the Tenth Revision of the International Classification of Diseases and Related Health



**Figure 1** Workflow of pharmaceutical care for patients in the study of Home Assistance Program developed by the University Hospital.

Adapted from Ref. [14].

Problems (ICD-10) and to the 22 categories of diseases at the first level of classification.<sup>15</sup> The medications were classified at the first level of the Anatomical Therapeutic Chemical system (ATC).<sup>16</sup>

### Recognition, classification and quantification of NOM

The pharmacist in this study only visited the PAD patients when accompanied by a medical team belonging to it. Thus, the doctor could certify that the goal of pharmacotherapy was not being achieved due to the clinical outcomes of the patient (lack of improvement in their health condition). In this way, the pharmacist could interview the patient and their caregivers trying to recognise the state of health or clinical signs diagnosed by a physician that could be related to the drug. Thus, all NMR were recognised, qualified and quantified. The problems related to the process of use that did not cause an NMR were not qualified or quantified in this study.

### Data analysis

The data were analysed using SAS software version 8.0. The total, average and percentage of patients with NOM were calculated as well as descriptive and inferential analysis of association between NOM and other variables. With the aim of testing whether there were associations between each of the variables involving socio-demographic data, the comorbidities were grouped according to the Tenth Revision of the International Classification of Diseases and Related Health Problems (ICD-10) and the medications were classified at the first level of the Anatomical Therapeutic Chemical system (ATC)<sup>16</sup> and the occurrence in each group of NOM. It was used the exact chi-square test of Pearson.

Furthermore, with the objective to study simultaneously studying the association between all variables and the occurrence of each group of NOM models, they were adjusted to a logistic regression. Variables were selected from the forward stepwise method with a test score for the inclusion of variables and a Wald test for exclusion. The level of significance for inclusion was 5% and the level for exclusion was 10%.

**Table 2** Characteristics of patients included in the present study.

|  |                          |
|--|--------------------------|
| <i>Average age</i>   | 66.2 years (1–97 years)  |
| <i>Adults, n (%)</i>                                       | 77 (88.5)                |
| <i>Children, n (%)</i>                                     | 10 (11.5)                |
| <i>Female, n (%)</i>                                       | 50 (57.5)                |
| <i>Male, n (%)</i>   | 37 (42.5)                |
| <i>Retired, n (%)</i>                                      | 54 (62.1)                |
| <i>Married, n (%)</i>                                      | 36 (41.4)                |
| <i>Main caregiver, n (%)</i>                               | 42 (48.3)                |
| <i>Still in primary school, n (%)</i>                      | 34 (39.1)                |
| <i>Average number of comorbidities</i>                     | 4.3 (1–10 comorbidities) |
| <i>Average number of medications</i>                       | 2.9 (1–15 drugs)         |
| <i>Frequency of comorbidities</i>                          |                          |
| Circulatory diseases, n (%)                                | 62 (71.3)                |
| Endocrine, nutritional and metabolic, n (%)                | 40 (46)                  |
| Nervous system disorders, n (%)                            | 25 (28.7)                |
| <i>The most groups of medications prescribed</i>           |                          |
| Medications for the alimentary tract and metabolism, n (%) | 64 (73.6)                |
| Medications for the nervous system, n (%)                  | 60 (69)                  |
| Medications for the cardiovascular system, n (%)           | 55 (63.2)                |

## Results

After the exclusion of patients who had not met the requirements to participate in the study ( $n=3$ ), the sample was obtained from 87 patients. Excluded patients were those patients who did not receive any medications at the beginning of the present study ( $n=2$ ) and those who gave up to participate in the study ( $n=1$ ). Table 2 describes the characteristics of the patients included. Problems with the storage of medications were found in 25.28% of the households involved. These problems attributed mainly to the drugs being stored at a temperature below the manufacturer's recommendation ( $n=2$ ), inappropriate exposure to the place of storage to direct sunlight, close proximity to children ( $n=26$ ), being stored with other unused medications or used by relatives ( $n=38$ ).

Among the 87 patients, 54 (62%) presented frequency of NOM, 33% one NOM and 29% more than one NOM. Thus, there was an average of 1.13 NOM per patient. The patients showed the following NOM (Table 3): untreated health problem in 18 patients (20.62%), effect of unnecessary medicine in 8 patients (9.1%), non-quantitative ineffectiveness in 30 patients (34.5%), quantitative ineffectiveness in 3 patients (3.4%), non-quantitative safety problems in 10 patients (11.4%) and quantitative safety problems in 3 patients (3.4%).

There was an association between the frequency of NOM of necessity category and the presence of endocrine, nutritional, and metabolic diseases and, the total number of

comorbidities. Among those patients with endocrine, nutritional and metabolic diseases, a prevalence of 35% was observed, whereas for the other group it was 17%. Among patients with 6 or more comorbidities the prevalence was 35%, whereas among those with up to 3 comorbidities it was 17% (data not shown).

There is evidence that several variables are associated with the occurrence of the NOM of effectiveness group. The prevalence of this NOM group was 19% among patients aged up to 64 years and 45% among those aged 65 or more. Widows showed a prevalence of 53%. Among patients who had not yet finished primary school, prevalence was 53%, whereas among those in higher education level it was 21%. There is also a higher average prevalence between patients with 3 or more cardiovascular diseases (60%) and with 6 or more diseases in total (60%). Even in this group, prevalence was also significant with respect to the use of 3 or more medications for alimentary tract and metabolism (56%), for the blood and blood forming organs (56%), using 2 or more medications for the cardiovascular system (54%) and a total of 8 or more medications (50%) (data not shown). For NOM of safety group, 22% of patients of up to 79 years of age showed this NOM; among widows prevalence was 3%; patients with nervous system diseases was 24%; and that influence the health status and contact with the server health (ICD Z00–Z99) was 25% who had greater than average prevalence at the sample.

Using the descriptive level of the exact chi-square tests, they were tested for different variables (socio-demographic, comorbidities and medicine classification). Considering a significance level of 5%, no variable that was studied shows evidence of an association with the occurrence of NOM group necessity. However, several variables have an association with the occurrence of NOM of effectiveness group, including marital status ( $p=0.0012$ ), schooling ( $p=0.0339$ ), total number of comorbidities ( $p=0.0463$ ) and medications for alimentary tract and metabolism ( $p=0.0160$ ), medications for the blood and blood forming organs ( $p=0.0033$ ) and the cardiovascular system ( $p=0.0160$ ). Only the age variable showed association with the occurrence of NOM of safety group ( $p=0.0129$ ) (Table 4).

In assessing the estimation, descriptive levels and odds ratios adjusted for the logistic regression model for NOM of the necessity, effectiveness and safety group it was observed that the chances of occurrence of NOM of the effectiveness group increased for patients aged between 65 and 74 years ( $p=0.0199$ ), those in primary education ( $p=0.0266$ ), the increase in the number of comorbidities ( $p=0.0461$ ), the use of medications for the digestive tract and metabolism ( $p=0.0475$ ) and medications for blood and blood forming organs ( $p=0.0466$ ). For NOM of the necessity group the chance of occurrence increased for patients with endocrine, nutritional and metabolic diseases ( $p=0.0587$ ) and for NOM of the safety group the chance of occurrence increased only for patients aged over 74 years ( $p=0.01809$ ) (Table 5).

## Discussion

The use of medications to improve, prevent and cure does not always produce the expected results due to factors such as the failure of therapy in patients with interaction between acute and chronic diseases and medications,



**Table 3** Absolute frequencies and the percentage of negative outcomes associated with medications (NOM) related to patients visited by the Home Assistance Program of the University Hospital of the University of São Paulo are included from January to August, 2008.

| NOM group     | NOM type                         | NOM quantity          |      |                              |       | NOM average |
|---------------|----------------------------------|-----------------------|------|------------------------------|-------|-------------|
|               |                                  | Patient with none NOM |      | Patient with one or more NOM |       |             |
|               |                                  | <i>n</i>              | %    | <i>n</i>                     | %     |             |
| Necessity     | Untreated health problem         | 69                    | 79.3 | 18                           | 20.62 | 0.2529      |
|               | Effect of unnecessary medicine   | 79                    | 90.8 | 8                            | 9.1   | 0.1494      |
| Effectiveness | Non-quantitative ineffectiveness | 57                    | 65.5 | 30                           | 34.5  | 0.5057      |
|               | Quantitative ineffectiveness     | 84                    | 96.6 | 3                            | 3.4   | 0.0345      |
| Safety        | Non-quantitative safety problem  | 77                    | 88.5 | 10                           | 11.4  | 0.1264      |
|               | Quantitative safety problem      | 84                    | 96.6 | 3                            | 3.4   | 0.0575      |
|               | Total NOM                        | 33                    | 37.9 | 54                           | 62    | 1.1264      |

**Table 4** Descriptive level of the exact chi-square tests for different variables.

| Variables   | NOM       |               |         | Any NOM |
|---|-----------|---------------|---------|---------|
|   | Necessity | Effectiveness | Safety  |         |
| Age   | 0.7083    | 0.0604        | 0.0129* | 0.5518  |
| Sex   | 0.6198    | 0.5074        | 0.3463  | >0.9999 |
| Occupation  | 0.3116    | 0.1750        | 0.7630  | 0.3626  |
| Marital status  | 0.7672    | 0.0012*       | 0.1299  | 0.2147  |
| Main caregiver  | 0.5097    | 0.2607        | 0.7086  | 0.5043  |
| Schooling   | 0.8202    | 0.0339*       | 0.9246  | 0.2225  |
| Endocrine, nutritional and metabolic diseases (E00–E90)                                 | 0.0824    | 0.3744        | 0.5343  | 0.1879  |
| Mental and behavioural disorders (F00–F99)  | 0.5785    | 0.7944        | 0.7252  | 0.2935  |
| Diseases of the nervous system (G00–G99)  | 0.4175    | 0.3326        | 0.0950  | 0.3290  |
| Diseases of the circulatory system (I00–I99)  | 0.3451    | 0.1119        | 0.6994  | 0.1217  |
| Diseases of the respiratory system (J00–J99)  | 0.4154    | 0.9625        | 0.1778  | 0.4512  |
| Diseases of the digestive system (K00–K93)  | 0.5156    | 0.2382        | 0.4642  | 0.3916  |
| Factors influencing health status and contact with health services (Z00–Z99)            | >0.9999   | 0.5728        | 0.2215  | 0.2707  |
| Other comorbidities   | 0.1797    | 0.5943        | 0.9207  | 0.5736  |
| Total number of comorbidities   | 0.3548    | 0.0463*       | 0.4133  | 0.0855  |
| Medications for the alimentary tract and metabolism                                     | 0.9579    | 0.016*        | 0.7864  | 0.4453  |
| Medications for the blood and blood forming organs                                      | >0.9999   | 0.0033*       | 0.2222  | 0.0140  |
| Medications for the cardiovascular system   | 0.6965    | 0.016*        | 0.9279  | 0.4117  |
| Medications for the systemic hormonal preparations, excluding sex hormones and insulins | 0.5428    | >0.9999       | >0.9999 | 0.7857  |
| Medications for the musculo-skeletal system   | >0.9999   | >0.9999       | 0.1165  | >0.9999 |
| Medications for the nervous system  | 0.6284    | 0.5507        | 0.3925  | 0.6218  |
| Medications for the respiratory system  | 0.7701    | 0.1124        | 0.7252  | 0.2935  |
| Others ATC groups   | 0.5790    | >0.9999       | 0.7250  | 0.8052  |
| Total number of medications   | 0.8594    | 0.0977        | 0.6672  | 0.4982  |

\*  $p < 0.05$  (Chi-square test).

**Table 5** Estimation, descriptive levels and odds ratios adjusted for the logistic regression model for NOM of the necessity, effectiveness and safety group.

| NOM                 | Variable   | Class                    | Estimation                | Standard error | p-Value | Odds ratio       |                           |
|---------------------|--|--------------------------|---------------------------|----------------|---------|------------------|---------------------------|
|                     |  |                          |                           |                |         | Point estimation | Confidence interval (95%) |
| Necessity group     | Intercept  |                          | -1.58                     | 0.39           | 0.0587  |                  |                           |
|                     | Endocrine, nutritional and metabolic diseases      | 0<br>1 or more           | Reference<br>0.97         | 0.51           |         | 2.6              | 1.0-6.9                   |
| Effectiveness group | Intercept  |                          | -4.87                     | 1.19           | 0.0199  |                  |                           |
|                     | Age  | 0-64<br>65 or more       | Reference<br>1.53         | 0.66           |         | 4.6              | 1.3-16.7                  |
|                     | Education level                                    | 1° more                  | Reference                 |                | 0.0266  |                  |                           |
|                     |  |                          | 1.51                      | 0.68           |         | 4.5              | 1.2-17.4                  |
|                     | Number of comorbidities                            | 1-5<br>6 or more         | Reference<br>1.27         | 0.64           | 0.0461  | 3.6              | 1.0-12.5                  |
|                     |  |                          |                           |                |         |                  |                           |
|                     | Medications for the digestive tract and metabolism | 0<br>1 or 2<br>3 or more | Reference<br>1.43<br>2.07 | 0.72<br>0.86   | 0.0475  | 4.2<br>7.9       | 1.0-17.4<br>1.5-42.9      |
|                     |  |                          |                           |                |         |                  |                           |
|                     | Medications for blood and blood forming organs     | 0<br>1 or more           | Reference<br>1,09         | 0.55           | 0.0466  | 3.0              | 1.0-8.7                   |
| Safety group        | Intercept  |                          | -1.16                     | 0.35           |         |                  |                           |
|                     | Age  | 0-74<br>75 or more       | -2.53                     | 1.07           | 0.0180  | 0.08             | 0.01-0.65                 |
|                     |  |                          |                           |                |         |                  |                           |

The forward stepwise method with a test score = for inclusion of variables and Wald test for exclusion. The level of significance for inclusion was 5% and the exclusion was 10%.

presence of the adverse reactions, errors in administration and lack of access to medications, among others. Through pharmaceutical care, the pharmacist can detect the negative outcomes associated with medications (NOM), using an algorithm based on the Third Consensus of Granada, which helps this professional to recognise, classify and quantify these results and therefore, take action to maximise the pharmacotherapy.<sup>10</sup>

But there are few publications that used the NOM classification as most of them focus on emergency services.<sup>7,13,17</sup> This low number is mainly due to the recent disclosure of the Third Consensus which was published in the end of 2007. However, there are many studies that used the DRP classification (First and Second Consensus of Granada), added to publications that used the term drug therapy problems, medicine-related problems and medications-related problems conducted by pharmacists in several countries.<sup>18</sup>

The present study showed that the profile of patients visited by Home Assistance Programme, Brazil, comprises, in most cases, adults, females, retirees (those older than 65 years of age), married people, those still in primary school and those with their own home. These results are similar to the data of other study conducted in 2002 where these groups were also studied.<sup>19</sup> In publications on DRP and NOM it was noted that the prevalence of females is higher than males with 58.4%, 51%, 63.60% and 74.0%.<sup>20-23</sup> According to Tuneau et al. this prevalence is due to the fact that women have a greater life expectancy and access health services more frequently than males.<sup>24</sup>

With regard to schooling, the majority of this group had completed primary school (39%). Illiteracy rates found in

22% of the patients was higher than the result found in 2002.<sup>19</sup>

In relation to age, there was an average of 66.2 years old (1-97 years). This average is similar to publications: 65 years old for hospital admission, 67.1 years old in institutionalised elderly patients and 63 years old in patients in the emergency services, respectively.<sup>23,25,26</sup> However, it is lower if compared with the average of 76.14 years old in patients visited in their homes in the study conducted at San Vicente de Alcántara, Spain.<sup>27</sup>

With regard to comorbidities, it was noted that there was a high frequency associated with the circulatory system (71%), which was related to the diagnosis of stroke, hypertension, myocardial infarction and atrial and ventricular fibrillation. The second highest frequency of comorbidities was that related to endocrine nutritional and metabolic diseases (46%) and it was linked to patients with diabetes mellitus, dyslipidemia and obesity. Thirdly it was found that the comorbidities of nervous system (29%) were related with Alzheimer's, Parkinson's and hemiparesis, among others. The frequency of 25% for the comorbidities that affect the respiratory system is the result of the presence of chronic obstructive pulmonary disease, emphysema and pneumonia in this group.

During our study it was observed that 44% of patients had 4-5 comorbidities. This result is lower than the work conducted in community pharmacies in Iowa, USA for the identification of DPR, which indicates the average of 6.1 comorbidities per patient.<sup>21</sup>

The ATC classification demonstrated that medications for the alimentary tract and metabolism were mostly used by

patients (73.6%). Therefore, our results are superior to publications that evaluated the presence of NOM or DRP and which found the prevalence of 19.1% for the presence of drugs for this system, recorded in the Dáder program.<sup>17</sup> The prevalence of these medications is 8.3% in patients belonging to the institutionalised geriatric group.<sup>26</sup> In a study conducted by Cautevilla et al., 15.89% of prescriptions for outpatients contained these groups of drugs.<sup>28</sup> Medications for the nervous system were present in 69% of prescriptions. These data were also higher than the frequencies of 16.4%, 47.8% and 19.69% for the works of García-Jiménez et al.<sup>17</sup>, Correia et al.<sup>26</sup> and Cautevilla et al.<sup>28</sup>. The frequency of prescriptions with medications for the cardiovascular system was 63.2%. This result is superior to the works of García-Jiménez et al.<sup>17</sup> (37.8%), Correia et al.<sup>26</sup> (36.4%) and Cautevilla et al.<sup>28</sup> (36.27%). With a frequency of 41%, the medications for the blood and blood forming organs appeared in fourth place.

The average number of drugs prescribed to our population was 6 and the maximum observed was 15, with 25% of patients using 8 or more. The average number of medications is similar to averages of 5.5 and 6.4.<sup>17,27</sup> On the other hand, the works with outpatient presented different values: Doucette et al. found an average of 4.6 medications per day; Cipolli et al. found the average of 3 medications per day for patients younger than 65 years old and 6 drugs per day for patients older than or equal to 65 years. It is different from the average of 3 drugs in the evaluation of the study with NOM classification of the Third Consensus of Granada in patients in the emergency services.<sup>7,21,29</sup>

From the 87 patients who took part in this study, 62% of patients were observed to have NOM, while 33% had one NOM and 29% had more than one. This finding is similar to 32% of patients visited at home who had DRP.<sup>30</sup> Compared with the studies that evaluated patients in the emergency services and using the term NOM, it was found that these results are less than in the present study, 52.1%, 28% and 33.17%.<sup>7,12,31</sup> To explain this disparity, it should be noted that the reality at home is different from that in emergency services because in the case of the latter the pharmacotherapy is described by a companion, when she/he knows about the pharmacotherapy of the patient; otherwise this information will only be obtained at another time.

The average of 3.4 DRP to hypertensive patient at home, 3.1 DRP per institutionalised patient, 3 DRP per institutionalised geriatric patients and 5.9 DRP per ambulatory patient were above the average of 1.13 RNM per patient found in this work, which were attended by the pharmacist only once.<sup>21,26,30,32</sup> However, this average is close to that found in studies of outpatients, i.e. 1.51 DRP per ambulatory patient and 1.6 DRP per patient in community pharmacy.<sup>33,36</sup>

In relation to NOM of Need group, which was related to untreated health problems, there was a prevalence of 20.62%. Thus, the patient suffers from a health problem that was not observed by a health professional and was identified at the time of the visit, such as constipation, pain aggravated by various comorbidities, muscular rigidity and signs of infections. This result is similar to several studies that found prevalence of 20.89% in patients treated in 22% community pharmacies, 23.6% in outpatients and 20% in home patients.<sup>22,28,30,33</sup>

The necessity group had a prevalence of 9.1% of patients with NOM of effect of unnecessary medicine. It was similar to 8% for ambulatory hypertensive patients studied in Niterói, city in Rio de Janeiro, Brazil.<sup>34</sup> This datum is less than 12.9% found in the study by Doucette et al., but it is much higher with respect to the prevalence of 3.6% of patients registered in the Dader program.<sup>17</sup> This fact is observed in patients who use over-the-counter (OTC) medications and as a result the presence of comorbidity persists, which worsens their health status. A clear example of misuse could be observed in a patient wrongly using an antibiotic to improve chronic pain in the knee after a fall and a patient using a topical antibiotic indicated friends to strengthen nails. With detection by a pharmacist and medical intervention, the patients began to receive proper treatment. Most of these negative outcomes associated with medications were the product of an attempt to minimise the health problems without consulting a specialist and the administration of these drugs may mask or worsen clinical outcomes.

Effectiveness group had a high prevalence of NOM due to the non-quantitative ineffectiveness (34%). All data in the literature were below the prevalence found in this study: 27.7% and 11.76%, both in emergency services, and 14.2% in ambulatory patients.<sup>7,28</sup> The occurrence of this type of NOM was very significant because of the problems related to the administration of medications or inappropriate storage, which may influence the chemical structure of the product. In many cases, Home Assistance Program patients have nasogastric tubes or difficulty in swallowing and need to receive diluted or crushed medications or have to take them with meals. However, these three forms of administration were counter-indicated by the manufacturer because it could affect the expected therapeutic effect of the medicine resulting in the continuation of a health problem. This health problem cannot be confused with the NOM of an untreated health problem as the patient is receiving the medicine indicated with the correct dosage and the frequency. For example, we can cite a case which is associated with crushing and dilution of omeprazole capsules for administration by nasogastric tubes. For the administration of this medicine by tube it must be handled with sodium bicarbonate solution of 8.4% in specialised pharmacies. Another common occurrence is linked to the administration of omeprazole or captopril with meals, when the indication is to administer during fasting.

The NOM of the non-quantitative ineffectiveness showed significant effects and varied according to age: 44% of patients who were between 65 and 79 years, 19% of patients younger than 64 years and, 39% of patients 80 years or more. The lowest prevalence was in patients older than 79 years and it may be due to the greater experience of the patient or their caregiver in relation to the administration of drugs, since this study included 33 patients aged 80 years or more and 27 patients aged between 65 and 79 years and it was expected that elderly patients would have higher prevalence of NOM. It is worth noting that a significant number of patients younger than 64 years were children ( $n = 10$ ) and had chronic comorbidities and received guidance on the use of medications, training and written instructions for administering them. The pharmaceutical care performed by a pediatric clinical pharmacist probably prevented the occurrence of such NOM in the children.



homes, included in this study. This NOM was also observed in 50% of widows, 47% of patients who had not finished primary school and 50% of patients who had 3 or more circulatory system diseases. As 53% of patients had one or more comorbidities of the circulatory system and 50% of patients who reached 6 or more comorbidities also had NOM of this group, i.e. patients with hypertension, congestive heart failure, dyslipidemia, diabetes mellitus, Parkinson's disease and depression. We found that 56% of patients who used 3 or more drugs of the alimentary tract and metabolism (omeprazole, dimeticone, mineral oil, bromopride associated with a hypoglycemic—NPH insulin, metformin or glibenclamide) and 50% of patients who used one or more medications for the blood and blood forming organs (warfarin, aspirin or enoxaparin) had NOM of the non-quantitative ineffectiveness type.

The caregivers who looked after the patients with the characteristics listed above probably pay more attention and spend more time on tasks related to the administration of food, hygiene care of the patient and of the environment, dressings and physiotherapy. Thus, when it comes to medications that apparently only need to be administered, the caregiver does not pay attention to this subject nor seeks a proper explanation from the doctor. All these data show that the group with the characteristics above had higher prevalence of NOM of the non-quantitative ineffectiveness type, i.e. patients with advanced age, the lowest level of schooling, with three or more comorbidities of the circulatory system, 6 or more comorbidities in general, use three or more drugs for the alimentary tract and the use of one or more medications for the blood and blood forming organs.

Also in the effectiveness group, it was noted that 3.4% of patients had NOM of the quantitative ineffectiveness type, i.e. the pharmacotherapeutic goal was not achieved because a lower dose of the medicine per day was administered. However, in some cases the patient received a lower dose than prescribed which lead to ineffective therapy. There is an extreme difference between the data of this study and the publications consulted in which values as 61.7%, 20.4%, 10.6% and 28.8% were found.<sup>7,17,28,31</sup>

The safety group of the non-quantitative safety problem type, i.e. not dependent on either the dose or the frequency, has a prevalence of 11.4%. The prevalence found in this NOM is not quantitatively superior to that found in works in emergency services: 8.8%, 2.45% and 5.45%.<sup>7,31,35</sup> However, it is lower than the data found by Triller et al. which was 16% in hypertensive patients visited at home.<sup>30</sup>

In the NOM of the quantitative safety problem, there was a prevalence of 3.4%, since these patients are constantly monitored by laboratory tests. This prevalence is lower than the impact on emergency services.<sup>7,22,35</sup>

In general, the only variable clearly associated with the occurrence of NOM of the need was with endocrine, nutritional and metabolic diseases ( $p=0.0587$ ) or the presence of these factors increases the chance of occurrence of NOM in both types. These diseases are, in general, diabetes mellitus, dyslipidemia and obesity. It was noted that the group which had a higher NOM was effectiveness, leading to the occurrence of various associations for the simple inferential analysis, which considered a significance level of 5%, with association to the variables found as marital status, schooling, number total of comorbidities, use of medications for

the alimentary tract, medications for the blood and blood forming organs and cardiovascular system. For the NOM of the security group there was only a strong association with age ( $p=0.0180$ ).

Thus, the factors that were related to the occurrence of NOM between patients treated by Home Assistance Program at a teaching Hospital and the occurrence of the NOM of the effectiveness group (which was the most expressive) were studied. The factors that increased the chance of occurrence were: an age of between 65 and 74 years, low schooling level, the increase in the number of comorbidities, use of medications for the alimentary tract and metabolism, and the use of medications for the blood and blood forming organs. The occurrence of NOM of necessity group increased chances for patients with endocrine, nutritional and metabolic diseases. The occurrence of NOM of the safety group had a greater chance for those patients who were younger than 74 years.

In this way, larger studies are needed to measure the acceptability of the clinical staff, patients or their caregivers as a way of assessing the cost of the presence of an NOM and to detect the NOM which could be avoided.

## Conflict of interest

The authors have no conflict of interest to declare.

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## Appendix I. Supplementary data

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