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Article

# Socioeconomic factors influencing access to drugs from the Specialized Component of Pharmaceutical Services in Paraná-Brazil: An observational, cross-sectional retrospective study

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The Specialized Component of Pharmaceutical Services (CEAF) is a crucial strategy for accessing medicines through the Brazilian Public Health System, holding the highest budgetary impact on outpatient pharmaceutical care. This study aimed to assess the association of socioeconomic factors with access to CEAF drugs in municipalities throughout Paraná from 2010 to 2019. It utilized a retrospective, observational, cross-sectional approach, evaluating dispensed medication units, medication expenditure, and average unit cost. Analyses were performed to identify a correlation between the use of CEAF drugs and socioeconomic indicators. In these 10 years, the number of dispensed units practically quadrupled, and the expenditure on these drugs doubled, from BRL 214 million to BRL 476 million. The Index of Paraná Institute for Economic and Social Development of Municipal Performance (IPDM) showed a greater association with the use of CEAF drugs, and no correlation was observed between gross domestic product (GDP) per capita and the municipal population. Overall, the IPDM index that includes income, education, and health are socioeconomic factors that influence the utilization of CEAF drugs. These findings emphasize the need for health education among users and adjustment of public policies to mitigate inequalities in the CEAF drug access for the citizens of Paraná.

**Keywords:** National drug policy. High-cost drugs. Pharmaceutical care. Multivariate analyses.

## INTRODUCTION

In Brazil, the provision of medications within the Unified Health System (SUS) is structured through pharmaceutical financing blocks: i) basic component of pharmaceutical services (CBAF), ii) strategic component of pharmaceutical services, and iii) specialized component of pharmaceutical services (CEAF). These components cater to medications and supplies in the context of primary care, medications for the treatment of epidemiologically relevant diseases, and medications for the treatment of less prevalent diseases with high financial impact, respectively (Vieira, 2010).

The CEAF is an important strategy for guaranteeing access to medicines in the Brazilian public health care system (SUS). Its main feature is the guarantee of the entirety of the drug treatment for all diseases covered by the CEAF, and access to these drugs must comply with criteria previously established in the Clinical Protocols and Therapeutic Guidelines (CPTG) published by the Ministry of Health (Brasil, 2017a).

At CEAF, treatments are contemplated for chronic degenerative diseases whose lines of care are defined in the CPTG, including rare diseases (Brasil, 2017a). Within the scope of this component, in 2021, drug treatment was offered for 106 clinical conditions, with the Ministry of

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Health being responsible for the acquisition of 114 drugs in 204 presentations (Brasil, 2022).

The drugs that integrate CEAF's lines of care are divided into three groups, with different characteristics, execution responsibilities, and forms of organization, so that each federal entity is responsible for the exclusive financing of a group of drugs (Brasil, 2017a). According to Consolidation Ordinance GM/MS nº 2/2017, CEAF drug groups are defined according to the following general criteria: a) complexity of disease treatment; b) guarantee of comprehensive treatment of the disease within the scope of the line of care; c) maintenance of financial balance between the spheres of SUS management (Brasil, 2017a).

Thus, regarding funding, the Union is responsible for the drugs in Group 1, where the most complex treatments and those with the greatest financial impact are found, while the drugs in Groups 2 and 3 are the responsibility, respectively, of the State Health Secretariats and the Federal District, and the Health Secretariats of the Federal District and Municipalities (Brasil, 2017b; CMAP, 2020).

The CEAF represents the greatest budgetary-financial impact on ambulatory pharmaceutical services in the SUS. To guarantee drug treatment for patients with the clinical conditions defined in CPTG, in 2021, the Ministry of Health acquired 628,518,721 medication units, which corresponded to an expense of BRL 4.76 billion, and 601.1 million medication units were distributed to the states (Brasil, 2022). In Paraná, in that same year, 130,044,267 medication units were distributed to the 22 Health Districts, equivalent to an expenditure of more than BRL 524 million (Paraná, 2022).

For a citizen to have access to CEAF medicines, they must meet the clinical and diagnostic criteria described in the CPTG. To request the medicine, the patient must present several documents, among them a medical prescription, Report for Request, Evaluation, and Authorization of Medicines of the Specialized Pharmaceutical Care Component, documents, and exams required in the CPTG, term of consent and a copy of personal documents. In some CPTG, it is established that the clinical diagnosis and medical prescription must be carried out by a specialist. The documentation presented by the patient is evaluated by a superior degree health professional to assess whether the patient meets the criteria set out in the CPTG. Only after this request is granted, patient can receive CEAF medications for the requested clinical condition (Brasil, 2017a).

The responsibility for carrying out the CEAF activities rests with the State Health Secretariats, and involves the steps of requesting, evaluating, authorizing, dispensing medication, and ensuring treatment continuity. Thus, it is up to the state management sphere to guarantee and organize patient access to the group of drugs included in this Component (Brasil, 2017a).

In Paraná, in addition to the medications covered by CEAF, there is a Complementary List (CL) provided by the State Health Secretariat. These medications are financed through state treasury resources, aiming to extend coverage for diseases and injuries not addressed by other policies (Paraná, 2016). The CL includes medications for chronic pain treatment, insulin analogues for patients with challenging-to-control Type 1 diabetes mellitus, medications and diets for individuals with cystic fibrosis, as well as medicines for treating opportunistic infections (OI) in HIV-infected individuals. Access to CL drugs operates on the same principles as CEAF, except for OI medications, which are dispensed through Medicine Dispensing Units along with antiretroviral medicines (Paraná, 2023).

Ensuring universal and equal access to medicines for all citizens is one of the crucial issues in the SUS, constituting the guiding axis of public policies established in pharmaceutical services. In this context, identifying and analysing the differences in the use of CEAF medicines is important and necessary to assess the universality and equity of access to these medicines, as well as to contribute to the orientation of public policies aimed at expanding access to medicines to the entire population.

This study aimed to assess the association of socioeconomic factors with access to CEAF drugs in municipalities throughout Paraná from 2010 to 2019, and also provide new insights into how the CEAF serves as a specialized approach to address challenges in medication accessibility. This emphasis on the CEAF as a strategic pillar fills a critical gap in understanding the role of pharmaceutical services in Brazilian healthcare.

The observed increase in the number of dispensed medication units and the corresponding rise in

expenditure on medications within the CEAF in the state of Paraná, Brazil, from 2010 to 2019, may be associated with socioeconomic factors, particularly those reflected in the IPDM. This study initiated with the hypothesis: Is there a correlation between higher IPDM scores in municipalities in Paraná and an increased utilization of CEAF medications?

## MATERIAL AND METHODS

### Study design and setting

This study follows the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines in order to enhance the reporting quality of this observational study (von Elm *et al.*, 2008).

This is a retrospective, observational, cross-sectional study in which the quantity and expenditure on CEAF medications dispensed in the 399 municipalities in the state of Paraná from 2010 to 2019 were analysed.

To carry out the study, the independent (predictor) variables analyzed, as well as the databases used, are described in Table I. The following dependent variables were also assessed: a) number of medication units dispensed from the CEAF and Complementary List (CL) by the municipalities of Paraná; b) the financial value waived from the CEAF and CL per municipality of Paraná; c) the average value per dispensed medication unit.

**TABLE I -** Demographic, socioeconomic, and health indicators analyzed regarding the association with the use of CEAF medications

| Independent variable | Year analyzed | Database |
|---|---|---|
| Municipal population | 2010 to 2019 | IBGE |
| Gross Domestic Product (GDP) per capita | 2010 to 2017 | IBGE |
| Number of professionals with medical specialty | 2012 to 2019 | DATASUS |
| Index of Paraná Institute for Economic and Social Development of Municipal Performance (IPDM, acronym in Portuguese)[1] | 2010 to 2016 | IPARDES |
| IPDM- Health[2] | 2010 to 2016 | IPARDES |
| IPDM - Income, Employment and Agricultural Production[3] | 2010 to 2016 | IPARDES |
| IPDM - Education[4] | 2010 to 2016 | IPARDES |

[1]The IPDM is a synthetic index that seeks to capture the socioeconomic conditions of the municipalities of the State of Paraná in their most significant dimensions: income (composed of income, employment, and agricultural production), education, and health, following a line like that of the Human Development Index (HDI) prepared by the United Nations Development Program (UNDP).

[2] IPDM – Health is composed of the variables: Percentage of more than six prenatal consultations per live births, Percentage of deaths from ill-deceased causes, Percentage of deaths of children under five years old from preventable causes per live births.

[3] IPDM – Income, Employment and Agricultural Production is composed of the variables: Average remuneration (absolute average remuneration and average remuneration growth rate), Formal employment (Index of formalization, Growth rate of Formal Employment Stock, Employment participation index formal), Agricultural Production (Participation of the Gross Value of Production - agricultural GPV of the municipality in the total and of the state, Growth rate of the agricultural GPV).

[4] IPDM – Education is composed of the variables: Early Childhood Education (daycare and preschool), Elementary and Secondary Education (age-grade non-distortion rate, Percentage of teachers with higher education, non-dropout rate, average education development index basic).

**a) Number of medication units dispensed from the CEAF and CL**

The total number of medication units dispensed was extracted from the computerized system used in the management of CEAF in Paraná - Sismedex, through the BI tool (Business Intelligence). To collect these data, reports were issued, year by year, in electronic spreadsheets, using the following filters: quantity dispensed per medication, patient´s county of residence, and year of dispensation. After the report was issued, the total amounts dispensed by municipality were summed, obtaining the total amount dispensed according to the municipality of residence of the patient attended.

**b) The financial value waived from the CEAF and CL per municipality of Paraná**

To obtain the financial value dispensed, reports were extracted from the computerized system for drug stock management in Paraná (Sysmed), using the BI tool (Business Intelligence). These reports were presented in electronic spreadsheets containing all acquisitions made by the Paraná State Health Secretariat of drugs from CEAF and CL and all drug shipments received from Ministry of Health. To issue the Sysmed report, the following filters were used: medicine, quantity acquired/received, unit value and year of acquisition/receipt. The weighted average price per drug was calculated each year, using Excel formulas. To obtain the total amount dispensed, the weighted average price of the drug was multiplied by the total amount dispensed by each municipality each year. Finally, the financial amount dispensed for all medications was summed, obtaining the total financial amount dispensed by municipality, year by year.

**c) The average value per dispensed medication unit**

To obtain the average value per medication unit, the total amount dispensed was divided by the number of medication units dispensed.

The relative variables were calculated dividing the absolute variables by the number of inhabitants of the municipalities. Relative variables were related to demographic, socioeconomic, and health indicators to identify the association of these variables with the use of CEAF medications. Table I shows the main indicators used and the database consulted.

**Data analysis**

A descriptive analysis of the dependent variables by municipality was performed, expressing the categorical variables in absolute and relative frequencies. Relative dependent variables were divided into quartiles and spatially represented, according to the quartile distribution, conforming to the municipal grid made available by IBGE, using the QGIS 3.16.15 software.

A model was created to calculate the municipality's permanence score in the distribution quartiles during the 10 years of the study. For each year that the municipality was in the 1st quartile, 1 point was attributed; in the 2nd quartile 2 points; in the 3rd quartile, 3 points and in the 4th quartile, 4 points, respectively. Thus, the score for remaining in the quartile ranged from 10 to 40 points. This score was used to measure the municipality's behavior over the 10 years analysed regarding the dispensing of CEAF and CL medications. The permanence score in the distribution quartiles was calculated for the 399 municipalities for the three dependent variables analysed. Finally, the quartile distribution of the permanence score was performed, and the spatial representation was performed again.

To test the association between dependent and independent variables, bivariate analyses were performed using Pearson's correlation test. The ranges considered for Pearson's correlation limits were 0.00 to 0.400 for a weak correlation, from 0.401 to 0.700 for a moderate correlation and greater than 0.700 for a strong correlation. The dependent variables analysed were the score for permanence in the quartiles of the distribution of the number of units dispensed per inhabitant and the score for permanence in the quartiles for the distribution of the amount dispensed.

**Multivariate analysis**

In the multivariate analysis that examined the permanence score in the quartiles of the distribution of

units dispensed per inhabitant as the dependent variable and included the following covariates: a) Permanence score in the quartiles of the distribution of value per dispensed unit; b) Average population over the period; c) Average GDP per capita 2010 - 2016, at current prices; d) IPDM - Health average 2010 – 2016; e) IPDM - Income, Employment, and Agricultural Production average 2010 – 2016; and f) IPDM - Education average 2010 – 2016.

A second model was conducted with the permanence score in the quartiles of the distribution of value dispensed per inhabitant as the dependent variable, and it included the following covariate: a) Permanence score in the quartiles of the distribution of the number of units dispensed per inhabitant; b) Average population over the period; c) Average GDP per capita 2010 - 2016, at current prices; d) IPDM - Health average 2010 – 2016; e) IPDM - Income, Employment, and Agricultural Production average 2010 – 2016; and f) IPDM - Education average 2010 – 2016.

### Ethical aspects

The present study did not analyse patient data; therefore, considering the current legislation, it was not necessary to submit the research to the Ethics Committee for Research in Humans.

## RESULTS

Paraná, with a population of approximately 11.4 million, ranks fifth in terms of population in Brazil, behind only São Paulo, Rio de Janeiro, Minas Gerais, and Bahia (IPARDES, 2022). The average per capita household income in 2018 was BRL 1,557.00, including salaries, pensions, social transfers, rentals, among other sources. This amount is 6.4% higher than the national average (BRL 1,337.00), placing the state in sixth position among the federative units, following the Federal District, São Paulo, Rio Grande do Sul, Rio de Janeiro, and Santa Catarina (IPARDES, 2022). The income distribution shows significant asymmetry, with the wealthiest 1% concentrating 10.2% of the total income, while the poorest 20% hold only 4.2% of the wealth.

Table II shows the total number of CEAF and CL medication units dispensed in the state of Paraná and the number of units dispensed per inhabitant, per year, from 2010 to 2019. In 2010, the population of Paraná was 10,439,601, while in the year 2019, the population of Paraná estimated by the IBGE was 11,433,957. Over this period, there is a consistent increase in both the total number of dispensed units and per capita medication units. In 2010, 47,902,251 units were dispensed, corresponding to 4.59 units per inhabitant. The figures steadily rise each subsequent year, reaching 162,181,021 dispensed units in 2019, with an average of 14.18 units per inhabitant. This data indicates a notable growth in the consumption of medication units over the specified timeframe.

**TABLE II -** Number of CEAF and CL medication unit dispensed in Paraná (2010-2019)

| Year | Number of dispensed units | Number of medication units dispensed per inhabitant |
|---|---|---|
| 2010 | 47,902,251 | 4.59 |
| 2011 | 54,576,574 | 5.19 |
| 2012 | 65,045,643 | 6.15 |
| 2013 | 73,850,783 | 6.72 |
| 2014 | 86,024,390 | 7.76 |
| 2015 | 95,366,670 | 8.54 |
| 2016 | 109,901,083 | 9.78 |
| 2017 | 127,923,793 | 11.30 |
| 2018 | 143,856,192 | 12.68 |
| 2019 | 162,181,021 | 14.18 |

Note: CEAF, specialized component of pharmaceutical services; CL, complementary list.

Table III describes the financial value of CEAF and CL medications dispensed in the state of Paraná during the study years, as well as the amount dispensed per inhabitant. From 2010 to the 2019, the financial values exhibit a noticeable upward trend. The financial figures surge from 214 million BRL in 2010 to BRL 476 million in 2019, reflecting a significant growth trajectory.

**TABLE III -** Financial value of CEAF and CL drugs dispensed in Paraná (2010-2019)

| Year | Financial value (BRL) | Financial value per inhabitant (BRL) |
|---|---|---|
| 2010 | 214,341,868,83 | 20.53 |
| 2011 | 233,496,928,95 | 22.21 |
| 2012 | 271,539,646,77 | 25.67 |
| 2013 | 291,422,932.94 | 26.50 |
| 2014 | 328,365,386.41 | 29.63 |
| 2015 | 357,778,015.37 | 32.05 |
| 2016 | 452,131,222.28 | 40.22 |
| 2017 | 452,898,702.26 | 40.01 |
| 2018 | 436,010,702.39 | 38.42 |
| 2019 | 476,097,944.73 | 41.64 |

Note: CEAF, specialized component of pharmaceutical services; CL, complementary list.

Table IV presents the annual average cost per medication unit dispensed each year from 2010 to 2019, revealing a fluctuating pattern in the data. The initial cost in 2010 was BRL 4.47. Over the subsequent years, there were variations, with the cost reaching its lowest point at BRL 2.94 in 2019. The analysis indicates a discernible downward trend in the average cost per medicine unit over the period from 2010 to 2019, ultimately settling at BRL 2.94 in 2019.

**TABLE IV -** Average cost (BRL) per medication unit dispensed (2010-2019)

| Year | Average cost (BRL) per medication unit dispensed |
|---|---|
| 2010 | 4.47 |
| 2011 | 4.28 |
| 2012 | 4.17 |
| 2013 | 3.95 |
| 2014 | 3.82 |
| 2015 | 3.75 |
| 2016 | 4.11 |
| 2017 | 3.54 |
| 2018 | 3.03 |
| 2019 | 2.94 |

Figure 1 illustrate the quartile distribution of the scores used to determine the categorization within quartiles. This classification is based on the distribution of the number of medication units per inhabitant, financial value per inhabitant, and average cost of medication units from 2010 to 2019. Municipalities falling within the 1st quartile dispensed the fewest medication units over the course of these 10 years. In contrast, municipalities in the 4th quartile were the highest dispensers in terms of the number of medication units. This categorization provides valuable insights into the distribution patterns and variations among municipalities in terms of their medication dispensing practices over the specified decade (Tables S1, S2, and S3, supplementary material).

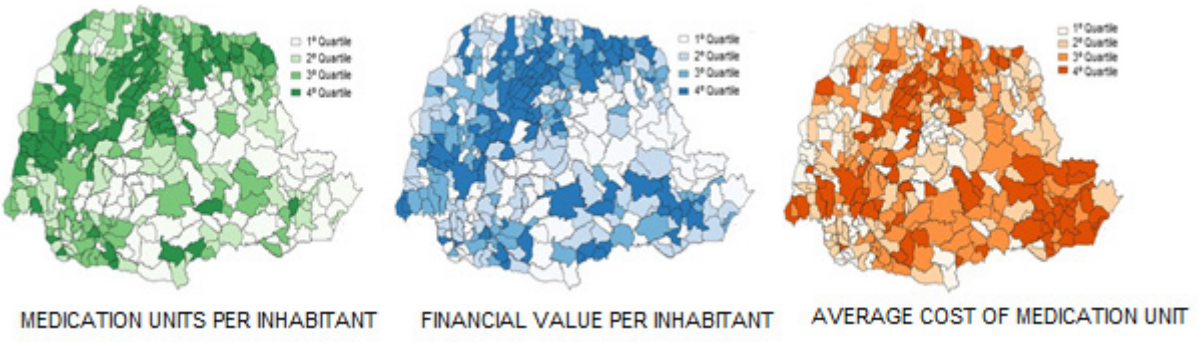


**FIGURE I -** Quartile distribution of the score used to identify the permanence of the municipality in the distribution quartiles.
Legend: Upper limit of the 1st quartile: 16; Upper limit of the 2nd quartile: 25; Upper limit of the 3rd quartile: 33; Upper limit of the 4th quartile: 40.

The highlighted values indicate the upper limits of quartiles, providing information on the distribution of average costs (in BRL) per medication unit over the years from 2010 to 2019. The first quartile, representing the point above which 25% of the data is located, ranges from 2.66 in 2010 to 1.78 in 2019. The second quartile, where the median (50% of the data) is situated, fluctuates from 3.64 in 2010 to 2.18 in 2019. The third quartile, indicating the value above which 75% of the data is distributed, varies from 4.78 in 2010 to 2.89 in 2019. Finally, the fourth quartile, covering the range between 75% and 100% of the data, ranges from 14.78 in 2010 to 9.15 in 2019.

## Multivariate analysis

An $R^2$ of 0.577 and a Durbin-Watson value of 2.041 were obtained, as shown in Table V. In the multivariate analysis, the variables "average population over the period" and "average GDP per capita 2010-2016" had a non-significant p-value ($p>0.05$), indicating no association with the dependent variable analyzed. Associations were observed with the variables "permanence score in the quartiles of the distribution of value per dispensed unit," "IPDM – Health average 2010-2016," "IPDM - Income, Employment, and Agricultural Production average 2010 – 2016," and "IPDM - Education average 2010 – 2016." "IPDM - Education average 2010 – 2016" was the variable that showed the strongest association.

**TABLE V -** Multivariate analysis with permanence score in the quartiles of the distribution of the number of units dispensed per inhabitant as the dependent variable

| Independent Variable | Beta adjusted | p-value | 95% CI | VIF |
|---|---|---|---|---|
| Score of permanence in the quartiles of the distribution of the value per dispensed unit | 0.198 | <0.001 | -0.298: -0.119 | 1.111 |
| Average population over the period | 0.060 | 0.204 | $2x10^{-6}$ : $1.4x10^{-5}$ | 1.288 |
| Average GDP per capita 2010 - 2016, at current prices | 0.025 | 0.619 | $-2.2 \times 10^{-5}$ :$1.2x10^{-4}$ | 1.503 |
| IPDM - Health average 2010 – 2016 | 0.144 | 0.002 | 5.521: 25.534 | 1.312 |
| IPDM - Income, Employment, and Agricultural Production average 2010 – 2016 | 0.128 | 0.024 | 1.952: 26.887 | 1.875 |
| IPDM - Education average 2010 – 2016 | 0.405 | <0.001 | 26.501: 43.0085 | 1.418 |

Note: Beta represents the standardized coefficients, p-value indicates the statistical significance, CI 95% is the confidence interval, and VIF is the variance inflation factor.

An $R^2$ of 0.464 and a Durbin-Watson statistic of 1.936 were obtained, as shown in Table VI. A correlation was observed between the "permanence score in the quartiles of the distribution of the value per dispensed unit", "IPDM – Health average 2010-2016," "IPDM - Income, Employment, and Agricultural Production average 2010 – 2016," and "IPDM - Education average 2010 – 2016." Once again, "IPDM - Education average 2010 – 2016" was the variable that showed the strongest association. The variables "average population over the period" and "average GDP per capita 2010-2016" once again had a non-significant p-value (p>0.05).

**TABLE VI -** Multivariate analysis with permanence score in the quartiles of the distribution of the value dispensed per inhabitant as the dependent variable

| Independent Variable | Beta adjusted | p-value | 95% CI | VIF |
|---|---|---|---|---|
| Score of permanence in the quartiles of the distribution of the value dispensed per inhabitant | 0.465 | <0.001 | 0.417: 0.582 | 1.111 |
| Average population over the period | 0.013 | 0.759 | $-7x10^{-6}$: $9x10^{-6}$ | 1.288 |
| Average GDP per capita 2010 - 2016, at current prices | 0.010 | 0.833 | $-6.3x10^{-5}$: $7.8x10^{-5}$ | 1.510 |
| IPDM - Health average 2010 – 2016 | 0.163 | <0.001 | 8.803: 27.115 | 1.312 |
| IPDM - Income, Employment, and Agricultural Production average 2010 – 2016 | 0.109 | 0.032 | 1.074: 23.939 | 1.875 |
| IPDM - Education average 2010 – 2016 | 0.349 | <0.001 | 23.046: 38.253 | 1.418 |

Note: Beta represents the standardized coefficients, p-value indicates the statistical significance, CI 95% is the confidence interval, and VIF is the variance inflation factor.

## DISCUSSION

Throughout this study, expressive growth was evidenced over the 10 years analysed in the amount of medication dispensed and the increase in expenses. In the period from 2010 to 2019, the total number of medication units dispensed through CEAF and CL in Paraná increased from 47 million units in 2010 to around 162 million units in 2019, indicating an increase greater than 330%. In this same period, the growth of the population of Paraná was 9%. The number of medication units dispensed per inhabitant increased in the same proportion, jumping from 4.59 to 14.18 units per inhabitant, tripling the number of units dispensed per inhabitant.

A factor that contributed to the increase in the number of units dispensed was the increase in medications incorporated within the scope of the SUS. An analysis of the evaluations made by the Commission for the Adoption of Technologies by the SUS (Conitec) between 2012 and 2019 shows that the disincorporation of medicines was much lower in relation to their incorporation, revealing an increase in the offer of these technologies in the SUS. In this period there were 191 recommendations for incorporation and only 40 for exclusion (Conitec, 2022).

Within the scope of the CEAF, it was observed that from 2010 to 2018, the number of drugs increased by 27%, going from 110 to 140, and the number of pharmaceutical presentations grew by 10%, jumping from 229 to 251, in the same period. Thus, in this period, the additional offer in 2018 was 30 drugs and 22 presentations, which reveals the increase in the number of drugs made available to the population through the SUS. In this same period, there was also an increase in the number of clinical conditions treated through the CEAF (Brasil, 2018).

Analysis of pharmaceutical expenditures verified that the increase was not proportional to the amount dispensed. In the analysed period, the amount dispensed increased 2.2 times, from BRL 214 million to BRL 476 million, and from BRL 20 to BRL 41 per inhabitant. In comparison with another state, Aguiar *et al.* (2020)

identified that Goiás spent BRL 423 million in three years, from 2016 to 2018, with the population of Goiás in 2018 being 6.9 million (Aguiar *et al*., 2020).

It is possible to verify that in the period from 2010 to 2016, the expenditure on medicines showed an average growth of 13% per year. In 2017, although there was an increase in the number of units dispensed (16.3%), the expense was similar to that in the previous year (BRL 452 million). In 2018, there was a slight drop of approximately 4%, and in 2019 the expense rose again with an increase of 40 million compared to the previous year, reaching the level of BRL 476 million. This growth was also observed by the Ministry of Health, which spent BRL 6.61 billion on CEAF medicines in 2019, while in 2018 it had spent BRL 6.04 billion (INESC, 2020).

The fact that there was no increase in expenditure in 2017, although there was an increase in the amount dispensed by more than 16%, may be due to the centralization of the acquisition of some medicines by the Ministry of Health, which until then were financed through transfers to the states. Among the drugs that in 2017 migrated to group 1A are products for which the difficulty of acquisition resulted in shortages and others whose purchase on a scale could generate significant savings for the public system. This rationalization of the purchasing process may have contributed to the drop in expenditures on the CEAF in recent times (INESC, 2019).

Regarding the results presented about the average cost per medication unit, it is possible to observe a decrease in cost from 2010 to 2019, from BRL 4.47 to BRL 2.94, a reduction of almost 35%. Here, it is important to point out that the average cost per dispensed medication unit includes the drugs available at the CEAF and CL of the Paraná State Health Secretariat. Probably, if the same analysis were performed with only CEAF drugs, the average cost per pharmaceutical unit would be higher.

Several factors contribute to the variation in the average cost of the medication unit, as incorporation of new drugs and the high value of these drugs, and changes in treatments that replace the use of cheaper drugs for more expensive ones. On the other hand, patent expirations, the increase in generic, and cheaper drugs and the reduction in the prices of drugs already available contribute to the reduction of this cost.

Between 2010 and 2019, new drugs made available by CEAF were incorporated, which could lead to an increase in the average cost of the medication unit. In general, the profile of incorporated drugs shows that they are newer products, with a single supplier in the country and, protected by patents, are under the monopoly of manufacturers, who abuse prices (CMAP, 2020; INESC, 2020). It should be noted that the incorporation of new medicines has been identified as an important driver for the increase in spending on medicines in countries around the world (Vieira, 2021).

It was possible to verify the difference in the amount dispensed and spent per inhabitant among the 399 municipalities in the state, which may reflect the difference in the population's access to CEAF medicines. Access to medicines in Brazil through the SUS involves problems related to the incorporation and supply of new medicines through the system but mainly with the difficulties faced by users accessing medicines already covered.

Although access to medicines through the SUS is universal, equitable, and free for all Brazilian citizens, in practice this is not yet a reality, as inequalities in access to medicines between regions of Brazil are visible. Regional differences in the organization, structuring and financing of services have an impact on the pharmaceutical services provided (Oliveira, Nascimento, Lima, 2019).

In Paraná, the majority of the population resides in households with a monthly per capita income ranging from more than ½ to 2 minimum wages. The two income brackets within this range represented, in 2018, 61.9% of the state's population. According to IBGE data, more than half (53.8%) of Paraná residents aged 25 or older did not complete high school. This group is distributed as follows: 5.9% have no formal education, 34.6% fall into the group of adults with incomplete primary education, 9.0% have completed primary education, and 4.3% have incomplete high school. On the other hand, those with completed high school represent 24.9%, surpassing the percentages of Paraná residents with incomplete (3.4%) and completed (17.9%) higher education (Paraná, 2020).

The economy of Paraná stands out for its diversification. According to IPARDES (2021), the Gross Domestic Product (GDP) of the state reached BRL 466.37 billion in 2019, corresponding to 6.31% of

the national GDP. The trade and services sector have significant weight, contributing 51.89% to the total goods and services produced in the mentioned year. Next is the industry sector (26.08%) and agriculture (8.47%). It is also worth noting the share of 13.57% related to taxes in Paraná (IPARDES, 2021). Paraná is one of the fastest-growing states in Brazil due to its intense industrialization, standing out as a major job generator. However, it is observed that development does not occur equitably, resulting in social inequalities, especially in access to basic services and economic opportunities, varying among different municipalities and regions.

In a study conducted by Rover *et al.* (2021), who analysed inequalities in the organization and results of access to high-cost medicines between Brazilian states, it was found that the analysed states presented differences in the indicators IDHM, IDSUS and GDP, which coincided with the data on the indicators of access to medicines and health services. The states with the highest GDP, IDHM and IDSUS (South and Southeast) also had greater access to medicines (Rover *et al.*, 2021). In this study, the IPDM - Education was the variable that showed the highest correlation with the score for permanence in the quartiles of the distribution of units dispensed per inhabitant and the score for permanence in the quartiles for the distribution of the amount dispensed per inhabitant.

In 2017, Almeida *et al.* carried out a systematic review that evaluated the socioeconomic determinants of access to health services by the elderly and demonstrated that there is a greater access problem among elderly people with lower income and education, varying to a greater or lesser extent according to the country and type of service used.

Education can exert an important influence on access to and use of health services. People with higher education tend to find it easier to recognize a health need and seek care (Almeida *et al.*, 2017). The literature has pointed out that people with greater purchasing power and higher education use health services more in general and receive more medical care, generating possible situations of inequity (Dilélio *et al.*, 2014; Dias *et al.*, 2016).

The greater use of health services by people with higher education was also observed in an international study, which described the relationship between educational inequalities and the use of health services by people aged 50 years or older, residing in 12 European countries. In this study, the presence of substantial educational inequality in the use of services was confirmed; those with a higher level of education have greater resources, whether cognitive, communicative and/or relational, which contribute to the autonomy of choices and decisions in health. However, the institutional organization can modify the inequality relationship due to lower schooling (Dias *et al.*, 2016).

According to Arruda, Mathias, Marcon (2017), schooling is a predictor of the use of health services, because it is associated with the level of knowledge about health and the adoption of healthier behaviors. The level of education implies, in addition to knowledge and the adoption of self-care actions, the occupational situation and working conditions (Arruda, Mathias, Marcon, 2017). In a study that evaluated access and adherence to CEAF medications in a city in Rio Grande do Sul, a significantly higher prevalence of adherence was identified in users with higher education and income (Fritzen, Motter, Paniz, 2017).

For most of the clinical conditions attended at the CEAF, the evaluation, treatment and follow-up of the user take place in a service of medium or high complexity. On many occasions, users are unable to receive medication from the CEAF due to difficulties in accessing specialized consultations and tests that confirm the diagnosis (Brasil, 2014). However, no association was identified between the number of specialist physicians and the permanence scores in the quartiles of the distribution of the number of units dispensed per inhabitant and in the quartiles of the distribution of the amount dispensed per inhabitant.

In a survey carried out in Santa Catarina, which aimed to analyse the perception of users, physicians, and pharmacists about the Specialized Pharmaceutical Care Component, it was observed that according to the interviewees, the procedures, such as consultations with specialists and exams, contained in the protocols (criteria diagnostic tools and mechanisms for clinical monitoring), are still not guaranteed to all who need it. Also, in this study, the authors mention that the provision and organization of health services contrast with the requirements established by the CEAF, creating

difficulties in accessing medication and/or monitoring treatments (Rover *et al.*, 2016).

Although this study has shown differences in the use of CEAF and CL medications between municipalities in the state, no factor that has a strong association with the consumption of these medications was identified. More in-depth studies are needed to elucidate the possible causes that impact consumption and expenses with these drugs. Considering the different clinical conditions and number of medications included in the CEAF, a detailed analysis, by CPTG and medication, may help to understand the results found and contribute to the construction of strategies, to reorient state public policies to expand and equalize access to this important group of medicines made available by the SUS.

### International context on access to medicines for chronic degenerative and rare diseases

In Europe, universal health coverage is still not a reality, thus there remains a significant need to address equity in access to medications for people living with rare diseases. Despite considerable advances in both healthcare and research, it is imperative to implement additional actions to ensure that these individuals receive a standard of healthcare that is equitable, safe, and high quality, aligned with the overarching goal of ensuring adequate access to medications (Tumienė, Juozapavičiūtė, Andriukaitis, 2024).

In Russia, access to medications varies for in-patients and out-patients. While in-patients have almost total coverage under Compulsory Medical Insurance, out-patients need to purchase medications unless they belong to eligible groups entitled to receive them for free, determined by socioeconomic factors such as war veterans, disabled individuals, and children up to 3 years old. For patients with rare and oncological diseases, the treatment is considered outpatient and is only covered by the state for eligible patients. Access to medications in Russia is more determined and influenced by institutional actors than by the daily routines of patients, doctors, and communities (Temina, Zvonareva, Horstman, 2023).

Medications for the treatment of rare diseases are expensive and contribute to the overall increase in healthcare costs. In the United States, the healthcare system is a mixed one, encompassing both public and private sectors, with eligibility often tied to socioeconomic factors. This system is characterized by notable challenges related to costs, access, and coverage. The FDA associates these medications with higher prices, leading to significant out-of-pocket expenses for patients (Althobaiti *et al*., 2023).

The National Reimbursement Drugs List in China aims to guide which medications will be reimbursed by the healthcare system, covering partial or full costs to facilitate access to treatments. The inclusion of medications intended for the treatment of rare diseases has been positive in improving access. However, challenges persist, especially due to socioeconomic factors that affect the availability and financial accessibility of these medications for patients with rare diseases. Therefore, additional adjustments in Chinese healthcare policies are necessary to enhance care for patients with rare diseases (Wang *et al*., 2023).

This study had some limitations. The indicators used in the statistical analysis do not include all the years analysed; however, they are the indicators that were available at the time of the analysis. In addition, it was considered that the prevalence of diseases whose treatments are contemplated in CEAF has a homogeneous distribution throughout the state of Paraná; however, this assumption may not be true, as potential differences would not influence the results of the analysis and, finally, the period from 2010 to 2019 was considered in the study to avoid potential interference from the pandemic situation in the analysis of the years 2020 to 2022.

## CONCLUSION

Understanding and addressing socioeconomic factors is crucial to promoting equitable access to medications, contributing to a more comprehensive improvement in the health of the population.

From variables medication units per inhabitant, financial value per inhabitant, and average cost of medication units, relevant differences were observed in the number of medication units dispensed and in expenditures per inhabitant among the 399 municipalities in the state.

The socioeconomical factors such as income, education, and health addressed by IPDM, which showed a significant correlation, being the variables that showed the greatest association with the dispensing of CEAF medications. Overall, it is essential to promote health education for users and readjust public policies to reduce inequalities in the use of medications from the specialized pharmaceutical assistance component.

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