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Prevalence of medicine use among Brazilian adults: a systematic review

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Abstract *The use of medicine in adults has been assessed by some population-based studies in Brazil, but to date there has been no overall estimate of the prevalence of drug consumption. We therefore aimed to estimate the prevalence of medicine use as measured in previously reported cross-sectional studies among Brazilian adults. We conducted a systematic review of the literature, searching in MEDLINE, Embase among others to a date ending January 2017. Two researchers selected the studies, extracted data and assessed methodological quality of those chosen for inclusion. The consumption prevalence were combined in meta-analyses, the heterogeneity measured by I^2 and investigated by subgroup analyses and meta-regression. The search identified 4,005 publications, of which 14 were ultimately included in the study. Most studies (12/14) measured the consumption over the previous 15 days, finding a consumption prevalence of 49.1% (95% CI: 48.5-49.6%, $I^2 = 100\%$). The recall period explains part of the heterogeneity found ($R^2 = 23\%$, $p = 0.048$), however the subgroup analysis did not allow for more homogeneous results. The use of medications occurs among almost half of all Brazilian adults. Appropriate pharmaceutical assistance and care are necessary to ensure the rational use of these technologies.*

Key words *Drug utilization, Cross-sectional studies, Review, Adult, Brazil*

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Introduction

Medicines play an important role in the delivery of care and in the impact on health. Therefore, issues of access and quality of consumption in Brazil have been at the center of several public policies over the years[1-4]. The improvement of pharmaceutical services has also been one of the millennium goals as a commitment to guarantee the right to health[5], highlighting the relevance of access to these technologies by the population.

Increased access to medicines is a benefit that carries inherent risks, such as adverse reactions and medication errors, generating more public spending on health[6,7]. Drug use studies can be useful tools in the development of strategies that favor proper and continuous consumption and access[8].

A review of drug use studies conducted in Brazil found that the analysis of the consumption pattern of these technologies and the profile of this consumption is the most common objective among surveys that draw mostly on population-based data[9,10].

Data regarding availability and access, required for the study of drug use, may also come from computerized systems[11]. Although these digital resources can offer a practical way of obtaining prescription data and consumption patterns, such systems are still not common in many countries including Brazil[12,13].

While the use of drugs in adults has been evaluated by some population-based studies in Brazil, summaries of the prevalence of drug consumption obtained in these studies have yet to be recorded.

The objective of the present study was to estimate the prevalence of drug use in adults in Brazil through a systematic review of cross-sectional population-based studies.

Methods

Outline and protocol recording

This is a systematic literature review, whose protocol was recorded in the International Prospective Register of Systematic Reviews (PROSPERO).

Eligibility criteria

We selected cross-sectional population-based studies that evaluated the prevalence of medicine use in adults (≥ 18 years) living in Brazil. Other delineations were not eligible due to the low external validity of studies lacking population representativeness.

Studies limited to the consumption of drugs in a particular class of medications, specific diseases or other special conditions were excluded, as well as those that restricted the research to the elderly or children, in order to ensure the population representativeness concerning consumption.

Information sources

We searched the Medline, Embase, Scopus, Latin American and Caribbean Health Sciences Center (Lilacs), Scientific Eletronic Library Online (SciELO) and Bank of Thesis of the Coordination of Improvement of Higher Education Personnel (CAPES) databases. The microdata of national surveys were also researched through contact with experts and surveys on institutional websites. (Last update was on 1/17/2017.) There was no restriction regarding language or date of publication in the search.

Search strategy

Search strategy on Medline (via PubMed) was: ("Drug Utilization"[TIAB] OR "Drug Utilizations"[TIAB] OR "Drug Utilization"[Mesh] OR "Pharmacoepidemiology"[Mesh] OR "Pharmacoepidemiology"[TIAB] OR "Pharmaceutical Epidemiology"[TIAB]) OR (("Health Surveys"[Mesh] OR "Surveys"[TIAB] OR "Survey"[TIAB] OR "Cross-Sectional Studies"[Mesh] OR "Prevalence"[TIAB] OR "Frequency"[TIAB]) AND ("Pharmacology"[TIAB] OR "Drug"[TIAB] OR "Drugs"[TIAB] OR "Medicine"[TIAB] OR "Remedy"[TIAB] OR "Medication"[TIAB])) AND ("Brazil"[Mesh] OR "Brazil"[TIAB] OR "Brasil"[TIAB]) AND ("Population"[Mesh] OR "Population" [TIAB] OR "Populations" [TIAB] OR "population-based study"[TIAB]). We adapted this strategy to the other bibliographic sources.

Study selection

Two researchers performed the selection (VPG, EBA) by screening the titles and abstracts. In cases of conflict, a third reviewer (TFG) took the decision. The selected articles were then analyzed in full text for quality assessment and data extraction. This step was performed in the Covidence system (www.covidence.org). The re-

viewers were not blind to the authorship of the manuscripts.

Extraction of data

Data were extracted by one author (VPG) and confirmed by another (TFG). The following variables were extracted: year of survey, location, sample type, age group, sample size, recall period, prevalence of drug use and type of drug evaluation. (In cases where information was not available or unclear, we contacted the authors.) From the studies that employed statistical models, we extracted factors positively associated with consumption and variables. The information needed to measure the consumption of drugs was extracted from adults between the ages of 18 and 65, when possible, or in the closest age group.

Quality assessment

For the assessment of quality we adapted the tool standardized by Loney et al.[14]. Nine items were evaluated: (i) Adequate sampling (probabilistic sampling or universe), (ii) Source of the sample list (census of the Brazilian Institute of Geography and Statistics [IBGE]), (iii) Size of adequate sample (statistically calculated) , (iv) Adequate measurement of outcome (confirmation of medical prescription and/or packaging of medication), (v) Recall period (up to 15 days) 14, (vi) Unbiased raters (trained interviewers), (vii) Adequate response rate (refusals and attrition of up to 70%), (viii) Presentation of results (prevalence with confidence intervals and relevant subgroups), (ix) Participants similar to the study (adults only included in sample). For each item that met the criteria, the study received a point.

Data analysis

Initially the local populations were obtained from the period in which each study was performed according to the IBGE[15] census, then the meta-analysis of the prevalence of medication consumption was calculated by means of the Freeman-Tukey double-arcosene transformation to stabilize the variances[16].

The prevalence was stratified by the recall period and heterogeneity was estimated using the inverse of the variance to calculate I^2 and chi-square ($p < 0.10$).

To verify the possible causes of heterogeneity we performed meta-regression and sensitivity analysis.

In the meta-regression by the modified Knapp-Hartung method[17] the effect of the variables (recall period, proportion of women, quality score, minimum age and year of research) was investigated in the variability observed among the prevalence studies. Surveys with discrepant results were excluded to verify their influence on the result.

In the subgroup analysis, only those studies with similar characteristics were included in the meta-analysis: recall period less than or equal to 15 days, research performed after year 2000, quality score = 9 and southeast region. Stata software version 14.1 was used for all analyzes.

Results

Selection of studies

In the literature review, 4,005 publications were retrieved, of which 37 were evaluated in full text. In the end, 14 studies[18-31] were judged to be worthy of inclusion, which in total involved the assessment of some 57,700 adults (Figure 1).

Study characteristics

Of the 14 articles included, nine collected data from the year 2000[23-31] and seven occurred in the southeast region[18,19,22,24,27,28,30]. All studies used probabilistic sampling based on the IBGE census. The recall period ranged from three to 90 days prior to the interview. Confirmation of the name of the drug occurred in half of the studies through the package or prescription (Table 1).

Quality assessment

Six studies met all criteria for methodological quality[23,24,27-30] as described in Table 1. With the exception of one study involving only adults aged 18-65 years[29], the others involved the elderly[18-28,30,31] and / or children[18-21,24,25,28] (Table 1). It was possible to obtain data on drug consumption of adults aged 18 years or older in 13 studies[18-20,22-31]. One survey did not report data from adults separately from those of children; For the purpose of calculations, we separated out participants over 12 years of age[21].

One study measured the use of medications for continuous use for chronic diseases without mentioning the recall period, and for drugs of occasional use the period measured was the previous 15 days[31]. In the present analysis, we there-

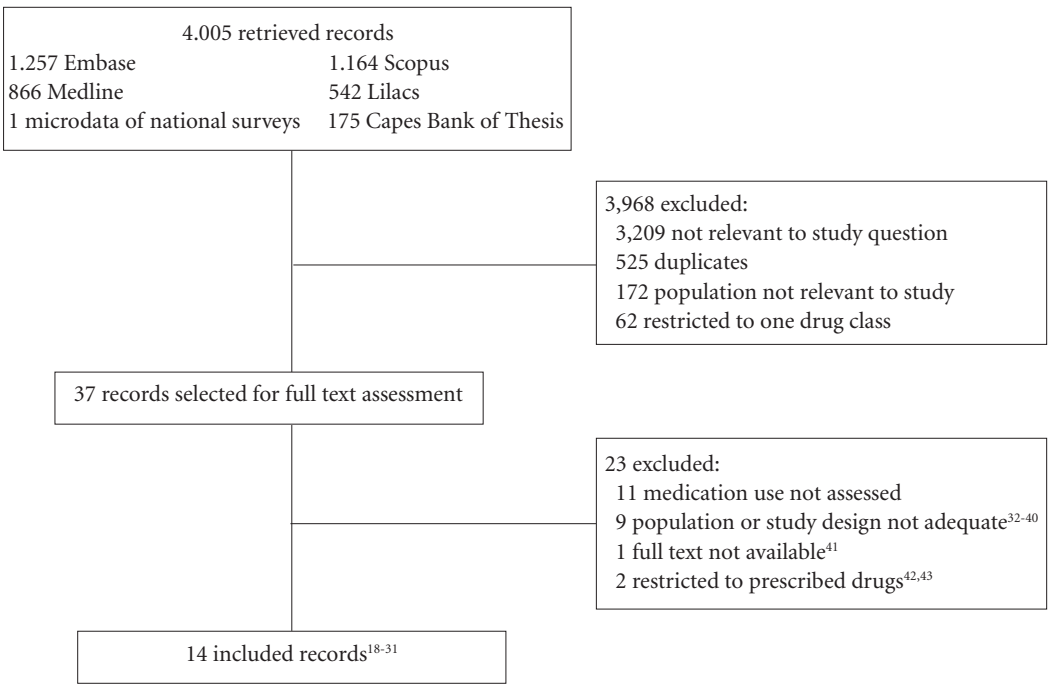

Figure 1. Process of search, selection and inclusion of studies

fore consider 15 days as the study recall period, with the interpretation that continuous use was also involved during the period.

Outcomes

Most of the studies (12) evaluated the consumption in the last 15 days prior to the interview, and the use of drugs was reported by 49.1%[18-20,23-31] The highest prevalence of drug consumption was 71.4% recalling the previous 90 days[22], followed by the prevalence of 70.0% in the month[21]. The prevalence in the previous week was evaluated in an investigation[29], being 35.7%; in the previous three days it was 44.7%, evaluated by four investigations[24,27,28,30]. The prevalence summary and respective confidence intervals (95% CI) are presented in the meta-analysis as a proportion, not converted to a percentage (Figure 2).

Estimates were of high heterogeneity, the subgroup analysis did not identify the possible causes for the differences between the results of the studies, nor did it lead to more homogeneous results (Table 2). The recall period explains 22.9% of the variance found ($p = 0.048$). A discrepant point was observed in the meta-regression in the study of a longer recall period (90 days)[22]. In order to ascertain the influence of this study it was excluded, and the association between the recall period and the variation between the studies lost significance. The other variables explored – year of data collection, methodological quality, proportion of women and minimum age of study participation' – were not significant ($p > 0.05$).

Among the articles included in the review, five performed adjustment models for drug consumption[22,23,25,28,29]. Among the associated factors, females were positively associated in all studies, while advanced age was associated in four of these and presence of chronic disease in three (Chart 1).

Discussion

About half of the Brazilian population has been using or has used some sort of medication in

Table 1. Characteristics of included studies.

Study	Year of research	City, Federative Unit	Sampling technique [a]	Age (adult), years [b]	Size of sampling (adult) [b]	Period, days	Type of medication assessment	Quality score
Barros 1983[b18]	1978	Ribeirão Preto, SP	Conglomerates	All (≥ 20-69)	6,988 (3,836)	15	Interview	7 [g,h]
Simões e Farache Filho 1988[19]	1985	Araraquara, SP	Conglomerates	All (≥ 20)	2,150 (1,343)	15	Interview	6 [d,f,g]
Simões 1991[20]	1987	Humaitá, AM	Systematic	All (≥ 20)	2,422 (881)	15	Interview	6 [d,f,g]
Vilarino et al. 1998[21]	1994-1995	Santa Maria, RS	Systematic and conglomerates	All (> 12)	413 (212)	30	Interview	6 [e,f,i]
Loyola Filho et al. 2002[22]	1996-1997	Bambuí, MG	Simple random	Adults (≥ 18)	1,086	90	Interview	8[e]
Bertoldi et al. 2004[23]	2002	Pelotas, RS	Systematic	Adults (≥ 18-65)	3,182 (2,790)	15	Interview, packing or prescription	9
Pelicioni 2005[24]	2001-2002	São Paulo, SP	Conglomerates and stratified	All (≥20)	3,646 (1,913)	3	Interview, packing	9
Arrais et al. 2005[25]	2002-2003	Fortaleza, CE	Stratified, census	All (20-64)	1,366 (754)	15	Interview	8[i]
Carvalho et al. 2005[26]	2003	Brasil	Stratified	Adults (18-59)	3,554 (2,930)	15	Packing	7[d,g]
Lima et al. 2008 [b27]	2001-2002	Botucatu, SP	Conglomerates and stratified	Adults (18-65)	1,023 (614)	3	Interview, packing	9
Costa et al. 2011[28]	2001-2002	Campinas, SP	Conglomerates and stratified	All (18-59)	941 (515)	3	Interview, packing	9
Galvão et al. 2014[29]	2012	Brasília, DF	Conglomerates and stratified	Adults (18-65)	2,051 (1,820)	7	Interview, packing	9
Costa et al. 2016[30]	2008	Campinas, São Paulo	Conglomerates and stratified	Adults (20-69)	2,476 (1,777)	3	Interview	9
PNAUM 2014[31]	2013-2014	Brazil	Conglomerates, stratified	Adults (18-65)	32,652 (26,633)	15	Interview, packing, prescription or leaflet	7 [g,h]

Notes: a, All the studies used the census of the Brazilian Institute of Geography and Statistics as source of sampling. b, Some data were obtained from contact with the author. c, The use of medicine for adults only in the age group considered by the study are reported in brackets. d, Unreported sample size calculation. e, Recall period greater than 15 days. f, Untrained evaluators. g, Unreported search response rate. h, Prevalence by subgroup not reported. i, Population included children and/or elderly.

recent weeks. The estimates emerging from the studies suggest great variability in the results, but nonetheless provide an approximate picture of drug use among Brazilian adults.

The recall period was the only factor significantly associated with the variability found. Large heterogeneity are indicative of the differences among the primary studies that provided the data to inform the meta-analyses. Because they are studies conducted in different periods and regions, differences between the estimated prevalence would be expected, despite being from the same population (adults) from the same country (Brazil).

High heterogeneity in prevalence studies is common[16]. Regional differences (income, access to services), outcome measures, population, year and/or period of the year in which the survey

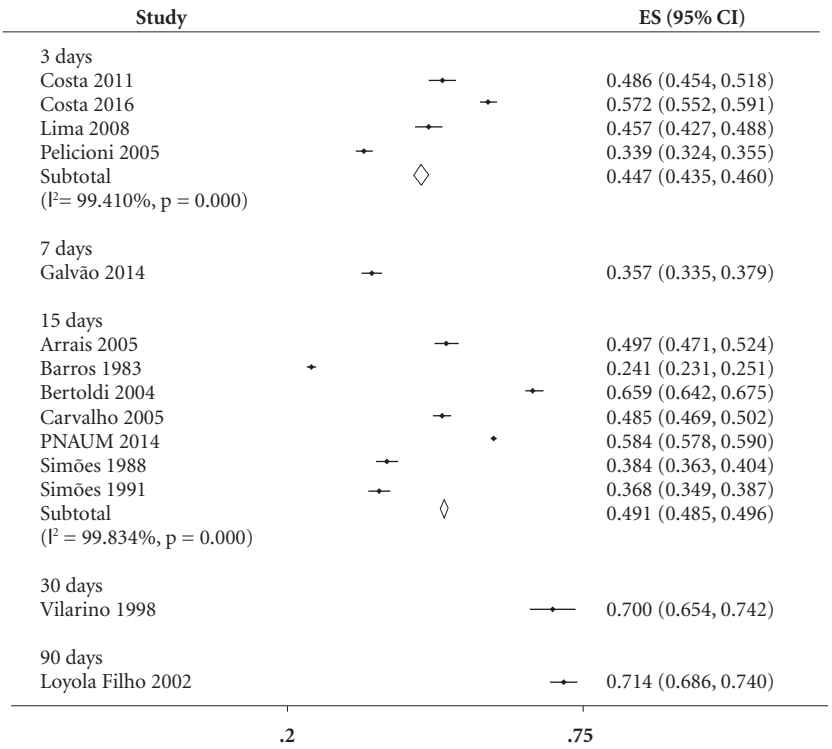

Figure 2. Prevalence of medicine consumption according to the recall period.

Table 2. Sensitivity analysis to investigate causes of heterogeneity.

Analyzed factors	Number of studies (reference)	Total of participants	Prevalence, % (95% IC)	Heterogeneity	
				I^2 (%)	p-value of Qui²
Recall period ≤ 15 days	12[18-20,23-31]	56,201	47,6 (47.2-48.1)	99.8	< 0.001
Research conducted from the year 2000	9[23-31]	44,641	54,0 (53.5-54.5)	99.4	< 0.001
Quality score = 9	6[23,24,27-30]	13,088	48,2 (47.2-49.3)	99.7	< 0.001
Southeast region	7[18,19,22,24,27,28,30]	18,310	41,2 (40.1-42.2)	99.6	< 0.001

Note: 95% IC 95, 95% confidence interval.

was conducted and rate of refusal were common causes of heterogeneity in prevalence reviews. In order to reduce and investigate heterogeneous results, we used proximal ages, categorized by similar recall period. We further evaluated the quality of the studies, analyzing separately those of higher quality – including only population-based studies – and explored the results by subgroup analysis and meta-regression[44].

The lack of methodological standardization and categorization of the age range of the included studies may have been some of the factors responsible for the high heterogeneity. Some recommendations such as a 15-day recall period,

Chart 1. Factors associated with medication consumption

Study	Statistical adjustment model	Variables of the model	Factors positively associated with medicine consumption
Loyola Filho et al. 2002[22]	Multinomial logistic regression adjusted for confounding variables.	Sex, age, number of residents and the following data in the last 12 months: number of medical consultations, consultation to the pharmacist and monetary expenses on medicines.	Female, age 18-39 years, and consult the pharmacist in the last 12 months.
Bertoldi et al. 2004[23]	Poisson regression adjusted with variables that remained significant p value between 5 and 20%	Age, schooling, economic status, current marital status, smoking, low physical activity, BMI and self-perception of health.	Female gender, advanced age, higher economic level, smokers and ex-smokers, low physical activity and poor self-perception of health.
Arrais et al. 2005[25]	Poisson regression adjusted by hierarchical model	Monthly family income, schooling, occupation, sex, age, marital status, number of residents at home, chronic diseases, health insurance, consultation in the last 3 months, hospitalization in the last 12 months and self-perception of health.	Female gender, advanced age, monthly family income greater than 3 minimum wages, schooling greater than 8 years, chronic diseases, health plan, consultations in the last 3 months.
Costa et al. 2011[28]	Poisson regression adjusted by sex and age	Sex, age, number of chronic diseases and morbidity in the last 15 days.	Female gender, advanced age, chronic disease, income from 4 minimum wages and morbidity in the last 15 days.
Galvão et al. 2014[29]	Poisson regression with robust variance adjusted by hierarchical model	Economic level, schooling, occupation, sex, age, marital status, number of residents per household, chronic self-reported diseases, access to medical care, self-perception of health status.	Female, advanced age, chronic illness, unemployed or retired, pain or discomfort, problems with self-care and consultations in the last 3 months.

Notes: articles that did not present adjustment models specifically for drug consumption: Barros 1983[18], Simões & Farache Filho 1988[19], Simões 1991[20], Vilarino et al. 1998[21], Pelicioni 2005[24], Costa et al. 2016[30], PNAUM[31].

categorization of age groups (children, adults, and the elderly) are proposed in the study area of medication use[29]. Such guidelines favor the measurement of the data and help in monitoring the drug use. Other important data, like the proportion of people with chronic diseases and the main drugs involved, would aid in the evaluation and explanation of the results, but were not systematically reported in the studies.

In spite of the heterogeneity found, the considerable proportion of the population that uses drugs underscores the importance that this consumption be accompanied by the necessary information for its rational use. Guidelines made by the pharmaceutical professional can minimize problems related to the use of medication and promote the quality, safety and efficacy of the drug through pharmaceutical care[45,46].

In addition to these aspects of the included studies, the present study has as a limitation the non-inclusion of primary data directly from health systems such as the National System of Controlled Products Management (SNGPC) and others from the Unified Health System (SUS), such as the National Pharmaceutical Services Management System (Horus), SUS electronic systems (e-SUS) and Outpatient Information System of the National Health System (SIA/SUS). On the other hand, it was sensitive and robust as far as it included studies published with population representativeness, bringing to light national estimates of drug consumption in the population. The results presented here therefore provide information about the general use of these technologies in the Brazilian population, allowing insight into its general scope and comparability with other contexts.

Of the factors associated with drug consumption, female sex stood out most significantly, supporting the findings of other countries[47-49]. The search for health care services is higher among women, with the concomitant effect of greater prescription and use of medicines among that demographic[49,50]. A survey of five community pharmacies randomly selected in northern Italy found that women are the most frequent patrons in the purchase of medications and supplements after obtaining information on the internet (30% compared to 20% of men, $p < 0.01$)[51].

Other factors that were associated were age and presence of chronic diseases. A population survey carried out in Spain in 2013 of 2,700 people observed that drug consumption increases with age and with the prevalence of chronic diseases: people over 65 years old consume about five more drugs than adults below this age[52]. The association between advanced age and the use of polypharmacy are factors that favor the occurrence of adverse reactions[53].

In Brazil, a descriptive study with data from the National Health Survey of 2013 observed that the prevalence of the use of drugs to treat chronic diseases was approximately 80% in the treatment of hypertension, diabetes and asthma[54]. The use changed according to region, sex and age. In hypertensive patients, for example, the prevalence of consumption was 82%, with greater use by women and individuals over 75 years of age[54] – a result similar to the one found in the present review in which drug use was shown to be influenced by gender, advanced age and presence of chronic diseases.

Although drug use is part of health care, it is important to emphasize that these technologies also pose risks to health, requiring their use in a rational way[55]. The consumption of medicines must be accompanied by the essential orientation for their proper use. A systematic review of clinical trials has shown that intervention through pharmaceutical care has significantly improved health-related quality of life, presenting itself as an auxiliary tool to promote well-being[56].

Medicines are the main cause of poisoning registered by Poison Control Centers (PCC) in different contexts. In the United States, about 2 million cases of exposure to toxic agents were reported in 2015, of which 1,473,638 were caused by pharmaceuticals[57]. Of the total number of drug poisonings, 275,979 (20%) were caused by therapeutic errors caused by: duplication of dose (30%), wrong product (17%), wrong dose (15%), wrong interval between doses (11%) and medication by another person (8%). In addition to causing most of the poisonings, medicines were the main responsible for deaths resulting from poisoning (1,108 cases, 80% of the total). Among the most involved were analgesics, stimulants and those acting on the cardiovascular system[57].

In Brazil, although there are no data identifying the most common class or active principle, the use of medicine has proven to be the main cause of poisoning attended by Brazilian PCC in recent years[58]. The reason for poisoning in general (drug specific data not available) is mainly individual accident (57%) and suicide attempt (16%).

An analysis of the 30-year time trend of toxicological treatment of North American PCC (1984-2013) revealed increased deaths and severity of poisoning[59]. Severity and lethality increased with exposure to a greater number of substances. During the period 2006-2013, it was observed that each additional product involved in one exposure led to an additional 221 deaths, an increase of 18% in the growth in fatalities related to consumption of three or more substances[59].

The increase in the number of poisonings per drug over the years in the United States has been accompanied by the growth of adult drug use. An analysis of the National Health and Nutrition Examination Survey surveys conducted between 1999 and 2012 noted that the prevalence of drug use in the last 30 days was 51% in the first decade, rising to 59% in the years 2011-2012[60]. This growth was statistically significant ($p < 0.001$), and the proportion of increase (around 10%) was similar to the increase in poisoning in the period[59]. Surveys included 37,959 adults in total.

Electronic health systems are tools that can provide useful information for both administrative and managerial purposes as well as patient care. Some information available on outpatient records includes laboratory results, procedures performed, diagnoses, dispensing records and the possibility of monitoring possible drug interactions[11].

In Brazil, the availability of electronic information is still limited, but enough to study the use of drugs in specific populations. The SIA/SUS[61] makes it possible to evaluate the dispensing of drugs from the Specialized Component of Pharmaceutical Care, released through the Authorization of High Complexity Procedures (APAC)[62,63]. The analysis of these data requires linkage of large databases in order to group the data of the patients who obtain the medicines

every three months. Such studies are still not frequent, but can nevertheless provide strategic information: a cohort of patients with Alzheimer's disease was elaborated from the APAC subsystem of the SIA/SUS. Developments in this cohort will enable the evaluation of the drug utilization profile through validated adherence measures, as well as patient follow-up within six months of replenishing prescription[63].

Another tool available from drug sales data is SNGPC, which contains the daily movements of drugs and substances subject to special control that are sent to the National Sanitary Surveillance Agency electronically from all pharmacies and drugstores licensed for sale[64]. From these data, an ecological study was developed that correlated the consumption of benzodiazepine anxiolytics and demographic characteristics of the regions[65]. Cities with a higher demographic density and higher concentrations of physicians had higher consumption of these drugs[65], which may be related to the higher purchasing power of the population of these cities[66], since the data used for this research were of commercial origin.

The Nordic countries (Denmark, Finland, Iceland, Norway and Sweden) have electronic systems that record all drugs dispensed and a database with potential for linkage in the follow-up of adverse reactions, routine care and the use of medicines. These systems are comprehensive in informing public and private data on the consumption of all types of drugs, not only those subject to special control[67].

In Brazil, electronic systems are fragmented, not providing complete and comprehensive information: the same patient may appear in more than one system and identifying that it is the same person is not always possible[63,65,68]. These limitations make cross-sectional population-based studies a necessity to properly assess the patterns of access and use of these technologies. A concrete example of this demand was the funding by the Ministry of Health of the National Survey on Access, Use and Promotion of the Rational Use of Medicines (PNAUM), with 41 thousand people interviewed throughout Brazil between 2013 and 2014[69].

In conclusion, the use of drugs is common among Brazilian adults and is more frequent in women. The results reported here have limitations due to differences between studies. In terms of practice, the results reveal a high demand for pharmaceutical care in society to enable the rational use of these technologies. Future investments should prioritize the development and analysis of comprehensive computer systems that provide better information regarding products and groups at greater risk.

Collaborations

VP Gomes, MT Silva and TF Galvão contributed to the design of the study, data analysis and writing of the manuscript. All have reviewed and approved the version submitted and agree to be responsible for all aspects of the work in order to ensure that issues related to the accuracy of the work are duly investigated and resolved.

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