ABSTRACT: Objective: Antidepressant use is increasing worldwide, but national data on psychotropic drug use by depressed patients in Brazil is lacking. Methodology: Between 2013 and 2014, a representative sample of urban adult individuals were asked if they had a diagnosis of chronic disease, had a medical indication for drug treatment, and were taking chronic medications at the time for each reported diagnosis. We analyzed the frequencies of reported depression and the medications related to this disease. Results: Overall, 6.1% of respondents reported depression. The prevalence increased with age — 9.5% among the elders — was higher among women (8.9%) and in the south of the country (8.9%). As a single disease, the prevalence of depression was higher among young people (17.6%). Among those with multimorbidity, the prevalence of depression rose to 25.7%. Of those who reported depression, 81.3% had medical indication for treatment and 90.3% were under treatment — this proportion was lower among young people (84.5%) and those living in the poorest region (78.6%). Antidepressants accounted for 47.2% of psychotropic drugs taken by respondents with depression, with regional differences — only 30% used antidepressants in the North. Polypharmacy was reported by 22% of those with depression and other chronic diseases. Conclusion: Depression in Brazil, is common among young adults as a single chronic disease and highly prevalent among people with chronic multimorbidity, especially the young. The treatment gap was larger among young people and in the less developed regions of the country.

INTRODUCTION

Depression is a systemic disease that can alter patients’ biorhythms (appetite and sleep), jeopardize emotional processing (feelings of hopelessness and guilt, suicidal ideation), impair cognition (memory and concentration), and cause psychomotor changes (psychomotor agitation or retardation). It is a relatively rare disease in childhood, with prevalence increasing from adolescence onward. On average, about 4.5% of the global population is affected, with a higher prevalence (5.2%) among women. With population aging, the prevalence of depression tends to increase significantly. Although depressive symptoms are associated with increased mortality, the major burden of depression is related to the impairment of functional capacity. In addition to increasing the incidence of other chronic conditions, such as cardiovascular disease and diabetes, depression decreases independence and autonomy in daily life. According to the World Health Organization, depression is one of the leading causes of years lived with disability.

Depression is commonly underdiagnosed — especially among the elderly, due to the misconception that negative moods are part of normal aging — and undertreated, due to the challenges posed by the adverse effects of antidepressants and the stigma associated with mental illness. Even so, there is a worldwide trend toward a significant increase in the prevalence of antidepressant use by the general population.

Although the psychopharmacotherapy of depression can be simple, with use of only one antidepressant controlling symptoms in the majority of cases, greater use of medicines by patients in pursuit of symptom relief is not uncommon. Medicines that are not always

RESUMO: Objetivo: O uso de antidepressivos está aumentando em todo o mundo, mas faltam dados nacionais sobre o uso de drogas psicotrópicas por pacientes deprimidos no Brasil. Metodologia: Entre 2013 e 2014, uma amostra representativa de indivíduos adultos urbanos foi questionada sobre a presença diagnóstica de doença crônica, a indicação médica para tratamento medicamentoso e o uso de medicamentos crônicos à época de cada diagnóstico relatado. Foram analisadas as frequências de depressão relatada e os medicamentos relacionados a essa doença. Resultados: No geral, 6,1% dos entrevistados relataram depressão. A prevalência aumentou com a idade (9,5% entre os idosos) e no sul do país (8,9%). Como doença única, a prevalência de depressão foi maior entre os jovens (17,6%). Entre aqueles com multimorbidade, a prevalência de depressão subiu para 25,7%. Dos que relataram depressão, 81,3% tinham indicação médica para tratamento e 90,3% estavam em tratamento — essa proporção foi menor entre os jovens (84,5%) e os que moram na região mais pobre (78,6%). Os antidepressivos representaram 47,2% dos medicamentos psicotrópicos tomados pelos entrevistados com depressão, com diferenças regionais — apenas 30% usavam antidepressivos no Norte. Polifarmácia foi relatada por 22% das pessoas com depressão e outras doenças crônicas. Conclusão: A depressão no Brasil é comum entre adultos jovens como doença crônica única e altamente prevalente entre as pessoas com multimorbidade crônica, principalmente os jovens. A lacuna de tratamento foi maior entre os jovens e nas regiões menos desenvolvidas do país.

appropriate (e.g., benzodiazepine-type anxiolytics) may lead to worsening of the condition and new symptoms, especially in older adults\textsuperscript{11}.

Until recently, national health surveys conducted in Brazil have not evaluated the use of medicines in depth, as the level of detail required by this topic would in itself take up much of the scope of any such research. The National Health Survey (PNS) in 2013 did evaluate the use of medications for several chronic diseases, including depression, but did not investigate which medications were being used\textsuperscript{12}. Few studies have assessed the use of psychotropic drugs in Brazil and, to date, none at the national scale\textsuperscript{13}.

The present study aims to provide nationwide data on the use of psychotropic drugs and other chronic medications by the Brazilian urban adult population, associating with the presence of self-reported depression and some sociodemographic characteristics.

\section*{METHODS}

The data used in the present analysis were obtained by the National Survey on Access, Use, and Promotion of the Rational Use of Medicines in Brazil (PNAUM), conducted between September 2013 and February 2014, an initiative of the Brazilian Ministry of Health\textsuperscript{14}. This was a population-based cross-sectional study with a probabilistic sample in three stages, where the first stage corresponds to the municipalities, the second stage are census tracts, and the third stage represents the households. The study population was residents in permanent private households in the urban area of the Brazilian territory. A total of 245 municipalities were included, and 41,433 people were interviewed in the 5 Brazilian geographic regions. The sample size was defined according to the estimates of access and use of drugs obtained from previous studies. Face-to-face interviews were conducted by 165 trained interviewers, and data were collected using tablets with a 3G and GPS connection. For the present study, only data from individuals aged 20 years or older (N = 32,348) were analyzed. Additional methodological details of PNAUM are described elsewhere\textsuperscript{15}.

Chronic use of medicines was investigated based on the reported reason for use, among eight directly investigated chronic non-communicable diseases (CNCDs): hypertension, diabetes, heart disease, hypercholesterolemia, stroke, pulmonary disease, arthritis/rheumatic disease, and depression. Respondents were asked whether they were on any chronic medications for each diagnosis they endorsed. The data collection instruments were developed by researchers from seven Brazilian universities, having been tested and standardized prior to implementation. Full questionnaires can be accessed on the PNAUM website (http://www.ufrgs.br/pnaum).

Point prevalence of self-reported depression and use of medications to treat depression were obtained from the following questions: “Has a doctor ever told you that you have depression?”; “Has a doctor ever told you that you should take any medication for depression?”; “Are you taking any such medication?”. Then, respondents were asked which medications they were taking for the treatment of depression and whether they had access to all of the medications they should be taking. As depression is commonly associated with other
CNCDs, it was often impossible to learn from the respondent which medications were used specifically for depression, and the drug use statistics included all medications mentioned by the respondent, in a variable that allowed identification of cases of polypharmacy (concurrent use of 5 or more medications)\textsuperscript{16}.

Medications described as being used by the self-reported depressed respondents were classified primarily as psychotropic and non-psychotropic drugs. Non-psychotropic drugs included all chronic medications reported by respondents with a diagnosis of depression, but which were being used to treat comorbidities often associated with depression. Psychotropic drugs were classified into six groups:

- those considered specific for the treatment of depression, \textit{i.e.}, antidepressants in general;
- benzodiazepines;
- hypnotics;
- antipsychotics;
- mood stabilizers;
- medicines used to treat dementia and parkinsonian syndromes (neurotropic drugs).

This classification is consistent with current guidelines for the treatment of depression and with the methodology of a previous epidemiological survey on the use of psychotropic drugs conducted in São Paulo, Brazil\textsuperscript{13,17}. To obtain supplementary data, we checked whether the psychotropic drugs endorsed by the respondents were present in the National Formulary of Essential Medicines (Rename) in force at the time of data collection\textsuperscript{18}.

The sociodemographic characteristics of interest were: sex, age group (20 to 39, young adults; 40–59, adults; 60 or over, older adults), socioeconomic level according to the Brazilian Economic Classification Criterion, stratified into classes (A/B, C, or D/E) by the Brazilian Association of Research Companies (ABEP)\textsuperscript{19}, and regions of Brazil, which also reflect the socioeconomic differences of the population (North and Northeast — poorer, less-developed regions; South and Southeast — richer, more developed regions).

Data on the multi-morbidity associated with depression, computed on the basis of reports of other chronic diseases, were also used for a supplemental analysis. Depression was classified as a single disease (when it was the only chronic disease present) or comorbid with one or more chronic diseases.

To calculate prevalence values with 95% confidence intervals, the total number of people aged 20 or older in the sample was used as the denominator. For the analyzes, we used post-stratum weights and statistical resources for complex samples (PASW Statistics 18, Release Version 18.0.0 (SPSS), Inc., 2009, Chicago, IL, www.spss.com). Pearson’s $\chi^2$ test was used for bivariate comparison of proportions.

This project was approved by the Brazilian National Research Ethics Committee (398.131 in 9/16/2013). All interviews were carried out after the prospective respondents or their legal guardians (when respondents could not complete the questionnaire themselves) had read and signed an informed consent form.
RESULTS

The prevalence of self-reported depression in the study population aged 20 years or older was 6.1% (95%CI 5.6 – 6.6). This prevalence increased significantly with age, from 3.5% in the under-40 age group to 9.5% in the 60-or-older group. It was highest among women (8.9%) and in the Southern region of the country (8.9%). There was no significant variation in prevalence across socioeconomic classes (Table 1).

Table 1. Prevalence of self-reported depression, medical indications for pharmacotherapy of depression, and use of medications for depression in the Brazilian population aged 20 years or older, stratified by sociodemographic characteristics. National Survey on Access, Use, and Promotion of the Rational Use of Medicines in Brazil (PNAUM), Brazil, 2014.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Prevalence of self-reported depression</th>
<th>Self-reported depression and medical indications for pharmacotherapy</th>
<th>Self-reported depression, medical indications for pharmacotherapy, and current pharmacotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>%a</td>
<td>95%CI</td>
<td>p</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>2.8</td>
<td>2.4 – 3.4</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Female</td>
<td>8.9</td>
<td>8.2 – 9.6</td>
<td></td>
</tr>
<tr>
<td>Age range</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20 to 39 years</td>
<td>3.5</td>
<td>2.9 – 4.0</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>40 to 59 years</td>
<td>7.6</td>
<td>6.9 – 8.4</td>
<td></td>
</tr>
<tr>
<td>60 years and older</td>
<td>9.5</td>
<td>8.6 – 10.6</td>
<td></td>
</tr>
<tr>
<td>Region of Brazil</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>North</td>
<td>2.7</td>
<td>2.1 – 3.4</td>
<td></td>
</tr>
<tr>
<td>Northeast</td>
<td>5.1</td>
<td>4.2 – 6.2</td>
<td></td>
</tr>
<tr>
<td>Southeast</td>
<td>6.2</td>
<td>5.4 – 7.0</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>South</td>
<td>8.9</td>
<td>7.9 – 10.1</td>
<td></td>
</tr>
<tr>
<td>Center-West</td>
<td>6.1</td>
<td>5.4 – 7.0</td>
<td></td>
</tr>
</tbody>
</table>
Table 1. Continuation.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Prevalence of self-reported depression</th>
<th>Self-reported depression and medical indications for pharmacotherapy</th>
<th>Self-reported depression, medical indications for pharmacotherapy, and current pharmacotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>%a  95%CI</td>
<td>p</td>
<td>%a  95%CI</td>
</tr>
<tr>
<td>ABEP socioeconomic classb</td>
<td>A/B 6.2  5.2 – 7.3  0.277</td>
<td>82.6  71.3 – 90.1  0.603</td>
<td>91.2  86.4 – 94.4  0.849</td>
</tr>
<tr>
<td></td>
<td>C 5.8  5.3 – 6.4</td>
<td>79.7  75.5 – 83.3</td>
<td>89.8  85.5 – 92.7</td>
</tr>
<tr>
<td></td>
<td>D/E 6.7  5.8 – 7.8</td>
<td>83.5  77.1 – 88.3</td>
<td>90.2  85.5 – 93.5</td>
</tr>
<tr>
<td>Total</td>
<td>6.1  5.6 – 6.6</td>
<td>81.3  77.5 – 84.7</td>
<td>90.3  87.6 – 92.4</td>
</tr>
</tbody>
</table>

*Percentages adjusted for sample weights and post-stratification by age and sex; aaccording to the Brazilian Association of Research Companies (ABEP)18; 95%CI: confidence interval of 95%.

The proportion of respondents with a medical indication for treatment of depression was 81.3% (95%CI 77.5 – 84.7), significantly higher (84.9%) in adults and lower (72.9%) in young adults. Among those who reported having a medical indication for treatment, most were receiving such treatment (90.3%, 95%CI 87.6 – 92.4). However, this proportion was significantly lower among young adults (84.5%) and residents of the North and Northeast regions (78.6 and 83.2%, respectively) (Table 1).

Among respondents who endorsed having only one CNCD, the prevalence of depression as a single disease was much higher than the general average (10.4%), and it was the third highest-prevalent disease in this population with a single disease, after hypertension and dyslipidemia. Among young adults, the prevalence was even higher (17.6%), whereas in older adults, the prevalence of depression as a single chronic disease was low (4.0%). Among those who reported more than one CNCD, the prevalence of depression as a comorbidity rose to 25.7%, reaching 45% among young adults with chronic comorbidities (see Supplementary Material 1).

Self-reported depression was commonly associated with other CNDCs and, consequently, with the chronic use of medicines for reasons other than pharmacotherapy of depression. Among respondents with at least one CNCD, 16.2% were not on any chronic medications, versus only 10.7% among those who specifically mentioned depression. Corroborating this finding, the prevalence of polypharmacy (five or more medications) was significantly higher among those who reported one or more CNCDs including depression (21.9%) than among those who did not report depression (12.1%) (Table 2).
Table 3 shows the groups of medications endorsed by patients with self-reported depression. More than two-thirds (69%) were non-psychotropic drugs, which is consistent with the high prevalence of comorbidities in cases of depression. It also lists all psychotropic drugs reported by the respondents, stratified into the six categories defined in the Methods section. Table 4 shows the proportion of use of each category of psychotropic drugs in relation to total intake of psychotropic drugs, for the sample as a whole and stratified by region. Nearly half of all psychotropic drugs mentioned by respondents were antidepressants, i.e., drugs specific for the treatment of depression (47.2%), followed by benzodiazepines (29.8%) and antipsychotics (12.1%). Use of antidepressants in cases of depression varied significantly across regions. In the South region, for instance, it was above the national average (55.4%), whereas in the North region, this rate was lower (29.7%), and use of antipsychotics was more prevalent than in any other region.

A total of 17 antidepressant drugs were reported, the most commonly reported was fluoxetine (30.1%), followed by amitriptyline (22.8%), sertraline (11.9%), and citalopram (8.2%). All others had a prevalence of use below 5% — paroxetine (4.8%), venlafaxine (4.5%), nor-triptiline (3.7%), escitalopram and imipramine (2.9%).

Table 2. Number of chronic medications reported and the number of chronic diseases reported from a list of 8 diseases, controlling for depression. National Survey on Access, Use, and Promotion of the Rational Use of Medicines in Brazil (PNAUM), Brazil, 2014.

<table>
<thead>
<tr>
<th>Chronic Medications</th>
<th>1 + CD</th>
<th>1 + CD and DEP</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>16.2%</td>
<td>10.7%</td>
<td>71.6%</td>
</tr>
<tr>
<td>1 to 4 med</td>
<td>71.7%</td>
<td>67.6%</td>
<td>24.3%</td>
</tr>
<tr>
<td>5 or more med</td>
<td>12.1%</td>
<td>21.9%</td>
<td>4.1%</td>
</tr>
</tbody>
</table>

CD: chronic disease; DEP: depression; Med: medications.

Table 3. Drug groups reported for the treatment of depression and its comorbidities. National Survey on Access, Use, and Promotion of the Rational Use of Medicines in Brazil (PNAUM), Brazil, 2014.

<table>
<thead>
<tr>
<th>Drugs reported for the treatment of depression</th>
<th>Prevalence (%)</th>
<th>95%CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-psychotropic drugs</td>
<td>69.0</td>
<td>[67.1 – 71.0]</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>14.6</td>
<td>[13.6 – 15.7]</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>9.2</td>
<td>[8.4 – 10.1]</td>
</tr>
<tr>
<td>Antipsychotics</td>
<td>3.8</td>
<td>[3.0 – 4.7]</td>
</tr>
<tr>
<td>Mood stabilizers</td>
<td>2.1</td>
<td>[1.7 – 2.6]</td>
</tr>
<tr>
<td>Hypnotics</td>
<td>0.7</td>
<td>[0.5 – 1.0]</td>
</tr>
<tr>
<td>Neurotropics</td>
<td>0.6</td>
<td>[0.4 – 1.0]</td>
</tr>
</tbody>
</table>

*Percentages adjusted for sample weights and post-stratification by age and sex; IC95%: interval of confidence of 95%.
DISCUSSION

In this population sample representative of the Brazilian urban adult population, we found a prevalence of self-reported depression of 6.1% among respondents aged 20 years or older. This prevalence is slightly higher than the overall prevalence estimated by WHO, but slightly lower than the 7.6% prevalence found in the 2013 National Health Survey, which used a similar methodology of self-report but applied to a broader age range (Brazilian population aged 18 and over).

The prevalence of depression in the North region was almost one third of that in the South region. This might be due to differences in the exposure to sunlight, much greater in the North, but also due to differences in availability of proper diagnosis, but these differences deserve to be further studied.

We observed a significant increase in the prevalence of depression with age, reaching 9.5% among older adults. Considering those individuals who reported only one of the eight CNCDs investigated directly by the PNAUM, the prevalence of depression as a single disease in the population aged 20 years or older rose to 10.8%, ranking third behind hypertension and dyslipidemias as isolated diseases. As such, the prevalence of depression was higher among young adults than among older adults with only one CNCD. Among those...
who reported at least one CNCD, the prevalence of depression was for times that found in the total population and more than twice the prevalence as a single disease. The most impressive finding was the extremely high prevalence of depression among young adults with chronic comorbidities, showing that self-reported depression is ubiquitous among young people with chronic multi-morbidity. We did not find in the literature other studies that have analyzed the prevalence of depression along with other comorbidities.

Considering that, according to WHO, depression is a leading cause of years lived with disability, the high prevalence of self-reported depression in the present sample, not only among the population with comorbidity, but also in young adults with depression as a single disease, is a matter of concern.

The vast majority of those who reported depression had a medical indication for treatment (81%); of those, most were indeed being treated. In general, 90% of those reporting depression were actually receiving some medication for depression. This proportion was significantly lower among the population living in the North (79%) and Northeast (83%) regions. This is probably a reflection of the lower accessibility in these poorer regions of the country, with less services and trained personnel. Also, the young population had a significantly lower rate of treatment of those reporting depression (85%). This might be due to the fear of side effects affecting libido or denial of the disease among the young, but this issue deserves further investigation and the attention from health workers treating depression in a young person. The high prevalence of older adults under treatment for depression (94%) is probably a reflection of the good access to prescribed medications for the other comorbidities that most of the interviewees reported having.

The higher prevalence of polypharmacy among respondents with self-reported depression is explained by the fact that depression is often accompanied by comorbidities that are treated with accessible drugs. Only 11% of those who reported depression with comorbidities were not on any chronic medication, and the prevalence of polypharmacy among those who reported depression was quite high (22%).

Although the majority of depressed patients who had indications for treatment were being treated, it is noteworthy that pharmacotherapy of depression is a chronic treatment based on psychototropic drugs, which are often expensive and are commonly absent from the National Formulary of Essential Medicines in Brazil; thus, treatment can be discontinued or neglected. This means that a significant proportion of depressed patients may not have continuously adequate and effective treatment over the years.

On the other hand, treatment of depression has become increasingly popular in recent years, in part due to a decrease in the stigma surrounding the disease and in part due to greater availability of effective medications with fewer side effects. There is a worldwide trend towards increased use of antidepressants. A U.S. study showed that, between 2000 and 2010, the number of people aged 18–44 who were on at least one antidepressant increased by almost 50%, from 6.6 to 9.8 million people — i.e., from 6.1 to 8.5% of the population.

We may consider it a positive fact that among the psychototropic drugs in use by those with self-reported depression, almost half were antidepressants, supposedly the drug of
choice to treat depression, as a single drug or associated to others. A total of 17 antidepressants were reported, with three agents accounting for 65% of reports — fluoxetine (30%), amitriptyline (23%), and sertraline (12%). It is worth noting that the two most commonly mentioned antidepressants were included in the National Formulary of Essential Medicines, as were nortriptyline and bupropion, both with a low reported frequency of use (3.7 and 1.8%, respectively).

Despite their lack of antidepressant effect, benzodiazepines were the most-represented group of psychotropic drugs in the sample after antidepressants, with use reported by almost one-third of depressed respondents. This is probably explained by the fact that depression is often comorbid with anxiety (which can lead to sleep disorders) and panic attacks. A population-based study conducted in São Paulo to evaluate the use of psychotropic drugs found that, as in the present study, anxiolytics and hypnotics are commonly prescribed as adjuncts to antidepressant pharmacotherapy in cases of depression, although these drugs can lead to dependence and are potentially inappropriate for older adults due to their negative effects on memory and balance. However, depressed patients in this sample may also have had other chronic diseases that were not considered in the analysis and are primarily treated with benzodiazepines. The same population-based study showed that, in some severe cases of depression with mood swings, a mood stabilizer — or even, in some cases, a second-generation antipsychotic — may be required. These classes were both included in the analysis, but were rarely reported by respondents. We observed significant differences in the prevalence of antidepressant and antipsychotic use across the different regions of Brazil, which probably reflects different prescribing patterns among physicians.

It bears stressing that most previous population-based studies on the prevalence of depression used DSM-IV criteria and/or validated screening instruments, which limits their comparability to the present study. But yet, self-reported diagnosis of depression has been previously validated and used in large surveys like the PNS in Brazil. On the other hand, self-report of depression increased the reliability of respondents’ reports of which medications they use. In most epidemiological drug surveys, these reports lack any linkage to the respondents’ reported health conditions. Another limitation of this study was that we did not have data on the timing or duration of diagnoses.

Depression is a growing public health challenge in the current paradigm of chronic diseases. Given its high prevalence in the population of chronic multimorbidity — especially among young adults — and high potential for inducing disability, its diagnosis and treatment should be a priority in primary care. This study shows original national data on the type of drugs that the urban adult population was using to treat depression in Brazil. Proper control of diagnosed depression through the rational use of antidepressant and anti-anxiety agents is essential to preserving the functional capacity of those affected, as well as to prevent polypharmacy, which is particularly common among patients with depression.

In summary, the present study shows that the treatment of self-reported depression involves mainly antidepressants but several other classes of psychotropic drugs are being used. A nationwide treatment protocol would be desirable, given the significant regional
differences in prescription patterns of medicines for depression in Brazil. The high prevalence of self-reported depression as an isolated chronic non-communicable disease and the extremely high prevalence as a comorbidity among young adults, along with the low proportion of cases being treated in this population group, warrant special attention.

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