

Prevalence of chronic respiratory diseases and medication use among children and adolescents in Brazil - a population based cross-sectional study

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Abstract

Objectives: to describe the prevalence of chronic respiratory diseases and their pharmacological management in children and adolescents in Brazil.

Methods: data from the Pesquisa Nacional de Acesso, Uso e Promoção do Uso Racional de Medicamentos no Brasil (PNAUM) (National Access Survey, Use and Promotion of Rational Use of Medicines in Brazil), a population-based cross-sectional study, were analyzed. Household surveys were conducted between September 2013 and February 2014. We included the population under 20 years of age with chronic respiratory diseases. Prevalence of disease, indication of pharmacological treatment, and their use were assessed.

Results: the prevalence of chronic respiratory diseases in children aged less than 6 years old was 6.1% (CI95%= 5.0-7.4), 4.7% (CI95%= 3.4-6.4) in those 6-12 years, and 3.9% (CI95%= 2.8-5.4) in children 13 years and older. Children under 6 showed a higher prevalence of pharmacological treatment indication (74.6%; CI95%= 66.0-81.7), as well as medication use (72.6%; CI95%= 62.8-80.7). Of those using inhalers, 56.6% reported using it with a spacer. The most frequent pharmacologic classes reported were short-acting β_2 agonists (19.0%), followed by antihistamines (17.2%).

Conclusion: children and adolescents who report chronic respiratory diseases living in urban areas in Brazil seem to be undertreated for their chronic conditions. Pharmacological treatment, even if indicated, was not used, an important finding for decision-making in this population.

Key words Epidemiological surveys, Medication use, Respiratory diseases, Chronic disease, Child, Adolescent



Introduction

Chronic respiratory diseases group are the tenth most prevalent illness among young people under 20 years old, accounting for 4.3% of prevalent cases of all chronic conditions worldwide.¹ Defined as a wide range of airways conditions and other structures of the lungs, they are characterized by similar symptoms,² but with different etiology, physiopathology, and prognosis.³

Asthma is the most common respiratory illness in children and a risk factor for airflow impairment in adulthood.⁴ Recurrent wheezing and bronchopulmonary dysplasia, along with asthma, are chronic respiratory diseases with higher prevalence in the pediatric population. Less prevalent conditions are primary ciliary dyskinesia, bronchiectasis is not associated with cystic fibrosis, plastic bronchitis and obliterating bronchiolitis.³ These conditions are leading causes of morbidity, poor quality of life, and an economic burden for the healthcare system.²

The similarity of symptoms among chronic respiratory conditions in childhood, the lack of biomarkers for supporting the diagnosis, and misinterpretation of wheezing lead to diagnostic misclassification and inadequate management.⁵ The scenario is even worst when both family members and health professionals do not recognize the chronic signals of these diseases.^{3,6,7} The Global Alliance against Chronic Respiratory Diseases (GARD) has been working to improve the quality of care and reduce the burden of these conditions, mainly in low and middle income countries.⁸ In Brazil, GARD has highlighted that, despite improvements, more commitment to the Ministry of Health is needed to address health policies for chronic respiratory diseases.⁸ To date, no populational studies have been conducted in Brazil for updating prevalence provided by the International Study of Asthma and Allergies in Childhood (ISAAC),⁹ and the Brazilian Ministry of Health guidelines for managing chronic respiratory diseases in children have not been updated in the last ten years.^{10,11}

In this regard, little is known about these conditions and current therapies for people under 20 years old in Brazil. Therefore, research in this area is needed for providing information, not only for caregivers and clinicians but also for supporting health policies and decision-making.⁴

This study aimed to assess the prevalence of chronic respiratory diseases among children and adolescents in urban areas in Brazil. We also assessed prescription and patterns of medication use, including the profile of inhalers use with spacers.

Methods

The reporting of the present study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement for cross-sectional studies.¹²

This was a population based cross-sectional study using data from the *Pesquisa Nacional de Acesso, Uso e Promoção do Uso Racional de Medicamentos* (PNAUM)¹³ (National Access Survey, Use and Promotion of the Rational Use of Medicines). The PNAUM study was based on a probabilistic sample with sampling defined by clusters in three stages: city (primary sampling unit); census tract; and household. Data collection took place between September 2013 and February 2014. The set of face-to-face interview questionnaires were applied by a team of trained interviewers. Data were recorded on tablets with software specifically developed for the study. The details about the sampling and logistics of data collection, and other information, were published in the methodological article.¹³

The PNAUM population's study was constituted by residents in urban areas in five regions, where data from 41,433 individuals in more than 20,000 households throughout Brazil were collected. After adjusting by region, sex and age, the study population represented approximately 171 million Brazilians residing in the urban areas of the country.

We analyzed data from children and adolescents. Our population was constituted of individuals between 0 to 19 years old. According to PNAUM methods, the population under 14 years old had their questionnaires responded by caregivers. Adolescents aged 15 or older responded the questionnaires themselves, and used the same questionnaires as for adults. Questionnaires for people with disabilities were excluded, considering this population were unable to communicate or self-report information properly.

The main dependent variable was chronic respiratory disease. The other dependent variables were medical indication for pharmacological treatment and medication use s and spacers.

For estimating the prevalence of chronic respiratory diseases, we used the following question: "Has a doctor ever told you that you have asthma, chronic bronchitis, emphysema or other lung diseases?" (yes, no). Although, PNAUM requested to specify the condition in case of an affirmative answer (asthma, chronic bronchitis, pulmonary emphysema, other lung disease, or does not know), we decided not to use this classification to reduce the possibility of misclassifying the disease. We assessed the prevalence of medical indications for

pharmacological treatment by asking “Do you have a medical indication to use any medicine for this disease?” (yes, no). For evaluating the prevalence of medication use in patients with chronic respiratory diseases who had treatment indications, we asked “Are you using any of these medications?” (yes, no). For these estimates, data from all the individuals interviewed from 0 to 19 years old were used as a denominator.

For individuals under 15 years old, the PNAUM interviewers questioned if they were using any type of inhaler. Those who answered affirmatively were asked about the current use of a spacer (yes, no). The source of obtention of spacers was examined (purchased, earned, or adapted). To note, the adapted devices are those produced at home using a plastic bottle.

To evaluate the medication use profile, the PNAUM interviewers requested to show the packaging and prescriptions, for each current medication. Detailed information about the product was collected (generic, expiration date, dosage form, concentration). We classified the products according to the pharmacological class used by the Global Initiative for Asthma (GINA).¹⁴ For this estimate, we used as denominator all medications reported for pulmonary disease. Dietary supplements, cosmetics and products recorded as “ignored” were excluded from our analysis.

We assessed the following sociodemographic characteristics: sex (female or male), age group (<6; 6-12; and ≥13 years old), *Critério Brasileiro de Classificação Econômica* (Brazilian Economic Classification Criterion) (A/B, C, D/E) (CCEB 2013/ABEP – <http://www.abep.org/>), Region (North, Northeast, Southeast, South, Central-West), and private health insurance (yes, no). Age was collected as a continuous variable and categorized by age groups, considering the profile of chronic respiratory diseases for this population.

The estimates of prevalence and confidence interval of 95% (CI95%) were reported while adjusting to sample weights and post-stratification by age and sex.¹³ The Pearson’s chi-square test for independence with Rao Scott adjustment was performed to evaluate associations between categorical variables, with a level of significance of 5%. All analyses were conducted using Software Stata/IC 15 (StataCorp LLC, TX), considering the complex sampling plan (svyset cluster) and applying the exclusion method in pairs.

The PNAUM study was approved by the National Ethics Council (Report number: 398,131 of 9/16/2013) and all the interviews were conducted after reading the Consent Term form and signed, either by the interviewed or legally responsible caregiver.

Results

Data of 9,062 children and adolescents living in urban areas in Brazil were assessed, of whom 5,973 (25%)

were <6 years old, 1,555 (37%) were 6-12 years old, and 1,534 (37%) were 13 years old or older (Figure 1). The prevalence of chronic respiratory diseases among the study participants according to sociodemographic characteristics is detailed in Table 1. The highest prevalence of chronic respiratory diseases was found in those less than 6 years old (6.1%; CI95%=5.0-7.4). When stratified by socioeconomic characteristics, higher prevalence was also observed among those younger than 6 years old, were boys, with a social status classified as “C”, and living in the Southeast region. Among those aged 6 to 12 years, who answered having private health insurance and having a higher prevalence of chronic respiratory disease was observed.

The overall prevalence of chronic respiratory diseases, prevalence of indication for pharmacological treatments, as well as their use are presented in Table 2. Regardless of age, children and adolescents who reported having chronic respiratory diseases are not adequately prescribed medications, neither used indicated medications, with prevalence for both treatment indications and medication use ranging from 56% to 75%.

Figure 2 shows that 57% of the children and adolescents aged 14 or less who had a prescription and were using inhalers to treat their chronic respiratory condition were also using a spacer. However, more than half (68%) were using a purchased device.

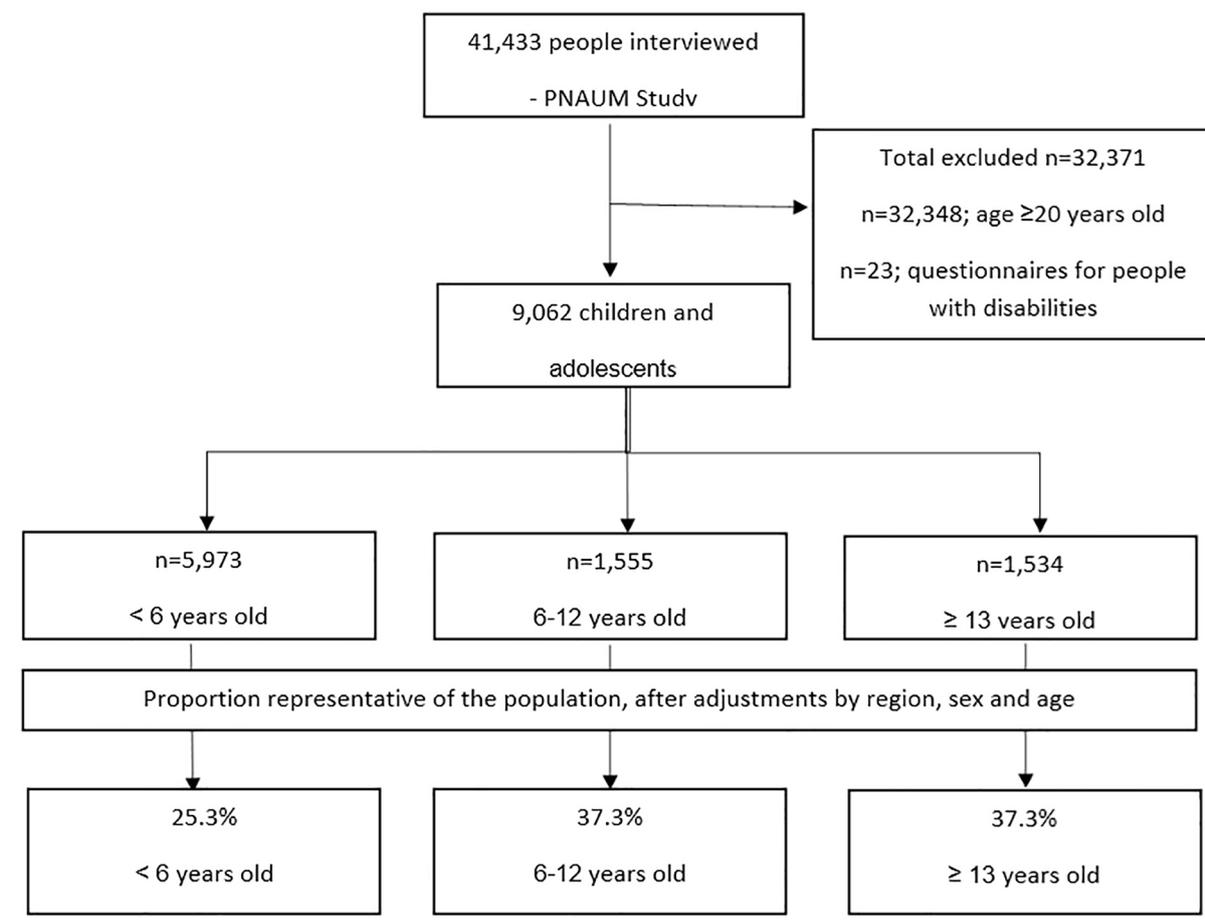
Table 3 shows the frequency and classes of medications reported among the study participants. Inhaled short-acting beta-2 agonist was the class most frequently reported (19.0%), followed by antihistamines (17.2%), inhaled and intranasal corticosteroids (both 11.4%). When combined, preventive medications like intranasal and inhaled corticosteroids and antileukotriens represented less than 50% of all medications reported. Children older than 6 years old showed less use of medication compared to the younger ones.

Discussion

Through the PNAUM data, we estimated the prevalence of chronic respiratory diseases and characteristics of pharmacological treatment in children and adolescents in Brazil between 2013 and 2014. The PNAUM study was the first drug utilization study representative of the Brazilian population living in urban areas. To our knowledge, there is no update for these estimates. Therefore, this is the only available source that allows us to understand the pharmacotherapeutic profile of children and adolescents with chronic respiratory diseases in Brazil. Our findings demonstrated that prevalence of chronic respiratory diseases in children and adolescents were lower than previously reported by other studies conducted in Brazil.^{9,15} Several reasons might be attributed

Figure 1

Study flow diagram.



to these lower estimates, including the study design, and the lack of proper diagnosis and recognition by parents and caregivers.⁶ The results concerning medication use must be interpreted in light of current guidelines when the study was conducted. A recent guideline for asthma management was published,¹⁶ however, a lack of national initiatives for updating guidelines still exists. Which made us rely on the hypothesis that no changes in estimates have occurred since 2014.

Prevalence of chronic respiratory diseases varied across the regions, with the highest in the Southeast, regardless of age range. Among children under 6, the lowest prevalence was found in the North, while for older children, lower prevalence was found in the Northeast region (less than 2%). Studies as ISAAC,⁹ ERICA¹⁷ and PeNSE¹⁵ have also found regional differences, mainly explained by socio-economic disparities throughout the country. Either ERICA and PeNSE were school-based national surveys that included children and adolescents across the country. Moreover, both studies adapted questions from the ISAAC study, assessing asthma symptoms and diagnosis provided by a physician. Although, we are not able to make direct comparisons,

considering those studies had a distinct design and included a different population, some issues might come up. Higher prevalence in the Southeast and lower prevalence in the North followed the same pattern, suggesting that chronic respiratory diseases could be under-diagnosed in those regions where access to healthcare is admittedly low.¹⁸ After applying weights, our sample was similarly distributed among the three ranges of age, with parents and caregivers as responsible for self-reporting the chronic conditions of their children. In light of this, we cannot rule out that our study underestimated prevalence, considering that only 6% of the parents and caregivers recognize chronic respiratory diseases as chronic conditions.⁶ On the other hand, overestimation from PeNSE, reaching near 18% of the students referring to asthma at least once in their lives,¹⁹ cannot be discarded. These results must be interpreted considering the study limitations, as memory bias and the ability of adolescents to properly answer the questions. For our study, we also hypothesize that environmental characteristics of different regions were contributing to differences found among regions.

Our study also found more than double the prevalence of chronic respiratory diseases in those aged 6-12 years old

Table 1

Prevalence of chronic respiratory diseases in children and adolescents according to sociodemographic characteristics. PNAUM, Brazil, 2014. (N=9,062)

Variables	< 6 years old			6-12 years old			≥ 13 years old		
	%	CI95%	p*	%	CI95%	p*	%	CI95%	p*
Sex			0.013			0.073			0.347
Male	7.3	5.7-9.3		6.0	4.0-8.9		4.5	2.9-6.9	
Female	4.8	3.6-6.3		3.4	2.1-5.6		3.3	2.0-5.4	
CCEB#			0.749			0.311			0.585
A/B	5.2	2.8-9.4		5.1	2.7-9.6		4.1	2.0-8.3	
C	6.4	4.9-8.2		5.3	3.6-7.8		4.3	2.8-6.6	
D/E	6.0	4.5-8.0		3.1	1.7-5.6		2.8	1.4-5.6	
Region			< 0.001			0.010			0.004
North	2.9	2.0-4.2		6.5	3.6-11.3		4.0	2.1-7.5	
Northeast	4.2	2.6-6.8		1.5	0.5-3.7		1.7	0.6-3.9	
Southeast	8.8	6.6-11.5		6.3	3.8-10.4		5.9	3.7-9.4	
South	5.3	3.7-7.7		3.8	2.3-6.1		2.2	1.2-4.1	
Central-West	5.0	3.6-7.0		5.6	3.3-9.3		2.6	1.3-5.4	
Private health insurance**			0.438			0.031			0.017
Yes	7.1	4.5-11.1		8.4	4.4-15.3		7.6	4.1-13.7	
No	5.8	4.7-7.2		3.9	2.7-5.5		3.2	2.1-4.8	
Total	6.1	5.0-7.4		4.7	3.4-6.4		3.9	2.8-5.4	

p* - Pearson's chi-square test for independence with Rao Scott adjustment. The percentages were adjusted according to sample weights and post-stratification by age and sex; # Classified according to *Critério de Classificação Econômica Brasil* 2013 (CCEB 2013 - Brazilian Economic Classification Criterion) of *Associação Brasileira de Empresas de Pesquisa* (ABEP - Brazilian Association of Survey Companies). Available from: <http://www.abep.org>; **Missing values: n=10.

Table 2

Chronic respiratory disease, indication for pharmacological treatment and prevalence on medication use in children and adolescents in Brazil. PNAUM, Brazil, 2014.

Characteristics	Numerator/ Denominator	< 6 years old		6-12 years old		≥ 13 years old		p*
		%	CI95%	%	CI95%	%	CI95%	
Chronic respiratory disease	410/9,052	6.1	5.0-7.4	4.7	3.4-6.4	3.9	2.8-5.4	0.092
Indication for pharmacological treatment	269/410	74.6	66.0-81.7	56.1	41.0-70.1	62.5	46.6-76.6	0.112
Medication use	176/269	72.6	62.8-80.7	65.5	44.1-82.0	73.6	52.9-87.4	0.729

p* - Pearson's chi-square test for independence with Rao Scott adjustment. The percentages were adjusted according to sample weights and post-stratification by age and sex.

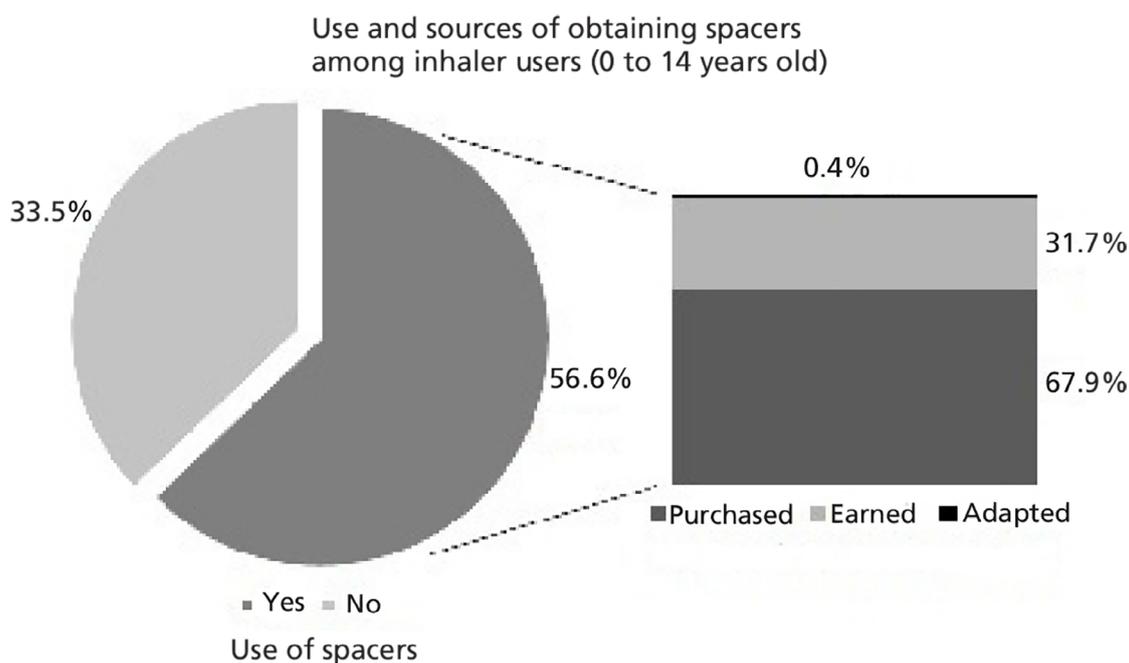
with private health insurance, compared to those without a private healthcare plan. This could be attributed to the fact that private health insurance would provide more access to healthcare services and therefore, a higher probability of diagnosis and pharmacological treatment. The private healthcare system does not necessarily provide better care, nevertheless, sometimes there is more opportunity to receive a diagnosis.

Regardless of the difficulty to diagnose chronic respiratory conditions in children under 6 years old, the estimates for the prevalence were higher among them, as well as treatment indication. According to the

pathophysiology of these conditions, a reduction is expected in the prevalence, with the increase of age,²⁰ a trend that seems to be confirmed in our study with those 13 years old and older showed a 4% prevalence of chronic respiratory conditions. Despite of the point estimates being different among the ranges of age, no statistical difference was observed for estimates of disease, treatment indication and medication use. The PNAUM study represented the largest survey conducted in Brazil for evaluating medication use, and the sampling strategy allowed, have a representative population for all ranges of age studied. However, when assessing the chronic respiratory disease

Figure 2

The proportion of using spacers among the population who reported using inhaler (n=73).



* Percentages adjusted according to sample weights and post-stratification by age and sex.

Table 3

Self-reported medication according to pharmacologic class and age range, PNAUM, 2014. (denominator medicines, n=268 medications).

Pharmacologic class	Total	< 6 years old	6-12 years old	≥ 13 years old
	%	%	%	%
Short-acting beta-2 agonists inhaler	19.0	36.5	37.5	26.0
Antihistamines	17.2	39.0	30.0	31.0
Inhaled corticosteroids	11.4	32.3	18.3	49.4
Intranasal corticosteroids	11.4	30.4	38.1	31.5
Systemic corticosteroids	7.8	50.0	30.0	20.0
Combination long-acting inhaled beta-2 agonist and corticosteroid inhalers*	7.7	10.1	56.6	32.3
Short-acting anticholinergic agent - ipratropium	7.4	35.2	40.4	24.2
Homeopathic and immunomodulators	3.4	45.1	54.9	-
Short-acting beta-2 agonists systemic - salbutamol‡	2.8	32.6	10.8	56.6
Others - Decongestants (topical and systemic)¥	2.7	85.1	14.9	-
Others - Antitussives/expectorants¥	2.5	71.9	12.1	16.0
Others - Oral corticosteroids + combinations	1.8	78.6	-	21.4
Others - Antibiotics	1.8	100	-	-
Antileukotrienes - montelukast	1.2	66.5	33.5	-
Others - Antipyretic / Anti-inflammatory /other combinations to treat symptoms¥	0.8	100.0	-	-
Combination short-acting beta-2 agonists and corticosteroid inhalers - beclomethasone/salbutamol	0.7	60.0	40.0	-
Others - General (not classified above)¥	0.3	100.0	-	-
Fresh plants, teas and homemade products	< 0.1	100.0	-	-

‡Salbutamol whose pharmaceutical form was solution or syrup were classified within this class; * Formoterol as monotherapy reported by a 6-19 years old user, included in this class but not presented here; ¥Herbal medicines included; ** Percentages adjusted according to sample weights and post-stratification by age and sex.

strata, numbers were sparsely contributing to the large confidence intervals for estimates and probably lack of power for demonstrating differences among children and adolescents.

Children aged 6-12 years old received fewer indications and used less medication compared to the rest of the study population. This could be either because treatment is mainly managed by parents with younger children than older ones,²¹ or due to remission of chronic respiratory diseases, for example, asthma, which may occur after 6 years old.²¹

Regarding the pattern of medication use, it is not surprising that short-acting inhaled beta-2 agonists were the most frequently reported class, as previously published.²² Salbutamol was and still is, provided either free-of-charge or at a low cost under Brazilian public health programs. Medications free of charge are recommended by GARD and, according to GINA protocol (considering the period in which the present study was carried out), recommended as needed as a first step in asthma management.¹⁴

Inappropriate asthma management with overuse of short-acting inhaled beta-2 agonists is well described,²³ representing an increased risk of adverse events. Equally a problem might be their underuse.⁶ Free of charge asthma medications provided by the Brazilian health system since 2011, showed to reduce by 30% the rate of hospital admission in those aged 19 years old and younger in Brazil.²⁴ Ipratropium bromide, beclomethasone dipropionate, and salbutamol are essential for managing asthma, however, health education for proper use is needed. Successful programs in Brazil for managing asthma in children and adolescents were established,^{25,26} but they are isolated and do not represent the needs of the entire Brazilian population.

Metered-dose device with spacer attached to the mask for children younger than four years old; and metered-dose device with spacer attached directly to the mouth for children between four and six years old were the recommendations for all children who prescribed inhaled medications.¹⁰ However, we observed a lower proportion (55%) of reported use of spacers. Additionally, most users were paying to receive their spacers, an expected finding considering these devices used to be expensive and not available free of charge.²⁵

Antihistamines play an important role in treating allergic diseases in children,²⁷ this class of medication was the second most reported in our study. For chronic respiratory diseases, specifically for asthma, their use remains controversial and no recommendation exists to be used as a first-line treatment or in monotherapy.^{10,14,28}

According to Ministry of Health recommendations for managing chronic respiratory conditions (2010), a low dose of inhaled corticosteroids should be the first-line

therapy for treating mild asthma, along with short-acting inhaled beta-2 agonists, for symptoms relief.¹⁰ Systemic corticosteroids were recommended for a short period of time and only for the treatment of exacerbations. Our findings were consistent with these recommendations for inhaled corticosteroids, but not for systemic medications. Since our study assessed medication use in those who were indicated for treatment, we were not expecting to find a higher proportion of medications used only for exacerbations.

Ribeiro and Fischer³ presented a summary of medications used for treating chronic respiratory diseases, and our findings were consistent concerning a large number of classes recommended for treating these conditions. Children younger than 6 years old were those reporting more diverse types of treatments, results expected when considering the profile of respiratory conditions in this population.

Trends have demonstrated stability in estimates for chronic respiratory conditions for both children and adults.^{9,29} However, we still need longitudinal studies to evaluate the effect of treatments or policies on the Brazilian population. Incorrect use of medication is as severe as a lack of its administration, and this should be a concern. Chronic respiratory conditions in which reevaluation and stepping up, or stepping down, of the treatment are highly dependent on the proper use of respiratory devices.¹⁴

The limitations of our study are those we expect to find when conducting surveys. Methodological challenges and general limitations related to the PNAUM study were described in the methodological paper.¹³ Beyond the implementation challenges of surveys, we highlight the limitations concerning the quality of the information obtained and other biases related to self-reported interviews. Self-report bias is a well-known type of information bias presented in observational studies.³⁰ For evaluating chronic respiratory diseases in children and adolescents we cannot rule out the possibility of recall bias. This bias may be related to parents or caregivers who do not remember receiving a diagnosis for their child's condition. The lack of diagnosis provided by a physician and recognition of the chronic respiratory disease, previously discussed, could also occur and may help to explain the lower prevalence observed in our study. Populational-based studies comparing the validity of self-reported diagnosis for chronic respiratory diseases in children and adolescents, not only for asthma are lacking in Brazil. Therefore, a need for future research in this area. For recording medication use, the package was not always available and inconsistent information between the declared disease and the therapeutic indication of the drug might be generated.¹³ For reducing the risk

of misclassifying the reason to use, we restricted the analysis of medications for those who declared a chronic respiratory condition. Finally, despite the study size and the balanced number of children and adolescents, when analyzing chronic respiratory diseases, the numbers were low, and wide confidence intervals were observed for the estimates.

The PNAUM study was the first large national survey that investigated medication use in detail with interviews performed in 2013 and 2014. The design and implementation of this national survey followed all the recommendations for conducting high-quality surveys, with results representative of the profile on medication use in the Brazilian population, including respiratory diseases for children and adolescents. Although, the interviews took place six years ago, there were no changes in the national policies for the management of chronic respiratory diseases in children and adolescents in Brazil since then. Therefore, we assume that our results are the best available knowledge about the profile of medication use by this population. Although the objective of our study did not cover the correct management of the therapy, it is important to focus on the pattern found, a high proportion of medications used for rescuing instead of as disease control and prevention. These findings are the only evidence currently available, allowing us to understand the management of chronic respiratory conditions in children in Brazil. We highlight that updated estimates are crucial to support strategic decisions related to pharmaceutical services in the Brazilian Public Health System.

In summary, children and adolescents who report chronic respiratory diseases living in urban areas in Brazil seem to be undertreated for their chronic conditions. Pharmacological treatment, even if indicated, was not used properly, an important finding for decision-making in this population.

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Author's contribution

Leal LF: Conception, analysis, interpretation of results, writing and approval of the final version of the manuscript. Tavares NUL: Conception, critical review of the intellectual content, writing and approval of the final version of the manuscript. Borges RB: Analysis, critical review of the intellectual content, writing and approval of the final version of the manuscript. Mengue SS: Conception, critical review of the intellectual content, writing and approval of the final version of the manuscript.

Fagundes SC: Critical review of the intellectual content, writing and approval of the final version of the manuscript. Masarwa R: Critical review of the intellectual content, writing and approval of the final version of the manuscript. Dal Pizzol TS: Conception, interpretation of results, critical review of the intellectual content, writing and approval of the final version of the manuscript. The authors declare no conflict of interest.

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