

Prevalence of asthma symptoms among adolescents in Brazil: National Adolescent School-based Health Survey (PeNSE 2012)

Prevalência de sintomas de asma entre escolares do Brasil: Pesquisa Nacional em Saúde do Escolar (PeNSE 2012)

Maurício Lima Barreto^I, Rita de Cássia Ribeiro-Silva^{II}, Deborah Carvalho Malta^{III,IV}, Maryane Oliveira-Campos^{III,IV}, Marco Antonio Andreazzi^V, Alvaro Augusto Cruz^{VI}

ABSTRACT: *Objective:* This study aims to describe the prevalence rates of asthma symptoms in Brazil, its Regions and State capitals, according to data from the National Adolescent School-based Health Survey, 2012. Furthermore, it aims to compare the prevalence of asthma in the capitals evaluated by PeNSE 2012 with previous results of the International Study of Asthma and Allergies in Childhood (ISAAC). *Methods:* Cross sectional study of 9th grade students at public and private schools of all Brazilian states and the Federal District (Brasília). A self reported questionnaire containing items from the ISAAC was applied in order to identify the presence of asthma symptoms. *Results:* The results of PeNSE indicate a high prevalence of asthma symptoms (23.2%) and of reports of a previous medical diagnosis of asthma (12.4%). Of the five state capitals in which the PeNSE results were compared to the ISAAC, São Paulo, Curitiba and Porto Alegre presented an increase in the prevalence of asthma symptoms. In Salvador, there was a reduction. *Conclusion:* Brazil is among the countries with the highest prevalence of asthma in the world, and the prevalence is still growing.

Keywords: Asthma. Wheezing. Prevalence. Adolescents. Schoolchildren. International Study of Asthma and Allergies in Childhood (ISAAC).

^IInstitute of Collective Health, *Universidade Federal da Bahia* – Salvador (BA), Brazil.

^{II}Departament of Science Nutrition at the School of Nutrition of *Universidade Federal da Bahia* – Salvador (BA), Brazil.

^{III}Departament of Disease and Non-Communicable Condition Surveillance and Health Promotion, Health Surveillance Secretariat, Ministry of Health – Brasília (DF), Brazil.

^{IV}*Universidade Federal de Minas Gerais* – Belo Horizonte (MG), Brazil.

^VBrazilian Institute of Geography and Statistics – Rio de Janeiro (RJ), Brazil.

^{VI}Nucleus of Excellence in Ashtma at *Universidade Federal da Bahia* – Salvador (BA), Brazil.

Corresponding author: Maurício L. Barreto. Instituto de Saúde Coletiva. Universidade Federal da Bahia. Rua Basílio da Gama, s/n, Campus Universitário, Canela, CEP: 40110-040, Salvador, BA, Brasil. E-mail: mauricio@ufba.br

Conflict of interests: nothing to declare – **Financing source:** none.

RESUMO: *Objetivo:* Descrever as prevalências de sintomas de asma no Brasil, regiões e capitais, segundo a Pesquisa Nacional de Saúde do Escolar (PeNSE), 2012. Além disso, comparar tais prevalências nas capitais – identificadas na PeNSE 2012 – com resultados de estudos anteriores do *International Study of Asthma and Allergies in Childhood* (ISAAC). *Métodos:* Estudo transversal em que foram incluídos escolares do 9º ano de escolas públicas e privadas de todos os estados brasileiros e do Distrito Federal. Um questionário estruturado autoaplicável com questões do ISAAC foi utilizado para identificar a presença de sintomas de asma. *Resultados:* Os resultados da PeNSE apontam para a alta prevalência de sintomas de asma (23,2%) e de relato de diagnóstico de asma no passado (12,4%). Entre as cinco capitais em que os resultados da PeNSE foram comparados com os do ISAAC, São Paulo, Curitiba e Porto Alegre apresentaram crescimento da prevalência de sintomas de asma ao longo dos inquéritos, e em Salvador houve uma redução. *Conclusão:* O Brasil está entre os países com mais altas prevalências de asma no mundo e esta prevalência ainda está em crescimento.

Palavras-chave: Asma. Sibilos. Prevalência. Adolescentes. Escolares. *International Study of Asthma and Allergies in Childhood* (ISAAC).

INTRODUCTION

Asthma is a chronic inflammatory disease characterized by the hyperresponsiveness of the lower airways and by the variable limitation to the airflow, which can be reversed spontaneously or with treatment. It can be clinically manifested by recurring episodes of sibilance, dyspnea, chest tightness, and cough, especially at night and in the morning, after waking up¹. It is estimated that 235 million people in the world have asthma², and an increment of more than 100 million cases of asthma is projected for 2025³. About half of all the cases begins to present symptoms before the age of 5, and 25% only present with symptoms after the age of 40³.

Despite the recent progress in the knowledge about the physiopathology of the disease and its treatment, the increased prevalence and persistence of mortality caused by asthma in the past decades are still a matter of concern⁴. Many factors have been proposed to explain the increased prevalence of asthma observed in the past decades, including environmental, nutritional, economic and psychosocial aspects⁵⁻¹⁰. However, environmental factors are probably the main determiners of the recent growth in the prevalence of this disease⁵.

Until the mid-1990s, epidemiological data about asthma were limited, which made it difficult to better understand the importance and the impact of this disease. The lack of standardized instruments that were highly sensitive and specific for epidemiological research about asthma made the comparison of results and the follow-up of its temporal tendency difficult. The aforementioned scenario was altered by the International Study of Asthma and Allergies in Childhood (ISAAC), which developed instruments and a protocol to assess the

prevalence of asthma and allergic conditions in different parts of the world by employing standardized methods (written self-applicable questionnaire and/or video-questionnaire); therefore, they were comparable^{11,12}. In Brazil, the instrument was translated to Portuguese, and its reproducibility and validity were assessed¹³. The question about respiratory sounds in the past 12 months and the global ISAAC score are the most recommended criteria for prevalence estimates of asthma symptoms.

The data from ISAAC, Phase 3, when compared to data from ISAAC, Phase 1, demonstrated that the prevalence of asthma symptoms is still increasing in several regions of the world (but not in all of them)¹⁴. Throughout the surveys, many geographic areas showed annual variation in the prevalence of asthma symptoms, with tendency to increase in the group of students in some parts of the world, including India (+0.06), North America (+0.32), Western Europe (+0.05%) and Eastern Mediterranean (+0.79%). Among adolescents, the tendency of annual increase is clear in countries of Africa (+0.16%), Latin America (+0.32%), North of Europe (+0.26), Eastern Europe (+0.26%) and India (+0.02%). On the other hand, there has been a tendency of stability or even reduction concerning the prevalence of the disease in other regions, such as Oceania (-0.76), especially in the group of adolescents¹⁵.

In Brazil, the global prevalence of active asthma ranged, from 1995 to 2002, from 21.3% to 24.4% (ISAAC Phase 1 and Phase 3)¹⁶. However, it is important to point out that only five centers (cities) participated in both phases of ISAAC. In these centers, adolescents showed reduced prevalence of asthma symptoms (27.7 *versus* 19.9%), but there was no variation in the prevalence of a medical asthma diagnosis (14.9 *versus* 14.7%)^{16,17}. The results of the ISAAC study, phase 3, pointed out to the highest prevalence of asthma symptoms in the following cities: Salvador (BA) (24.6%) and Vitória da Conquista (BA) (30.5%), and the lowest presence in Maceió (AL) (14.8%) and Itajaí (SC) (12.3%), and the mean prevalence between Brazilian adolescents is close to 20%¹⁵.

Even though asthma symptoms present high prevalence in many Brazilian cities, the true magnitude of the prevalence of the disease in the different regions of the country is unknown. This fact makes it difficult to plan and execute programs that aim at its prevention and control. In this context, knowing the prevalence of asthma among adolescents in several regions of Brazil is very relevant, since such knowledge will enable the planning and the implementation of adequate strategies to prevent and control this disease.

Therefore, the study aims at describing the prevalence of asthma in Brazil, regions and capitals, according to the National Adolescent School-based Health Survey (PeNSE), 2012. Besides, it aims at comparing the prevalence of the disease in the capitals pointed out by PeNSE 2012 with results from previous ISAAC studies.

METHODS

This cross-sectional study was conducted in 2012 by the Ministry of Health in Brazil, together with the Brazilian Institute of Geography and Statistics (IBGE). The study

population is composed of 9th grade students of public and private schools of all of the Brazilian states and the Federal District. The sample of PeNSE 2012 represented Brazil, its five regions, 26 capitals of the states and the Federal District (n = 109,104). For the sampling plan, the national territory was stratified as follows: each of the 26 state capitals, and the Federal District, was defined as a geographic stratum, and the other cities were grouped in each of the five major geographic regions, thus forming other five geographic strata. The sample of each stratum was allocated proportionally to the number of schools, according to the administrative dependency of the schools (private and public). For each stratum, a conglomerate sample was selected in two stages, as follows: in the first stage, school; and, in the second stage, eligible classrooms in the selected schools (9th grade, elementary school).

In the strata formed by cities that were not capitals, it was chosen to group conglomerates according to homogeneity and neighboring criteria, thus forming groups of 300 to 600 classrooms, approximately. One sample of these groups was selected in each region, and afterwards, the schools were selected. For cities that are not capitals, the primary sampling units were the groups of cities, and the secondary units were schools; the classrooms of these schools were the tertiary sampling units. In both cases, all of the students in the selected classrooms who were present on the day of data collection formed the sample of student and were invited to participate in the study.

Schools with less than 15 students in the analyzed grade were excluded. Even if they represented about 10% of the schools, they accounted for less than 1% of the total of students. Classrooms from the evening period were also excluded, because in general these students were older to the others, therefore, they could present with different risk factors in relation to other 9th grade students. The methodology is described in PeNSE, 2012¹⁸.

The ninth grade was chosen because the students in this grade, mostly aged between 13 and 15 years old, have already acquired the necessary skills to answer the self-applicable questionnaire, and because they are already prone to being exposed to several risk factors, and because the resulting data would enable the comparison with other countries¹⁹. The self-applicable structured questionnaire was inserted in a smartphone without about 120 questions. In 2012, some adjustments were made to the questionnaire, in order to improve it, to introduce new themes, as well as to adjust its comparability with data obtained by the WHO survey, Health Behavior in School-Aged Children¹⁹.

With the objective of improving the knowledge about the prevalence of asthma symptoms among students, PeNSE, in 2012, incorporated this theme, including questions that were also investigated in ISAAC (Phase 1, Phase 3)²⁰. In order to know if the student had wheezing chest in the 12 months prior to the survey, the following question was asked: "In the past 12 months, did you have wheezing (or chirping) chest?" (yes/no). And to analyze the presence of asthma at least once in life, the following was asked: "Have you ever had asthma?" (yes/no).

STATISTICAL ANALYSIS

The prevalence of asthma was estimated with a 95% confidence interval (95%CI), according to sex (male/female), its regions and state capitals. The collected information was inserted in a data base, being analyzed with the statistical package SAS, v.14.

PeNSE was approved by the Ethics Research Committee of the Ministry of Health, report n. 192/2012, concerning registration n. 16805, of CONEP/MS, on 27/03/2012.

RESULTS

From the total of students that were initially selected, 47.6% of them were male and 52.4% of them were female participants, mostly aged 14 years old (46.7%). The prevalence of asthma symptoms (wheezing chest in the past 12 months) in the country was of 23.2% (95%CI 21.1 – 25.3), ranging from 24.9% (95%CI 20.0 – 29.8) to 19.8% (95%CI 18.7 – 20.8) in the Southeast and the Northeast regions, respectively. In the capitals, the prevalence of asthma symptoms was of 25.2% (95%CI 24.4 – 25.9), ranging from 18.2% (95%CI 16.4 – 20.1) in São Luís (MA), to 29.5% (95%CI 27.4 – 31.65) in São Paulo (SP). Wheezing chest was more frequent among girls (24.9%; 95%CI 23.3 – 26.4) than boys (21.4%; 95%CI 18.4 – 24.4) ($p < 0.001$) (Table 1, Figures 1 to 3).

Of the students, 12.4% (95%CI 11.4 – 13.5) reported having been diagnosed with asthma at least once, ranging from 18.4% (95%CI 17.3 – 19.5) in the North region to 11.4% (95%CI 9.5 – 13.2) in the Southeast region. Among the capitals, the mean was of 16% (95%CI 15.4 – 16.5), ranging from 29.3% (95%CI 26.4 – 32.1) in Porto Alegre to 12.2% (95%CI 10.0 – 14.4) in Cuiabá (Table 1, Figures 1 and 2).

Table 1. Percentage of 9th grade students who had wheezing (or chirping) chest in the last 12 months and asthma episodes at any point in their lives, by sex, indicating the 95% confidence interval, in the Brazilian total and the Capitals' total.

	Total		Sex			
			Male		Female	
	%	95%CI	%	95%CI	%	95%CI
Wheezing chest in the past 12 months						
Brazil	23.2	21.1 – 25.3	21.4	18.4 – 24.4	24.9	23.3 – 26.4
All capitals	25.2	24.4 – 25.9	22.9	21.9 – 23.9	27.3	26.4 – 28.3
Asthma episode at any point						
Brazil	12.4	11.4 – 13.5	12.8	11.6 – 14.1	12.1	11.1 – 13.0
All capitals	16	15.4 – 16.5	16.0	15.2 – 16.7	16	15.3 – 16.8

DISCUSSION

The results from PeNSE point out to the high prevalence of asthma symptoms (23.2%) and of the report of asthma diagnoses in the past (12.4%) among 9th grade students, elementary school, who are usually aged between 13 and 15 years old. Such high prevalence was also observed in other regions of the world, like North America (21.5%), Latin America (18.8%) and Oceania (26.7%)¹⁵.

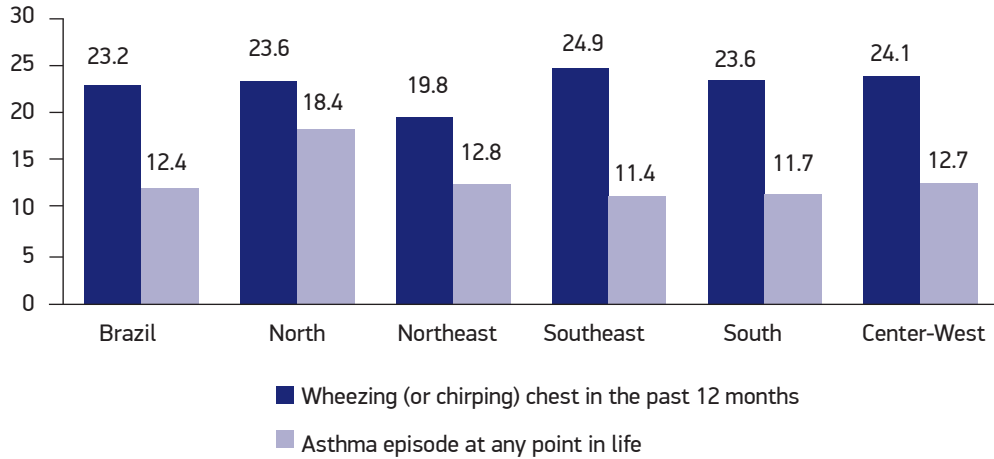


Figure 1. Percentage of 9th grade students who had wheezing (or chirping) chest in the last 12 months and were diagnosed with asthma in the five Brazilian regions.

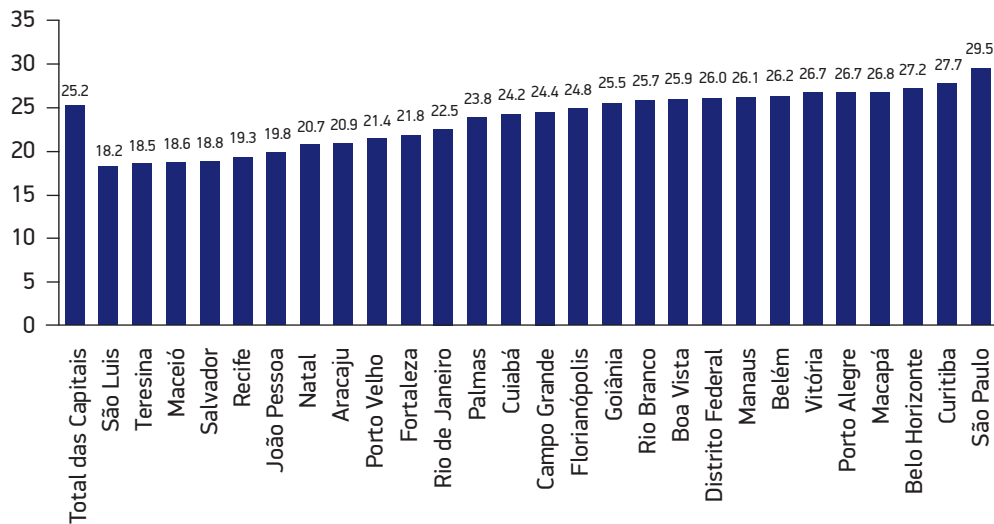


Figure 2. Percentage of 9th grade students who had wheezing (or stridor) chest in the last 12 months in Brazilian state capitals.

The analyzed age group is close to the age group of adolescents who participated in ISAAC (13 – 14 years old). Therefore, the sample from PeNSE is comparable to the one from ISAAC surveys conducted in Brazil, as well as in other parts of the world. The results of PeNSE, in comparison to those of ISAAC Phase 1 and Phase 3, indicate the increment concerning the prevalence of asthma symptoms in the population of students in some capitals of the country¹⁷.

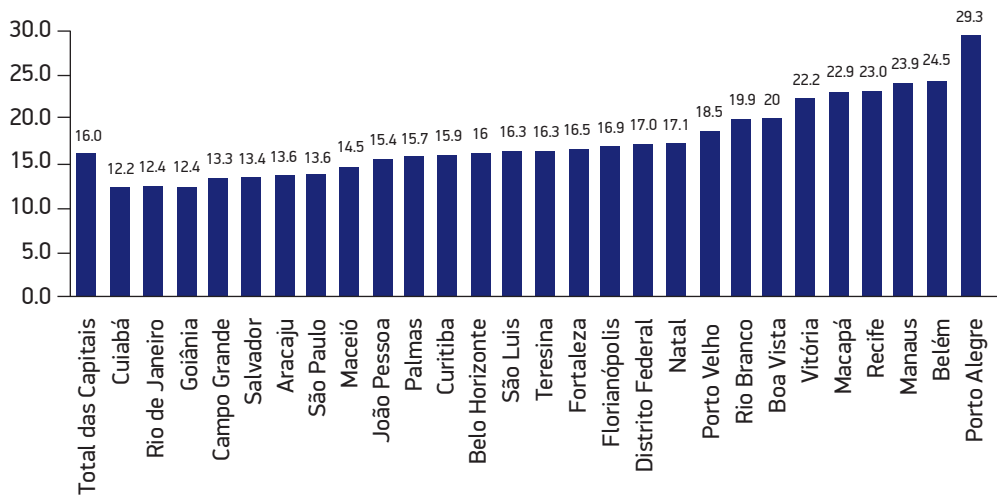


Figure 3. Percentage of schoolchildren of the 9th grade who were diagnosed with asthma at any point in their lives in Brazilian state capitals.

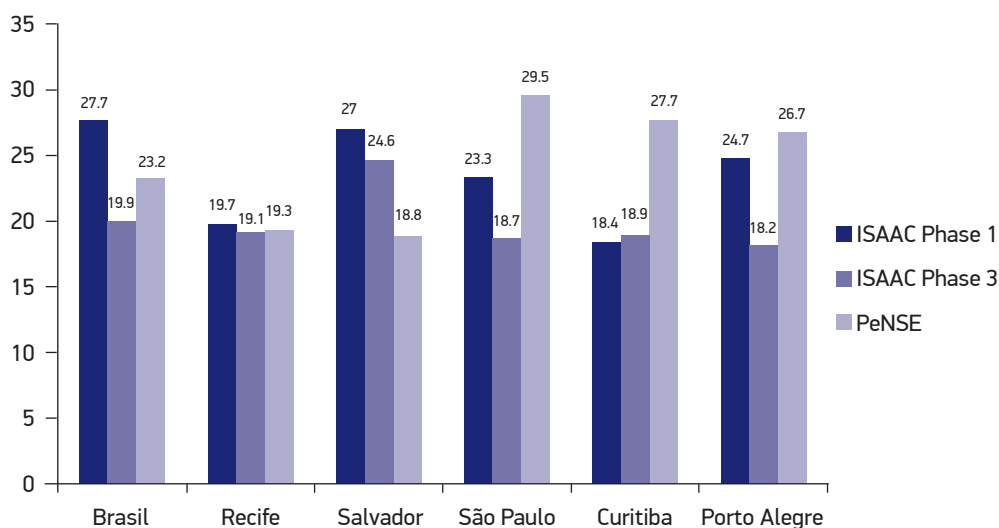


Figure 4. Prevalence of asthma symptoms among schoolchildren studied in Brazil (ISAAC Phase 1, Phase 3, PeNSE).

Of the Brazilian capitals included in PeNSE, five of them conducted ISAAC surveys in both of its phases. Out of these five, São Paulo (23.3%, 18.7% and 29.5%), Curitiba (18.4%, 18.9% and 27.7%) and Porto Alegre (24.7%, 18.2% and 26.7%) presented increased prevalence of asthma symptoms, in the surveys, among adolescents. Salvador was an exception, since prevalence presented a reduction from 27% (ISAAC Phase 1) to 18.8% (Figure 4). In this city, there is an extensive public program to control asthma (ProAR), in which patients with severe asthma are provided with free medical care and medications. Besides, health professionals are trained to prevent and control this disease, since 2003, and this reveals a significant impact on the reduced number of hospitalizations caused by asthma in the city²¹. Initiatives for asthma control have been observed in several Brazilian cities²², and they contributed for the reduced morbimortality by asthma registered by DATASUS indicators in the past few years; however, there are very clear regional inequalities²³.

In this study, the prevalence of asthma was higher among female students. These results are compatible with the ones from several studies, in which asthma is more prevalent among boys during childhood and among girls during adolescence^{24,25}. There seems to be an inverse relationship between age group and prevalence of asthma as to sex. This difference would possibly be a result of hormone and behavioral changes in female teenagers, genetic polymorphisms, among other factors that are still not identified²⁶.

The findings reported here indicate the magnitude of the morbidity caused by asthma at a point of the natural history of the disease, pointing out how important this public health issue is among adolescents in the whole country. The natural history of asthma is little understood, and it is not possible to transform the observations extracted from studies, especially longitudinal ones, into clear comprehension about the evolution of the disease and its prognosis. Asthma is a chronic condition that can begin during childhood. However, infants and preschool children with recurring respiratory sounds present with varied evolutions, which are possibly related to different subjacent immunopathological mechanisms that lead to limited airflow²⁷. Three out of four children with asthma in school age do not present with symptoms of the disease once they become middle-aged adults. The risk of asthma persistency increases according to the severity of the condition, with the sensitivity to allergens, smoking and the fact of being female²⁸. The probability of asthma remission from adolescence on is inversely related to the severity of the disease²⁹. However, it is clear that asthma is also a relevant health issue during adulthood. In a representative sample of the adult Brazilian population, 12.5% of the individuals reported asthma diagnosis, and 22.6% claimed to have had asthma symptoms in the past year³⁰.

Among the explanations for the expressive increase in allergic conditions in the past decades, one is based on the hygiene hypothesis, which interprets the increasing occurrence of allergic diseases as the effect of the reduced exposure to infections at early stages in life. This would be a consequence of the general improvement in sanitary conditions of the human population in general, especially in developed regions³¹. Some registers indicate that a large percentage of asthma cases is not exclusively attributed to atopy, and this percentage would be higher in developing countries^{32,33}, especially in rural areas³⁴. Little is known about the causes of non-atopic asthma³⁵, which include factors related to poverty³⁶, besides psychosocial aspects⁹. In order to

subsidize the planning of interventions to prevent and control asthma, it is important to better identify risk factors in diversified environments.

CONCLUSION

The results of PeNSE confirm prior evidence, which puts Brazil among the countries with the highest prevalence of asthma in the world. They also reveal that this prevalence is probably growing in the population of students. These results require further investigations, which can allow us to understand the determiners of the high levels of asthma in this age group. However, the set of existing evidence is not sufficient to define asthma as a relevant health problem in the Brazilian population.

REFERENCES

1. Global Initiative for Asthma. The global strategy for asthma management and prevention. GINA; 2002.
2. Organização Mundial da Saúde. Fact sheet N°307: Asthma [Internet]. Disponível em: <http://www.who.int/mediacentre/factsheets/fs307/en/>. (Acessado em 13 de junho de 2013).
3. Masoli M, Fabian D, Holt S, Beasley R. The global burden of asthma: executive summary of the GINA Dissemination Committee report. *Allergy* 2004; 59(5): 469-78.
4. O'Byrne PM. Global guidelines for asthma management: summary of the current status and future challenges. *Pol Arch Med Wewn* 2010; 120(12): 511-7.
5. Asher MI. Recent perspectives on global epidemiology of asthma in childhood. *Allergol Immunopathol (Madr)* 2010; 38(2): 83-7.
6. Cooper PJ, Rodrigues LC, Barreto ML. Influence of poverty and infection on asthma in Latin America. *Curr Opin Allergy Clin Immunol* 2012; 12(2): 171-8.
7. de Cassia Ribeiro Silva R, Assis AM, Cruz AA, Fiaccone RL, Dinnozeno S, Barreto ML, et al. Dietary Patterns and Wheezing in the Midst of Nutritional Transition: A Study in Brazil. *Pediatr Allergy Immunol Pulmonol* 2013; 26(1): 18-24.
8. Silva Rde C, Assis AM, Goncalves MS, Fiaccone RL, Matos SM, Barreto ML, et al. The prevalence of wheezing and its association with body mass index and abdominal obesity in children. *J Asthma* 2013; 50(3): 267-73.
9. Feitosa CA, Santos DN, Barreto do Carmo MB, Santos LM, Teles CA, Rodrigues LC, et al. Behavior problems and prevalence of asthma symptoms among Brazilian children. *J Psychosom Res* 2011; 71(3): 160-5.
10. Alves Gda C, Santos DN, Feitosa CA, Barreto ML. Community violence and childhood asthma prevalence in peripheral neighborhoods in Salvador, Bahia State, Brazil. *Cad Saude Publica* 2012; 28(1): 86-94.
11. Asher MI, Keil U, Anderson HR, Beasley R, Crane J, Martinez F, et al. International Study of Asthma and Allergies in Childhood (ISAAC): rationale and methods. *Eur Respir J* 1995; 8(3): 483-91.
12. Worldwide variation in prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema: ISAAC. The International Study of Asthma and Allergies in Childhood (ISAAC) Steering Committee. *Lancet* 1998; 351(9111): 1225-32.
13. Solé D, Vanna AT, Yamada E, Rizzo MC, Naspitz CK. International Study of Asthma and Allergies in Childhood (ISAAC) written questionnaire: validation of the asthma component among Brazilian children. *J Investig Allergol Clin Immunol* 1998; 8(6): 376-82.
14. Asher MI, Montefort S, Björkstén B, Lai CK, Strachan DP, Weiland SK, et al. Worldwide time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in childhood: ISAAC Phases One and Three repeat multicountry cross-sectional surveys. *Lancet* 2006; 368(9537): 733-43.
15. Chong Neto HJ, Rosário NA, Solé D. Asthma and Rhinitis in South America: How Different They are From Other Parts of the World. *Allergy Asthma Immunol Res* 2012; 4(2): 62-7.
16. Pearce N, Ait-Khaled N, Beasley R, Mallol J, Keil U, Mitchell E, et al. Worldwide trends in the prevalence of asthma symptoms: phase III of the International Study of Asthma and Allergies in Childhood (ISAAC). *Thorax* 2007; 62(9): 758-66.

17. Solé D, Melo KC, Camelo-Nunes IC, Freitas LS, Britto M, Rosario NA, et al. Changes in the prevalence of asthma and allergic diseases among Brazilian schoolchildren (13-14 years old): comparison between ISAAC Phases One and Three. *J Trop Pediatr* 2007; 53(1): 13-21.
18. Brasil. Instituto Brasileiro de Geografia e Estatística. Pesquisa Nacional de Saúde Escolar (PeNSE) – 2012. Rio de Janeiro (RJ): IBGE; 2012. Disponível em: http://portalsaude.saude.gov.br/portalsaude/arquivos/pdf/2013/Jun/20/pense_2012_arquivo_web.pdf (Acessado em 13 de outubro de 2013).
19. Organização Mundial da Saúde. Social determinants of health and well-being among young people. Health behaviour in school-aged children (HBSC) study: international report from the 2009/2010 survey. Copenhagen: WHO; 2012.
20. Sole D, Wandalsen GF, Camelo-Nunes IC, Naspitz CK. Prevalence of symptoms of asthma, rhinitis, and atopic eczema among Brazilian children and adolescents identified by the International Study of Asthma and Allergies in Childhood (ISAAC) - Phase 3. *J Pediatr (Rio J)* 2006; 82(5): 341-6.
21. Souza-Machado C, Souza-Machado A, Franco R, Ponte EV, Barreto ML, Rodrigues LC, et al. Rapid reduction in hospitalisations after an intervention to manage severe asthma. *Eur Respir J* 2010; 35(3): 515-21.
22. Fontes MJ, Affonso AG, Calazans GM, de Andrade CR, Lasmar LM, Nader CM, et al. Impact of an asthma management program on hospitalizations and emergency department visits. *J Pediatr (Rio J)* 2011; 87(5): 412-8.
23. Souza-Machado C, Souza-Machado A, Cruz AA. Asthma mortality inequalities in Brazil: tolerating the unbearable. *ScientificWorldJournal* 2012; 2012: 625829.
24. Mandhane PJ, Greene JM, Cowan JO, Taylor DR, Sears MR. Sex differences in factors associated with childhood and adolescent-onset wheeze. *Am J Respir Crit Care Med* 2005; 172(1): 45-54.
25. Subbarao P, Mandhane PJ, Sears MR. Asthma: epidemiology, etiology and risk factors. *CMAJ* 2009; 181(9): E181-90.
26. Anthracopoulos MB, Pandiora A, Fouzas S, Panagiotopoulou E, Liolios E, Priftis KN. Sex-specific trends in prevalence of childhood asthma over 30 years in Patras, Greece. *Acta Paediatr* 2011; 100(7): 1000-5.
27. Bisgaard H, Bønnelykke K. Long-term studies of the natural history of asthma in childhood. *J Allergy Clin Immunol* 2010; 126(2): 187-97; quiz 98-9.
28. Sears MR, Greene JM, Willan AR, Wiecek EM, Taylor DR, Flannery EM, et al. A longitudinal, population-based, cohort study of childhood asthma followed to adulthood. *N Engl J Med* 2003; 349(15): 1414-22.
29. Bousquet J, Mantzouranis E, Cruz AA, Ait-Khaled N, Baena-Cagnani CE, Bleecker ER, et al. Uniform definition of asthma severity, control, and exacerbations: document presented for the World Health Organization Consultation on Severe Asthma. *J Allergy Clin Immunol* 2010; 126(5): 926-38.
30. To T, Stanojevic S, Moores G, Gershon AS, Bateman ED, Cruz AA, et al. Global asthma prevalence in adults: findings from the cross-sectional world health survey. *BMC Public Health* 2012; 12: 204.
31. Strachan DP. Family size, infection and atopy: the first decade of the "hygiene hypothesis". *Thorax* 2000; 55(1): S2-10.
32. Alcantara-Neves NM, Veiga RV, Dattoli VC, Fiaccone RL, Esquivel R, Cruz AA, et al. The effect of single and multiple infections on atopy and wheezing in children. *J Allergy Clin Immunol* 2012; 129(2): 359-67.
33. Figueiredo CA, Amorim LD, Alcantara-Neves NM, Matos SM, Cooper PJ, Rodrigues LC, et al. Environmental conditions, immunologic phenotypes, atopy, and asthma: new evidence of how the hygiene hypothesis operates in Latin America. *J Allergy Clin Immunol* 2013; 131(4): 1064-8.
34. Moncayo AL, Vaca M, Oviedo G, Erazo S, Quinzo I, Fiaccone RL, et al. Risk factors for atopic and non-atopic asthma in a rural area of Ecuador. *Thorax* 2010; 65(5): 409-16.
35. Bousquet J, Kiley J, Bateman ED, Viegi G, Cruz AA, Khaltayev N, et al. Prioritised research agenda for prevention and control of chronic respiratory diseases. *Eur Respir J* 2010; 36(5): 995-1001.
36. Barreto ML, Cunha SS, Fiaccone R, Esquivel R, Amorim LD, Alvim S, et al. Poverty, dirt, infections and non-atopic wheezing in children from a Brazilian urban center. *Respir Res* 2010; 11: 167.

Received on: 11/10/2013

Final version presented on: 02/11/2014

Accepted on: 02/12/2014