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**Educational aims**

The reader will come to appreciate that:

- Pediatric asthma in low-income countries (LMICs) is increasing, causing significant burden to both children and the health system.
- In several LMICs, the prevalence of pediatric asthma is similar to that of high income countries.
- In some LMICs, local strategies for asthma treatment, which includes providing essential asthma medication, have shown promising results.

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SUMMARY

Pediatric asthma has been increasing in LMICs (Low Middle-Income Countries), leading to an important burden for both children and national health systems. Implementing measures to achieve control are influenced by the degree of organization health systems have, the availability and affordability of essential asthma medications, and the effective implementation of asthma programs and asthma guidelines. In this review authors give an updated view of the current situation of these components of asthma management in LMICs.



## INTRODUCTION

Asthma is the most common chronic disease in children worldwide. Several studies have been published regarding childhood asthma in low and middle-income countries (LMICs). These countries are a diverse group of nations that contrast widely in terms of geographical dimensions, urbanization, income distribution, infrastructure, life styles, and health systems [1]. In a number of LMICs, public health data are difficult to obtain or are incomplete. Furthermore, heterogeneous methodology and outcome measures in epidemiologic studies, including individual or local (mis)interpretation of key terms, such as "wheezing", might also contribute to variability in pediatric asthma data from LMICs [2,3]. Recently,

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a Lancet commission on asthma highlighted the wide spectrum of the disease and the need to develop specific treatment approaches to each type of asthma, urging a better definition of the specific airway disease with targeted management options in order to get better disease outcomes [4]. This is an enormous challenge in LMICs where health needs usually exceed available resources. Consequently, it is important to understand the current epidemiology and management strategies in LMICs, in order to develop more targeted approaches for childhood asthma.

We aimed to provide and updated review on both epidemiological information and management strategies on pediatric asthma in LMICs. Due to the difficulties in diagnosing asthma in young children, this review focuses on children older than 5 years of age.

We searched for publications on epidemiology and management strategies in LMICs in PubMed and regional databases, as well as publications and information from the Global Asthma Network and the Global Initiative for Asthma. In some cases, we complemented our data by searching available online country-specific official healthcare public information and contacting their healthcare representatives by e-mail. Fig. 1 graphically depicts the elements that contribute to lower burden of asthma in LMICs.

## EPIDEMIOLOGY

Undeniably, the International Study of Asthma and Allergies in Childhood (ISAAC), has been the most important resource to provide worldwide comparable information on the epidemiology of pediatric asthma. The ISAAC Phase 3 research included 1.2 million children from 233 centers in 98 countries distributed in all WHO regions [5]. The main and most consistent findings of the study were the large variability of asthma prevalence between regions, continents, countries, and centers in the same country. Fig. 2 depicts the worldwide prevalence of asthma in children, according to ISAAC-3.

Country-wise, higher prevalences of asthma have been usually found in high-income countries, but also in some LMICs such as Brazil, South Africa and Costa Rica [6]. However, the overall prevalence of asthma symptoms seems more severe in less affluent nations [6] and among underprivileged communities of both developing and developed countries [7]. Local studies can illustrate this; a recent one, from Senegal, found that 62% of children with asthma had severe symptoms [8]. The other one, from Brazil, found that 11% of asthmatic school-age children fulfilled criteria for severe asthma, but 22% of all asthmatics had one or two severe asthma symptoms [9]. Other LMICs with an increased prevalence of severe asthma symptoms in children include Costa Rica, Uruguay, Peru, Panama, Kenya, Ethiopia and Nigeria [3].

Results from ISAAC phase 3 compared to ISAAC 1 also showed a rising in prevalence in LMICs, mostly in Latin American countries and some African Countries [6]. Several factors may account for this, particularly environmental changes associated with urbanization [10,11]. For instance, a study in 59 rural communities, from Ecuador, found a dose–response effect of increasing urbanization in the frequency of symptoms of asthma in children [12]; asthma prevalence was higher in communities connected to the national electrical grid compared to those not connected. Other important environmental exposures to consider, common in many LMICs, are domestic smoke-producing fuels and tobacco products, which are well-known risk factors for asthma exacerbations and respiratory morbidity [2,13]. The overuse of antibiotics, not only a problem in LMICs, is now recognized as another factor associated with an increasing asthma prevalence [14].

Data on pediatric asthma admissions in LMICs are very scarce. One of the few studies with information from different parts of the world found that Portugal had the lowest admission rates (<3 per 10,000) and Australia had the highest (56 per 10,000). The information was obtained on a country-by-country basis by direct enquiry, but authors were not able to obtain it in LMICs [15]. As WHO recognizes, in many LMICs, statistical and health information

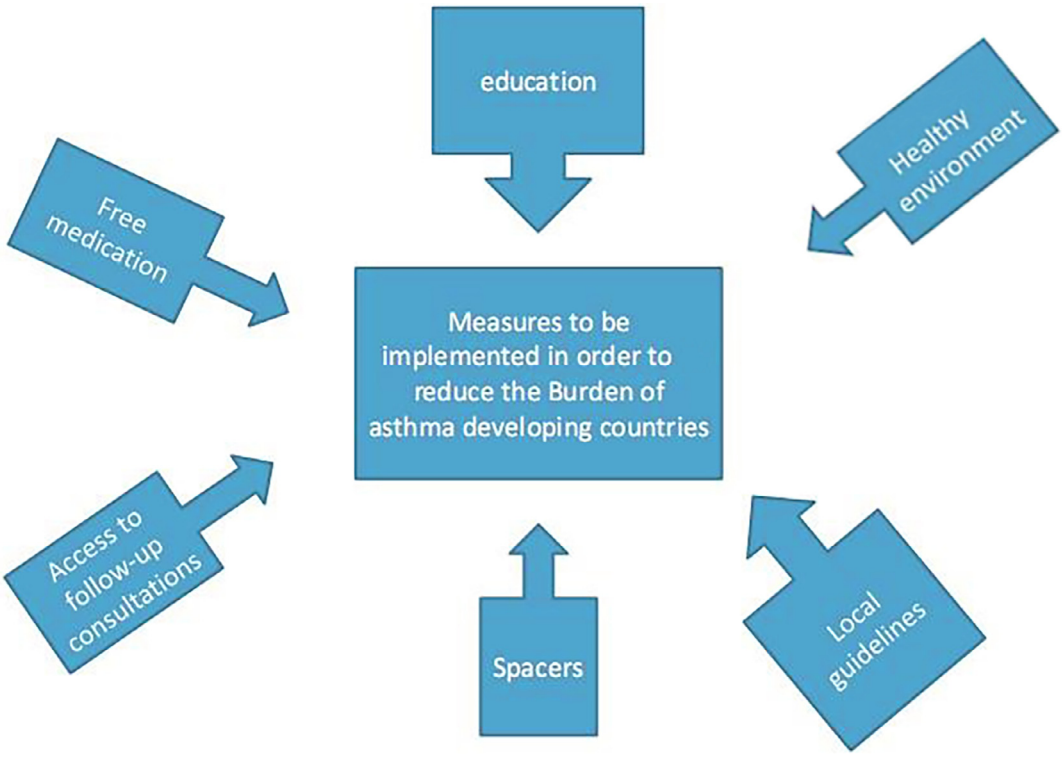


**Fig. 1.** Contributing factors to lower the burden of childhood asthma in LMICs.

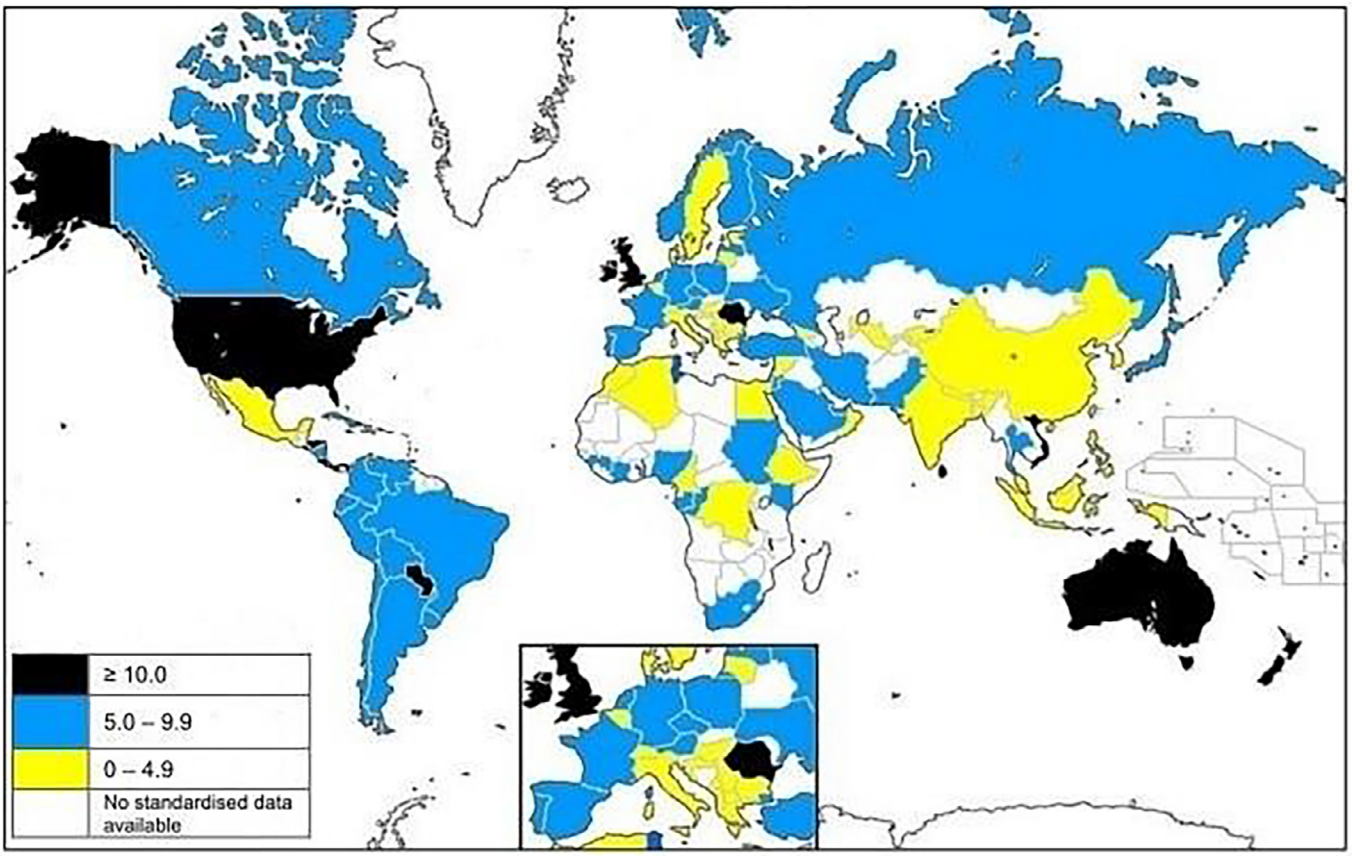


**Fig. 2.** World map of the prevalence of current asthma in children aged 13–14 years. Data from ISAAC Phase 3 reproduced with permission. Black regions on the map have the highest prevalence of asthma in children [percent of the population].

systems are weak, and the underlying empirical data may not be available or may be of poor quality [15]. Admission rates for childhood asthma in LMICs are situated within the same wide range of high-income countries. Admission numbers have shown a reduction over time in countries where access to essential asthma medication, that is, inhaled corticosteroids (ICS) and short-acting beta agonists (SABA) has increased through some form of subsidies [16–18]. According to a Brazilian study, the availability of ICS and SABA free-of-charge was the main reason that led to a reduction in asthma admissions, from 90 to 60 per 10,000 in a few years [17]. Similarly, in Costa Rica, along a 12–15-year period, a clear reduction in hospitalization and mortality due to asthma was seen with the introduction, at no cost, of ICS, and the start of a national asthma program [18]. Other studies based on national registries have found a similar trend once ICS and SABA have become available, with some exceptions [16]. For instance, in Chile, admissions were stable between 2001 and 2014 for children aged 10–15 years, but it doubled in children aged 6–9 years during the same period for unclear reasons. This may reflect the difficulty of diagnosing and treating younger children [19].

Respiratory viruses, especially the respiratory syncytial virus [RSV], have been described as risk factors for future asthma or exacerbations. The ubiquitous human rhinovirus type C (HRV-C) has recently gained particular attention for its association with subsequent asthma. For instance, a recent study from Costa Rica showed that HRV is a very important risk factor for exacerbations in previously sensitized asthmatic children, when compared to a non-sensitized group [20]. Unfortunately, virus monitoring is not common in LMICs to plan, prepare or promote better preventive measures against virus transmission.

When it comes to important asthma comorbidities, allergic rhinitis represents an additional unrecognized concern [21,22], since it is a well-known risk factor for poor asthma outcomes and up to 80% of asthmatic children and adolescents suffer from it. In LMICs, however, nasal corticosteroids are less frequently available as essential medicines, compared to ICS and SABA. The lack of nasal corticosteroids increases the number of emergency department visits and hospitalizations for asthma [23]. Different than rhinitis, obesity is an inflammatory, non-respiratory comorbidity affecting asthmatic adults, children and adolescents [24]. It has independently but steadily increased over recent decades, in both high-income countries and in LMICs [25] and a bi-directional causal relationship has been found between them [26]. Obesity is a risk factor for developing asthma and for more severe asthma, and asthma is also a risk factor for obesity in pediatric subjects. A recent national-level study in Brazilian adolescents even found that severe asthma is clearly associated with the metabolic syndrome [27]. These complex relationships between asthma, obesity and metabolic imbalance are not yet clearly understood, highlighting the need for more studies to investigate the epidemiological impact of this association. Other co-morbidities, such as anxiety, mood disorders or gastroesophageal reflux disease are beyond the scope of this review.

Asthma mortality is a rare event in children, worldwide. The ISAAC study (Phase 3) provided relevant and specific pediatric asthma mortality information along 2 different points in time from countries in most continents. It found that child mortality, similar to adults, showed a decrease in time but, also, that mortality estimates in children are directly associated with severe asthma symptoms. Similarly, it found that numbers vary among LMICs with

values as low as 0.01 per 1,000,000 (Chile) and as high as 0.44 per 1,000,000 (Panama), with middle values for Costa Rica, Mexico and Thailand [16]. Unfortunately, the study summarizing worldwide mortality data is a decade old, and updated information on both actual and mortality trend is lacking.

Recently, the Global Asthma Report 2014 found a higher age-standardized asthma mortality rate, for ages 5–34 years, in LMICs, compared to high-income countries [28]. Nonetheless, the specific contribution of children and adolescents to those numbers is difficult to establish through mortality statistics, which include them in the same group with younger adults. Two studies from Brazil exemplify this confusion; the first study found a mortality rate of 0.47 per 1,000,000 in 2007 (age group 5–34 years) [29] while the other found a mortality rate of 0.15 per 1,000,000 (age group 5–19 years) for the same year [30]. Therefore, care should be taken when interpreting mixed child–adult data.

## ASTHMA TREATMENT: (STILL) AN UNMET NEED

To reduce the life-long burden of asthma by lowering the risk of exacerbations, and the risk for hospitalization, efforts should be intensified on ways to improve the control of asthma symptoms. A relevant and critical issue related to asthma among LMICs is the availability and affordability of essential asthma medications [31]. According to global estimates, medicines account for over 50% of health spending in LMICs, up to three times more than high-income countries. For the majority of the population in developing countries, medicines come second to food in family expenditures [32]. Among the 300 million people that suffer from asthma worldwide, many have difficulties in accessing essential asthma medicines. In terms of affordability, a study from Mexico estimated the amount a patient with controlled asthma would spend per year was approximately 1.7 times a monthly minimum wage. In cases of uncontrolled, severe asthma, these figures could rise to six times the minimum monthly wage [33]. In terms of medication availability, a study that included 52 LMICs found that 37 (71%) did not have SABA and/or ICS on their list of essential medicines, as recommended by the WHO [34]. The same study demonstrated that, at retail-pharmacies, generic ICS were available in 19% and 46% of public and private hospitals, respectively. The cost of a single beclomethasone inhaler device (100 mcg/dose) was rather expensive: from half a day's wages (Afghanistan), to over 5 days of work (El Salvador, Ethiopia, Madagascar and Malawi), or even to 14 days of work (Madagascar) [34]. There are successful initiatives toward offering asthma medication at lower costs under universal healthcare policies. These policies can have an important impact on both asthma control and the economy of the involved families as well. That was the case for a group of severe asthmatic patients seen in follow-up at a tertiary-care center in Brazil whom were given medicines and multidisciplinary care at no cost. After one year of follow-up, their family net income had recovered the equivalent to seven times the minimum wage, considering the reduction in both, parent's lost days of work, and the savings in asthma expenses [35]. In contrast, a study in the U.S.A. found that, when co-payments doubled, patients with asthma reduced their medication by 32% [36]. It has been demonstrated that an irregular supply of asthma medicines due to affordability issues, leads to higher risk for non-scheduled emergency visits, hospitalization and school absenteeism in asthmatic children [37].

Increasing access to proper treatment in LMICs is feasible and cost-effective, reducing direct and indirect costs and increasing patient's productivity and quality of life. How this access (availability and affordability) is achieved within LMICs, differs among sub-region and healthcare system. In approximately half of Latin American countries, the universal healthcare coverage model prevails. They provide salbutamol and beclomethasone to asthmatic patients, either once a prescription has been filled (Brazil, Costa Rica) or only after the diagnosis has been confirmed by a physician and through a specific formulary (Chile). Access to regular follow-up is also crucial to achieve adequate asthma control. All asthmatic children should have regular consultations, and those with severe asthma should be seen more frequently. Questions related to asthma control should be reviewed at each visit, and lung function tests should also be requested if available. Spacers are mandatory in children, to achieve an adequate medication delivery to the lungs using metered dose inhaler [MDI]-based drugs. The use of spacers, however, adds further costs, either to the health system, to the families or both. Very few LMICs offer spacers, at reduced or no cost, along with asthma medication. Parents must buy them or improvise them at home. Well-constructed valve spacers are the best option, although studies have proven that a low-cost adapted plastic bottle-spacer could reasonably substitute commercial ones [38]. Unfortunately, scarce data on these additional but fundamental aspects of asthma management (i.e., frequency of visits, lung function testing and spacers) is available from LMICs.

## NATIONAL ASTHMA STRATEGIES, ASTHMA GUIDELINES, CLINICAL PATHWAYS AND INTEGRATED CARE GUIDELINES: NOT MANY IN PLACE, NOT MANY IN USE

From the public health standpoint, population-based Asthma Control strategies have demonstrated the greatest impact on reducing the burden of asthma [38].

Global guidelines for asthma are available and can be adapted to the local context. The International Union Against Tuberculosis and Lung Diseases (IUATLD) Asthma Guidelines, and the GINA guidelines are used in several LMICs [39] but must be adapted to the local and cultural situation [40], and medications must be available and/or affordable. Moreover, guidelines have been based mostly, on clinical trials carried out in high-income countries. It is important to note that the IUATLD asthma guidelines, since its inception, have positioned for less affluent countries. They have included an approach based on effective practices with tuberculosis case-management, adapted to asthma, and have progressively added successful local experiences to the newer editions of the guidelines; unfortunately, the last edition was published in 2008 [41].

Developing or fully updating evidence-based guidelines is a time and resource-consuming task as is the implementation of them. A few LMICs have followed the lead and adapted international guidelines (mostly GINA's) or developed their own, while others have given some importance to asthma care within the Integrated Management of Childhood Illness program (respiratory diseases module), focusing only on acute care [42]. Some LMICs have promoted, at primary care level, the use of the Integrated Management of Adolescent and Adult Illness [43], the use of integrated care pathways (which include multidisciplinary care plans) [44], and non-disease specific respiratory guidelines (to optimize the opportunity of identifying other prevalent respiratory diseases) [45]. The South African experience with this different approach to traditional asthma care is very promising [45], albeit the methodological quality of its guidelines has raised concerns [46].

According to the Global Asthma Network public registry, from a list of 124 LMICs [1], only thirty-two countries (25,8%) have in use, at least, one pediatric asthma management guideline developed at national level [47]. Unfortunately, most were published more than 5 years ago and have not been updated. LMICs are distributed in 11 geographical sub-regions, and South America is the one with a greater proportion of guidelines (8 guidelines in 10 countries),

and both Central Africa and the Caribbean are sub-regions without a single guideline [1,47]. Although these numbers, based on published information, may be outdated, the number of guidelines is far from optimal.

Despite the importance of asthma guidelines, the existence of a national asthma program or strategy can really make the difference. However, only five developing countries (4%) have them in place. In larger LMICs, there are some successful local strategies (city, district or province level), without reaching a country-wide impact. The city of Salvador (Bahia, Brazil) [48], and the Anhui Province, China [49], are two examples of bigger geographical areas with their own asthma strategy. The former was locally developed and maintained, and the latter was financed by the World Bank and supported by the IUTLD and local authorities. Smaller cities can also achieve good outcomes with an asthma program; a study in Itabira (Brazil), found a significant difference in emergency visits and regular use of ICS in asthmatic children within the city asthma program, compared to those not in the program [50]. Table 1 lists the number of asthma guidelines and/or asthma programs by LMICs sub-regions [1].

Two other studies illustrated difficulties and successful experiences of implementing asthma guidelines/programs in LMICs during the last decade [52,53]. The experiences in Benin [54] and Sudan [55], supported by the IUATLD and the World Bank, demonstrated that political will, an outcome-oriented plan, education (healthcare providers and patients alike), and availability of both low-cost ICS and SABA can achieve important health improvements in asthmatic patients. Other experiences have not been successful due to physician-related barriers, patient mistrust on continuous medication and lack of government strategic support [52,50]. To tackle these difficulties requires intense, persistent and concentrated efforts not always found in developing countries [56,57].

The lack of an asthma management program/strategy in many LMICs contributes to an insufficient registry of both prescription patterns and patient characteristics. This is particularly important in the outpatient setting as it makes implementing and proving cost-efficient improvements in asthma care more challenging if there is a lack of baseline information from which to benchmark change. Inadequate training in the diagnosis and management is common, resulting in overuse of some drugs, such as oral corticosteroids or salbutamol, underuse of ICS and spacers, and poor emphasis on the patient's asthma education [58,59].

**Table 1**
Number of Asthma Guidelines and Pediatric Asthma Programs in LMICs by geographical sub-region.

| Continent regions | Number of Countries | Number of Asthma Guidelines | National Asthma Strategy/Program |
|---|---|---|---|
| *Africa* | | | |
| North Africa | 7 | 1 | 0 |
| Southern Africa | 11 | 1 | 0 |
| Central Africa | 7 | 1 | 0 |
| East Africa | 12 | 2 | 0 |
| West Africa | 15 | 1 | 0 |
| *Asia* | | | |
| East Asia | 22 | 4 | 0 |
| South Asia | 9 | 1 | 1 |
| Western Asia | 13 | 1 | 1 |
| *Latin America/Caribbean* | | | |
| Caribbean | 8 | 0 | 0 |
| Mexico/Central America | 6 | 2 | 2 |
| South America | 11 | 6 | 1 |

Source derived from: [1,47,51].

## CONCLUSION

The high burden of childhood asthma worldwide is more pronounced in LMICs and strategies to strengthen diagnosis and management should be implemented. Successful initiatives should be followed or adapted accordingly, guidelines and essential asthma medicines, ICS, SABA and spacers, should be provided universally. Health professionals should have access to continued education to appropriate asthma management.

## DIRECTIONS FOR FUTURE RESEARCH

- Epidemiological studies on asthma admissions and mortality in children from LMICs.
- Studies on efficacy of asthma programs adapted to LMICs.

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## References

[1] United Nations DoEaSA, Development Policy and Analysis Division. World Economic Situation and Prospects 2018: United Nations Publication; 2018 2018. 206.
[2] Zar HJ, Levin ME. Challenges in treating pediatric asthma in developing countries. Pediatric Drugs 2012;14(6):353–9.
[3] Pearce N, Aït-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.
[4] Pavord ID, Beasley R, Agusti A, Anderson GP, Bel E, Brusselle G, et al. After asthma: redefining airways diseases. The Lancet 2018;391(10118):350–400.
[5] Mallol J, Crane J, von Mutius E, Odhiambo J, Keil U, Stewart A, et al. The International Study of Asthma and Allergies in Childhood (ISAAC) Phase Three: a global synthesis. Allergol Immunopathol (Madr) 2013;41(2):73–85.
[6] Lai CKW, Beasley R, Crane J, Foliaki S, Shah J, Weiland S. Global variation in the prevalence and severity of asthma symptoms: Phase Three of the International Study of Asthma and Allergies in Childhood (ISAAC). Thorax 2009;64(6):476–83.
[7] Fattore GL, Santos CA, Barreto ML. Social determinants of childhood asthma symptoms: an ecological study in urban Latin America. J Community Health 2014;39(2):355–62.
[8] Hooper LG, Dieye Y, Ndiaye A, Diallo A, Fan VS, Neuzil KM, et al. Estimating pediatric asthma prevalence in rural Senegal: a cross-sectional survey. Pediatr Pulmonol 2017;52(3):303–9.
[9] Simões SDM, Cunha SSD, Barreto ML, Cruz ÁA. Distribution of severity of asthma in childhood. J Pediatr 2010;86(5):417–23.
[10] Ellwood P, Asher MI, Billo NE, Bissell K, Chiang C-Y, Ellwood EM, et al. The Global Asthma Network rationale and methods for Phase I global surveillance: prevalence, severity, management and risk factors. Eur Respir J 2017;49(1):1601605.
[11] Ponte EV, Cruz AA, Athanazio R, Carvalho-Pinto R, Fernandes FLA, Barreto ML, et al. Urbanization is associated with increased asthma morbidity and mortality in Brazil. Clin Respir J 2018;12(2):410–7.
[12] Rodriguez A, Vaca M, Oviedo G, Erazo S, Chico ME, Teles C, et al. Urbanisation is associated with prevalence of childhood asthma in diverse, small rural communities in Ecuador. Thorax 2011;66(12):1043–50.
[13] Padhi BK, Padhy PK. Domestic fuels, indoor air pollution, and children's health. Ann N Y Acad Sci 2008;1140(1):209–17.
[14] Metsala J, Lundqvist A, Virta LJ, Kaila M, Gissler M, Virtanen SM. Prenatal and post-natal exposure to antibiotics and risk of asthma in childhood. Clin Exp Allergy 2015;45(1):137–45.
[15] Duke T, Yano E, Hutchinson A, Hwaihwanje I, Aipit J, Tovilu M, et al. Large-scale data reporting of paediatric morbidity and mortality in developing countries: it can be done. Arch Dis Child 2016;101(4):392–7.
[16] Anderson H, Gupta R, Kapetanakis V, Asher M, Clayton T, Robertson C, et al. International correlations between indicators of prevalence, hospital admissions and mortality for asthma in children. Int J Epidemiol 2008;37(3):573–82.
[17] Comaru T, Pitrez PM, Friedrich FO, Silveira VD, Pinto LA. Free asthma medications reduces hospital admissions in Brazil (Free asthma drugs reduces hospitalizations in Brazil). Respir Med 2016;121:21–5.
[18] Soto-Martinez M, Avila L, Soto N, Chaves A, Celedon JC, Soto-Quiros ME. Trends in hospitalizations and mortality from asthma in Costa Rica over a 12- to 15-year period. J Allergy Clin Immunol Pract 2014;2(1):85–90.
[19] Herrera AM, Cavada ChG, Mañalich J. Hospitalizaciones por asma infantil en Chile: 2001–2014. Rev Chilena Pediatr 2017;88(5):602–7.

[20] Soto-Quiros M, Avila L, Platts-Mills TA, Hunt JF, Erdman DD, Carper H, et al. High titers of IgE antibody to dust mite allergen and risk for wheezing among asthmatic children infected with rhinovirus. J Allergy Clin Immunol 2012;129 (6). 1499–1505. e5.
[21] Van Den Nieuwenhof L, Schermer T, Bosch Y, Bousquet J, Heijdra Y, Bor H, et al. Is physician-diagnosed allergic rhinitis a risk factor for the development of asthma? Allergy 2010;65(8):1049–55.
[22] Padilla J, Uceda M, Ziegler O, Lindo F, Herrera-Pérez E, Huicho L. Association between allergic rhinitis and asthma control in Peruvian school children: a cross-sectional study. Biomed Res Int 2013;2013.
[23] Lasmar L, Fontes MJ, Mohallen MT, Fonseca AC, Camargos P. Wheezy child program: the experience of the Belo Horizonte pediatric asthma management program. World Allergy Organ J 2009;2(12):289.
[24] Roncada C, de Oliveira SG, Cidade SF, Sarria EE, Mattiello R, Ojeda BS, et al. Burden of asthma among inner-city children from Southern Brazil. J Asthma 2016;53(5):498–504.
[25] Mistry SK, Puthussery S. Risk factors of overweight and obesity in childhood and adolescence in South Asian countries: a systematic review of the evidence. Public Health 2005;129(3):200–9.
[26] Leinaar E, Alamian A, Wang L. A systematic review of the relationship between asthma, overweight, and the effects of physical activity in youth. Ann Epidemiol 2016;26(7). 504–510.e6.
[27] Kuschnir FC, Felix MMR, Kuschnir MCC, Bloch KV, Jordão EADOC, Solé D, et al. Severe asthma is associated with metabolic syndrome in Brazilian adolescents. J Allergy Clin Immunol 2018.
[28] Group GANS. The Global Asthma Report 2014. Auckland, New Zeeland: Global Asthma Network; 2014.
[29] Graudenz GS, Carneiro DP, Vieira RDP. Trends in asthma mortality in the 0- to 4-year and 5- to 34-year age groups in Brazil. J Bras Pneumol 2017;43:24–31.
[30] Prietsch SOM, Zhang L, Catharino AR, Vauchinski L, Rodrigues FE. Asthma mortality among Brazilian children up to 19 years old between 1980 and 2007. J Pediatr 2012.
[31] Ait-Khaled N, Enarson DA, Bissell K, Billo N. Access to inhaled corticosteroids is key to improving quality of care for asthma in developing countries. Allergy 2007;62(3):230–6.
[32] World Health Organization. WHO guideline on country pharmaceutical pricing policies, 2015. Geneva, Switzerland, 2015.
[33] Martínez GGCA, Díaz SN, Rodríguez GG. Costos derivados de la atención médica del asma en un grupo de niños del Noreste de México. Rev Alerg Mex 2007;54(3):82–5.
[34] Lessing CMC, Bissell K. The availability, pricing and affordability of three essential asthma medicines in 52 low-and middle-income countries. Pharmacoeconomics 2013;31(11):1063–82.
[35] Franco R, Nascimento HFD, Cruz A, Santos A, Souza-Machado C, Ponte EV, et al. The economic impact of severe asthma to low-income families. Allergy 2009;64(3):478–83.
[36] Goldman DP, Joyce GF, Escarce JJ, et al. Pharmacy benefits and the use of drugs by the chronically ill. JAMA 2004;291(19):2344–50.
[37] Patel MR, Brown RW, Clark NM. Perceived parent financial burden and asthma outcomes in low-income, urban children. J Urban Health 2013;90(2):329–42.
[38] Rodriguez-Martinez CE, Sossa M, Lozano JM. Commercial versus home-made spacers in delivering bronchodilator therapy for acute therapy in children. Cochrane Library 2008.
[39] IUATLD. Applying the Union model to asthma. International Union against Tuberculosis and Lung Disease; 2018. Available from https://www.theunion.org/what-we-do/technical-assistance/lung-health-and-ncds/asthma.
[40] Boulet L-P, FitzGerald JM, Levy ML, Cruz AA, Pedersen S, Haahtela T, et al. A guide to the translation of the Global Initiative for Asthma (GINA) strategy into improved care. Eur Respir J 2012;39(5):1220–9.
[41] Aït-Khaled N, Enarson DA, Chen-Yuan Ch, Marks G, Bissel K. Management of asthma: a guide to the essentials of good clinical practice. 3rd ed. Paris, France: International Journal of Tuberculosis and Lung Disease; 2008.
[42] Ministério da Saúde OP-AdS, Fundo das Nações Unidas para a Infância. Manual of procedures: IMCI Child: 2 months to 5 years: Editora MS; 2017.
[43] Ashwin V, Andrew E, Stephen DL, Sandy G, Manzi A, Neil G, et al. Integrated care as a means to improve primary care delivery for adults and adolescents in the developing world: a critical analysis of Integrated Management of Adolescent and Adult Illness (IMAI). BMC Med 2014;12(6).
[44] Bousquet J, Addis A, Adcock I, Agache I, Agusti A, Alonso A, et al. Integrated care pathways for airway diseases (AIRWAYS-ICPs). Eur Respir J 2014;44 (2):304–23.
[45] English RG, Bateman ED, Zwarenstein MF, Fairall LR, Bheekie A, Bachmann MO, et al. Development of a South African integrated syndromic respiratory disease guideline for primary care. Prim Care Respir J 2008;17(3):156–63.
[46] Machingaidze S, Zani B, Abrams A, Durao S, Louw Q, Kredo T, et al. Series: Clinical Epidemiology in South Africa. Paper 2: Quality and reporting standards of South African primary care clinical practice guidelines. J Clin Epidemiol 2017;83:31–6.
[47] Network GA. Asthma Management Guidelines for Children: Globalasthma network.org; 2018 [Available from: http://www.globalasthmanetwork.org/management/child.php.
[48] Cruz A, Souza-Machado A, Franco R, Souza-Machado C, Ponte E, Santos P, et al. The impact of a program for control of asthma in a low-income setting. World Allergy Organ J 2010;3(4):167–74.
[49] Kan XH, Chiang CY, Enarson DA, Rao HL, Chen Q, Ait-Khaled N, et al. Asthma as a hidden disease in rural China: opportunities and challenges of standard case management. Public Health Action 2012;2(3):87–91.
[50] Andrade W, Camargos P, Lasmar L, Bousquet J. A pediatric asthma management program in a low-income setting resulting in reduced use of health service for acute asthma. Allergy 2010;65(11):1472–7.
[51] Network GA. The Global Asthma Report 2014. Auckland, New Zealand: Global Asthma Network; 2014.
[52] Lalloo U, Walters R, Adachi M, De Guia T, Emelyanov A, Fritscher C, et al. Asthma programmes in diverse regions of the world: challenges, successes and lessons learnt. Int J Tuberc Lung Dis 2011;15(12):1574–87.
[53] Chiang CY, Ait-Khaled N, Bissell K, Enarson DA. Management of asthma in resource-limited settings: role of low-cost corticosteroid/beta-agonist combination inhaler. Int J Tuberc Lung Dis 2015;19(2):129–36.
[54] Ade G, Gninafon M, Tawo L, Aït-Khaled N, Enarson D, Chiang C. Management of asthma in Benin: the challenge of loss to follow-up. Public Health Action 2013;3(1):76–80.
[55] El Sony A, Chiang C, Malik E, Hassanain S, Hussien H, Khamis A, et al. Standard case management of asthma in Sudan: a pilot project. Public Health Action 2013;3(3):247–52.
[56] Asher I, Haahtela T, Selroos O, Ellwood P, Ellwood E, Global Asthma Network Study G. Global Asthma Network survey suggests more national asthma strategies could reduce burden of asthma. Allergol Immunopathol 2017;45 (2):105–14.
[57] Tan WC, Aït-Khaled N. Dissemination and implementation of guidelines for the treatment of asthma. Int J Tuberc Lung Dis 2006;10(7):710–6.
[58] Arıkan-Ayyıldız Z, Işık S, Çağlayan-Sözmen Ş, Anal Ö, Karaman Ö, Uzuner N. Efficacy of asthma education program on asthma control in children with uncontrolled asthma. Turk J Pediatr 2016;58(4).
[59] Jose BP, Camargos PA, Cruz Filho AA, Correa Rde A. Diagnostic accuracy of respiratory diseases in primary health units. Rev Assoc Med Bras 2014;60 (6):599–612.