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GAPP Italy: “A survey on asthma on Italian physicians and patients”

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SUMMARY

Guidelines recognize the importance of achieving and maintaining asthma control: the treatment strategies now available allow the control of the great majority of patients with asthma but despite many efforts only 5% of patients achieve guideline-defined asthma control. The GAPP (The Global Asthma Physician and Patient survey) is a global quantitative survey with the aim of identifying barriers to optimal management of asthma. Physicians and adult patients with persistent asthma have been interviewed with closed-ended questions questionnaire. This study has been conducted in 16 countries. In Italy the survey has revealed that physicians prescribe a combination of ICS and LABA more often in the other countries. They consider ICS the first-line treatment for mild persistent asthma. They are not completely satisfied with ICS because of local and systemic side effects. At the same time, the reason why patients change asthma medication is the potential for side effects. The two group responses were found to differ about the time spent discussing how to improve the management of asthma. A better communication between physician and patient and a new treatment option with lower side effect profile could be the key point to achieve asthma control in a larger number of patients.

Introduction

During the last 25 years a large number of studies on asthma have been made with the aim to improve the knowledge of this worldwide disease. Nowadays we have a clear global and regional view of asthma deriving from the two main important epidemiological studies, the ISAAC (1) and the ECRHS (2).

Relevant advances in the pathogenesis of asthma have been achieved: starting from the knowledge of inflammatory mechanisms (3), through the smooth muscle pathophysiology (4, 5), to the new insight into remodeling (6). At present asthma diagnosis is mainly based on clinical features and on spirometric lung function evaluation, but other

new instruments seem to be useful, such as induced-sputum, eNO, pulmonary function in infants, HRCT, etc.

The treatment strategies now available allow the control of a great majority of patients affected by asthma; new drugs such as anti-IgE, are important in severe asthma therapy. Moreover, the Global Initiative for Asthma guidelines (GINA), its successive updating (7) and National Institute of Health guidelines (NIH) (8) have been published with the aim to divulge a clear trace in the management and treatment of this world spread disease. Unfortunately, despite these tools, only 5% of patients achieve guideline-defined asthma control (9). Four important studies have been conducted to evaluate how asthmatic patients are assessed and treated in real life, covering almost every continent of the world.

The AIRE study (Asthma Insight and Reality in Europe) revealed that asthma has an important impact on different daily life aspects (9, 10).

A large survey has been conducted in the United States to explore asthma prevalence, the frequency and severity of symptoms, the use of emergency care, quality of life, and quality of care issues. The study revealed that the asthma management has not reached the goals established by the National Heart, Lung, and Blood Institute (NHLBI) (11). The same findings have been shown in the south of America by the AIRLA survey (12).

Despite the strong efforts, there is evidence that asthma is far from a good control in the great majority of cases and it seems that part of the energy invested in its management is wasted in some elements of the system. For these reasons and because of the unanswered questions from AIRE and the other studies it has been necessary to develop another study, the Global Asthma Physician and Patient (GAPP) survey, that was designed to uncover asthma attitudes and treatment practices among physicians and patients, with the goal of identifying barriers to optimal management (Fig. 1).

The GAPP is a global quantitative survey with the aim to evaluate the same themes both in patients and physicians by asking similar questions in the two groups. It has been conducted during 2005 in 16 countries (Australia, Belgium, Brazil, Canada, France, Germany, Ireland, Italy, Japan, the Netherlands, Poland, South Africa, Spain, Switzerland, the UK and the US).

This survey was announced and supported by the World Allergy Organization (WAO) and the American College of Allergy, Asthma and Immunology (ACAAI) scientists. The main objectives were:

- Enhance understanding and awareness of likely contributors to suboptimal asthma management.
- Explore the content and dynamics of physician-patient communications.
- Enhance treatment compliance and outcomes.

Physicians (including primary care physicians/family practitioners, pulmonologists and allergists) and adults affected by persistent asthma have been interviewed with a 20-minute questionnaire with closed-ended questions.

The key global findings regard the compliance of patients that can be enhanced by improving the communication between physician and patients and through their education on asthma. Moreover, this important goal can be achieved by administering treatment options with lower side effect profiles.

The GAPP survey in Italy

Patients and methods

5,480 physicians and patients worldwide have been evaluated.

In Italy a group of 105 adults affected by asthma has been recruited and screened from Harris Interactive online panel; the patients were at least 18 years aged.

101 physicians were recruited and screened from existing national databases. All of them used to treat adults and 51 were generalists (including general practitioners and internal medicine practitioners) and 50 were specialists (allergists and pulmonologists). To be included in this study they were required to be practicing medicine at least for three up to thirty years, see at least three adult asthmatic patients per week and write at least one asthma treatment prescription per week.

The number of interviews was determined to guarantee statistical significance when the data were measured globally and in each country. The interviews were performed by experienced interviewers in their native language. Before being used, the questionnaire was tested on 10 people from each country to ensure that the questions had been understood.

The patients were asked screening questions to ensure that they were affected from asthma. Chronic obstructive pulmonary diseases patients were not excluded.

Table 1 and table 2 contain patients' and physicians' questionnaire. Patients and physicians were not requested to sign a specific informed consent, however they agreed their responses could be used in public in an aggregate, anonymous and confidential way.

Figure 1 - Global key findings of GAPP Survey.



Data management and analysis

In Italy, as well as in the other countries except for USA, the data were not weighed. These samples are not probability samples: since simple size is 100 the margin of error was ± 10 .

Results

Mild, moderate and severe asthma show a homogeneous distribution globally in the study, both in Europe and in Italy when the patients' self-reported perception of asthma severity is considered. The 50% of patients describe their

Table 1 - Survey questions for patients

Q1a	Which type of doctor or healthcare professional do you usually see to treat your asthma?
Q2a	Overall, based on your symptoms, how would you describe your asthma? a) Mild b) Moderate c) Severe
Q3a	Overall, how much has your asthma limited your ability to do your daily activities? a) A great deal b) Somewhat c) Not much d) Not at all
Q4a	During the past 12 months, have you [insert options] for your asthma? a) Made unscheduled calls to your doctor because of your asthma b) Made unscheduled visits to your doctor because of your asthma c) Gone to a hospital emergency room because of your asthma d) Been admitted to hospital because of your asthma
Q5a	Which of the following medications are you currently taking to treat your asthma?*
Q6a	Overall, how satisfied or dissatisfied are you with the following features of you current asthma medication(s)? a) Ease of use d) How many times per day you take it b) Effectiveness e) Potential for side effects c) Fast acting f) Safety
Q7a	Since being diagnosed with asthma, have you ever switched from one medication to another or discontinued an asthma medication because...? a) Your asthma symptoms lessened or went away b) You experienced side effects c) You were concerned about the potential for side effects d) The asthma medication was too expensive e) The asthma medication was difficult or inconvenient to use
Q8a	After you doctor told you your asthma can be triggered by allergies, has he or she...? a) Told you how to avoid allergic triggers b) Explained that you should be on continuous preventer medication c) Referred you to an allergist or other specialist
Q9a	Who at your doctor's office typically explains your treatment options and techniques for successful management of your asthma? a) Treating physician b) Nurse c) No one
Q10a	During a typical visit with your doctor or health care professional, what percentage of the time do you or did you spend discussing how to improve techniques for successful management of your asthma?

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- Q11a Does your doctor or other healthcare professional in his or her office discuss any of the following with you?
- a) A plan for treating asthma
 - b) Correct inhaler technique
 - c) Keeping daily symptom/ medication diaries
 - d) Monitoring peak expiratory flow
 - e) Contacting patient support organizations
-
- Q12a Is the following statement true or false or are you not sure? Asthma attacks can be fatal in patients with mild asthma.
-
- Q13a When you discuss or discussed side effects of asthma medications with your doctor or other health care professional, who typically brings up the topic, you or your doctor or health care provider?
-
- Q14a How often do you or did you discuss short-term side effects or your asthma medications related to your mouth or throat – such as fungal infection, sore throat or hoarseness – with your doctor or other health care professional?
- a) Never
 - b) Rarely
 - c) Sometimes
 - d) Always
-
- Q15a How often do you or did you discuss long-term side effects of your asthma medications – such as weight gain, weakening of the bones or changing bone density, cataracts or glaucoma – with your doctor or other health care professional?
- a) Never
 - b) Rarely
 - c) Sometimes
 - d) Always
-
- Q16a The following is a list of potential side effects of inhaled corticosteroids. ON a scale of 1-10 where "1" mean "not at all concerned" and "10" means "extremely concerned", how concerned have you been with the following potential side effects, or were you not previously aware of these as potential side effects?
-
- Q17a The following is a list of potential side effects of inhaled corticosteroids. ON a scale of 1-10 where "1" mean "not at all concerned" and "10" means "extremely concerned", how concerned have you been with the following potential side effects, or were you not previously aware of these as potential side effects?
-
- Q18a While taking asthma medications, have you experienced....?
- a) Decreased cortisol production
 - b) Long-term side effects
 - c) Short-term side effects
-
- Q19a Have any of the asthma medication side effects you experienced since being diagnosed caused you to....?
- a) Consider switching medications
 - b) Switch medications
 - c) Consider skipping doses
 - d) Skip doses
 - e) Consider stopping medications
 - f) Stop taking medications
 - g) Change dosage
-

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- Q20a What percentage of the time do or did you take your asthma medication according to your doctor or other health care professional's instructions?
-
- a) Never
 - b) 1-25%
 - c) 26-50%
 - d) 51-75%
 - e) 76-99%
 - f) All
-
- Q21a On a scale of 1- 10 where "1" means "not at all important" and "10" means "extremely important", how important are the following reasons you don't or didn't always take your asthma medication as instructed?
-
- Q22a Have you ever experienced the following if you don't or didn't take your asthma medication as instructed? (Asked to patients who took asthma medication less than 100% of the time)
-
- a) Increased symptoms
 - b) Limited physical activity
 - c) Increased use of bronchodilator
 - d) Nighttime awakenings
 - e) More frequent asthma attacks or exacerbations
 - f) More severe asthma attacks
 - g) More physician visits
 - h) More hospitalizations or ER visits
 - i) Absences from work
 - j) Life-threatening asthma attacks
 - k) Less interaction with friends and family
-
- Q23a Do you think there is a need for new medication options for people with asthma?
-
- Q24a If a new inhaled corticosteroid asthma medication were to become available, using a scale of 1 -10 where "1" means "not at all important" and "10" means "extremely important", please rate how important each of the following would be to you.
-
- a) Lower potential for unwanted long-term side effects
 - b) Works at least as well as other ICS
 - c) Fewer side effects in the mouth and throat
 - d) A drug that is activated in the lung
 - e) Once-daily dosing
 - f) No mouth rinse issues
 - g) A dose counter
 - h) Quickly eliminated from the body
 - i) Can use without a spacer
 - j) High lung deposition
-

asthma as mild, while around the 40% say their asthma is moderate and the 11% of patients consider it as severe.

In Italy, more than in the other countries of the GAPP study, patients' daily activities are limited since up to one third of them state that their abilities are somewhat reduced. Moreover, around the 24% of the asthmatic pa-

tients paid unscheduled visits, the 8% applied to the emergency department and the 5% has been admitted to the hospital due to asthma.

In Italy the 54% of asthmatic patients are treated by the specialist: this percentage is higher than the global (31%) and the European (36%) one; unfortunately, on the other

hand, we have one fifth of subjects who don't see any doctor, PCP either or the specialist.

In Italy the 86% of patients have taken asthma medication at any time; in the 65% of cases they have been treated with the combination of inhaled corticosteroids (ICS) and long acting beta2-agonist: this percentage is much higher than in the other countries of the survey. Inhaled corticosteroids are considered the "gold standard" treatment for asthma, as a matter of fact they are used most frequently as a first-line treatment for all patients; there is a wide agreement in the treatment of the inflammation with the aim to reduce the risk of broncho-constriction. At the same time physicians are not completely satisfied with local and systemic side effects.

On this topic the patients' responses are similar: they are satisfied with medication efficacy, but they are not with potential side effects.

What's interesting is that in Italy, more than in other countries, physicians prefer to prescribe corticosteroids as first-line treatment for mild intermittent asthma both in combination and singularly. The 72% suggests the beta2-short acting; moreover, Italy has the highest percentage of doctors who give leukotriene receptor antagonist for this kind of asthma.

The 74% of Italian patients with mild persistent asthma have been given the combination, but the difference with those who received only inhaled corticosteroids was small. In the same view, physicians administer leukotriene antagonist much more often than in other countries (53% versus 36% in Europe and 42% considering all countries). The average physicians' satisfaction with corticosteroids administered as monotherapy in Italy is the lowest compared to the other countries; accordingly physicians' satisfaction with ICSs is the lowest on both systemic and local side effect issues. In parallel, patients' satisfaction with current asthma treatment is much lower on "potential for side effects" compared to other countries of the survey (51% versus 72%) and the reasons why patients change asthma medications concern potential side effects.

Both patient and healthcare provider recognize the importance of taking care of the patient's education and agree that the physician is the most responsible healthcare provider for this task.

Physicians appear available and helpful on discussing about the asthma management plan, the inhaler use technique and about the usefulness and side effects of steroids and bronchodilators.

In Italy the 43% of physicians says that they spend the whole time of the visit discussing how to improve tech-

niques for the successful management of patients' asthma; on the other side, only the 32% of patients say that the whole visit has been spent for this topic. Anyway, a very low number of subjects followed for asthma say that the percentage of time used for this issue was less than at least the 50%.

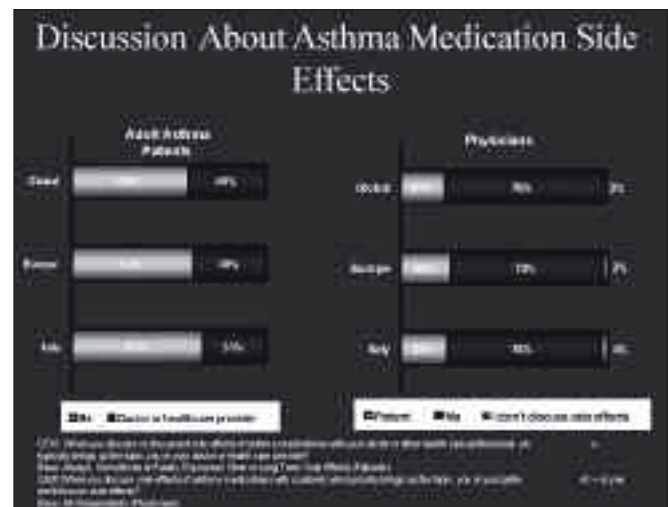
Even if these results are encouraging, a lot of work has to be done yet.

Indeed, asthma education is not ideal, since three-quarters of the patients in Italy don't recognize that asthma attacks in mild patients can be fatal; moreover, the physician's perspectives on side effects differ deeply from patient's point of view: patients are more concerned about long-term side effects than physicians and their opinions differ about who must start the discussion on asthma medication side effects. In Italy as well as in the other countries of the survey, more than the 60% of patients (67% in Italy) state that they bring up the topic "drug side effects", while, at least the 73% of physicians say that they do (Fig. 2).

Both patients and physicians are most concerned about the long-term side effects of ICS, compared to the short-term ones. More often in Italy, this leads patients to consider switching medication, skipping or changing doses or stopping the therapy; according to physicians this seems to be due to fear of steroids and the concern for side effects (Figs. 3, 4)

Compared with the rest of the world in Italy adult patients with asthma and physicians are, on average, discussing asthma management less frequently and a greater proportion of adult asthmatic patients don't know that

Figure 2 - Different opinion about who must initiate the discussion on asthma medication side effects.



asthma attacks can be fatal in patients with mild asthma. In addition, patients are equally aware of side effects and they are concerned about the decreased production of cortisol and short term side effects but are less likely to be concerned about long term side effects.

Italian physicians need new asthma medication more than physicians of other countries, while their patients believe that there's a need for new asthma drugs only in the 47% of cases, a percentage very low compared to other countries where it is estimate around 70%.

When doctors and patients were asked which specific attributes were of primary importance if a new inhaled cor-

ticosteroid medication were to become available, the physicians' replay was the once-daily dosing, together with at least the same efficacy, fewer side effects in the mouth and throat and a lower potential for unwanted long-term side effects; this attitude confirms their awareness of the necessity to apply strategies to enhance the subjects' compliance (Tab. 3).

In confirmation of this aspect, a study evaluated the adherence to twice-daily inhaled corticosteroid therapy in 50 adults with moderate-to-severe asthma monitoring electronically for 42 days. Average adherence was the 63%; the 54% of patients recorded at least the 70% of the prescribed number of inhaled steroid actuations; the compliance to the therapy decreased progressively over the weeks of the study. Factors associated with poor adherence included: less than 12 years of formal education, poor patient-clinician communication, household income lower than \$ 20,000, non-English-speaking patient and minority status (12).

Ciclesonide is a new inhaled steroid that has to be taken once-daily; a study showed that at 160 or 40 mcg/day it had no detectable effects on growth velocity, as assessed by stadiometer height, in children with mild persistent asthma (13-15). CIC demonstrated no effect on the growth in children from different regions, while differences in growth rates between children with asthma from North and South America may reflect genetic and socioeconomic differences. This drug could improve patients' adherence to therapy since it can be taken only once daily.

Figure 3 - Actions taken by patients due to medication side effects.

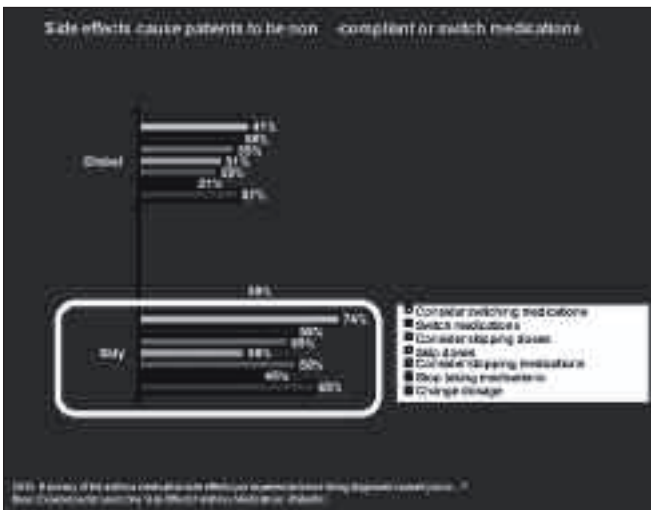
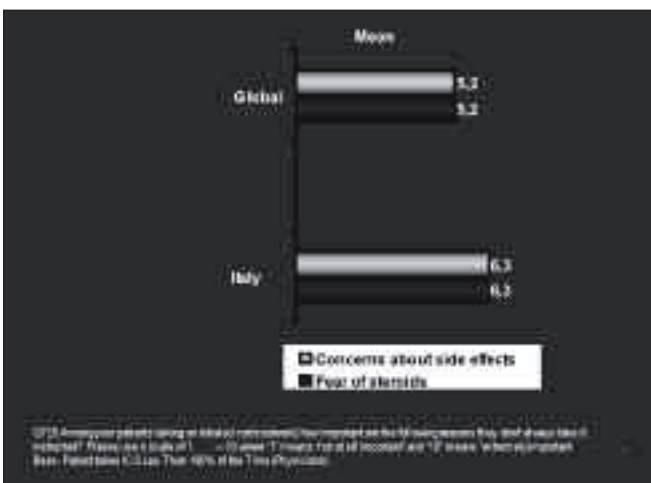


Figure 4 - Physicians' Perceptions of Why Patients Do Not Always Take ICS as Instructed.



Discussion

The GAPP survey has studied the current management and treatment of asthma by evaluating patients' and physicians' point of view.

Both groups were questioned on asthma diagnosis and symptoms, communications with their respective patients or physician, the quality of life, their experience with asthma medications, side effects from asthma drugs, the concern and awareness of side effects and interest in new drugs for asthma.

The GAPP has the aim to identify barriers to optimal management of asthma through enhancing the understanding and the awareness of likely contributors to sub-optimal asthma management, exploring content and dynamics of physician-patient communications, finally enhancing treatment compliance and outcomes.

Table 3 - Main results in Italy, Europe and globally.

	Italy	Europe	Global
Patients activities are limited	36%	32%	31%
Unscheduled visits to doctor	24%	28%	27%
Patients admitted to hospital due to asthma	5%	6%	6%
Patients treated by specialist	54%	31%	36%
Patients not treated by doctors	20%	11%	11%
Patients treated with combination ICS+LABA	65%	29%	27%
ICS considered the gold standard treatment for asthma by physicians	80%	95%	95%
Leukotriene antagonist in mild persistent asthma	53%	36%	42%
Patients assert to start discussion on asthma medication side effects	67%	62%	60%
Physicians assert to start discussion on asthma medication side effects	74%	73%	76%
Patients believe there is a need for a new asthma medication	47%	73%	76%
Physicians believe there is a need for new asthma medication	98%	80%	81%

From the evaluation of the patients' self-reported perception of asthma severity, unscheduled resources use and limitation to daily activities it is evident that asthma is far from a satisfactory control. This could be due to the patients' lack of knowledge or awareness about their disease or to the physicians' inability to face key issues. Moreover, in Italy the 20% of patients is not treated by any doctor.

Both patients and healthcare providers recognize the importance of the provider in patient education. However, there is disagreement about the time devoted to asthma education and discussing how to improve techniques for the successful management of asthma.

The most frequent asthma treatment taken is the combination of ICS and LABA. Italian physicians agree that it is important to treat bronchial inflammation and that ICS are the gold-standard therapy for asthma: in this view these are the first-line treatment for mild persistent asthma; at the same time, they are not fully satisfied with their potential local and systemic side effects. In Italy, more frequently than in the other countries, patients are treated with leukotriene antagonist.

The GAPP survey also revealed that potential side effects are for the cause of patients' concern and this is considered one of the key points that can lead to switch medication, to skip doses, or to stop taking medication. Another important point is the time devoted to patients' information by the health provider. Patients' information should improve awareness of the disease and educate on the necessity to take medication in order to cure and prevent

symptoms. The barriers to adherence can be identified in the relationship between the patient, the provider and the health care system. As a matter of fact, poor provider-patient communication can lead to a poor understanding of the disease and of the benefits and risks of treatment by the patients. Moreover, the patient has a poor understanding of the medication if the physician prescribes a complex course of treatment or switches to different formulation.

Despite our knowledge and our efforts on asthma treatment, some unmet needs still exist. As a matter of fact, even if GINA guide lines greatly improved asthma therapy approach over the time, asthma control is still too low, Quality of Life has a significant impact on patients' lives, side effects are relevant and compliance is not ideal. Moreover, the 70% of asthma death could be prevented. Asthma patient education seems to be a crucial point to exploit and must be improved through discussions with physicians during office visits.

References

1. Asher MI, Anderson HR, Stewart AW, et al. worldwide variations in prevalence of asthma symptoms: the International Study of Asthma and Allergies in Childhood (ISAAC). *Eur Respir J* 1998; 12: 315-35.
2. Chinn S, Burney P, Jarvis D, Luczinska C for ECRHS. Variation in bronchial responsiveness in the European Respiratory Health Survey. *Eur Respir J* 1997; 10 (11): 2495-501.
3. Tillie-Leblond I, Montani D, Crestani B, et al. Relation between

- inflammation and symptoms in asthma. *Allergy* 2009; 64 (3): 354-67.
4. An SS, Bai TR, Bates JH, et al. Airway smooth muscle dynamics: a common pathway of airway obstruction in asthma. *Eur Respir J* 2007; 29 (5): 834-60.
 5. Brusasco V, Crimi E, Baroffio M. Allergic airway inflammation and beta-adrenoceptor dysfunction. *Cell Biochem Biophys* 2006; 44 (1): 129-38.
 6. Folli C, Descalzi D, Scordamaglia F, Riccio AM, Gamalero C, Canonica GW. New insights into airway remodelling in asthma and its possible modulation. *Curr Opin Allergy Clin Immunol* 2008; 8 (5): 367-75.
 7. Global Initiative for Asthma (GINA). Global strategy for asthma management.
 8. NIH Publication 02-3659 issued January 1995 (Updated 2006. <http://www.ginasthma.com>).
 9. Rabe KF, Vermeire PA, Soriano JB, Maier WC. Clinical management of asthma in 1999: the asthma insights and reality in Europe (AIRE) study. *Eur Respir J* 2000; 16: 802-7.
 10. Lai CK, De Guia TS, Kim YY, et al. Asthma control in the Asia-Pacific region; the Asthma Insights and reality in Asia Pacific Study. *J Allergy Clin Immunol* 2003; 111 (2): 263-8.
 11. www.asthmainamerica.com
 12. Neffen H, Fritscher C, Schacht FC, et al. Asthma control in Latin America: the Asthma Insights and Reality in Latin America (AIRLA) survey. *Rev Panam Salud Publica* 2005; 17 (3): 191-7.
 13. Apter AJ, Reisine ST, Affleck G, Barrows E, ZuWallack RL. Adherence with twice-daily dosing of inhaled steroids. Socioeconomic and health-belief differences. *Am J Respir Crit Care Med* 1998; 157 (6 pt 1): 1810-7.
 14. Skoner DP, Maspero J, Banerji D; Ciclesonide Pediatric Growth Study Group. Assessment of the long-term safety of inhaled ciclesonide on growth in children with asthma. *Pediatrics* 2008; 121 (1): e1-14.
 15. Baena-Cagnani CE, Passalacqua G, Gómez M, Zernotti ME, Canonica GW. New perspectives in the treatment of allergic rhinitis and asthma in children. *Curr Opin Allergy Clin Immunol* 2007; 7 (2): 201-6.