ORIGINAL ARTICLES

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# Asthma management among different specialists: results from a national Italian survey

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## KEY WORDS

Asthma; diagnosis; follow-up and monitoring tools; treatment

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#### Summary

In Europe more than 50% of asthmatic treated patients have a not well-controlled asthma. The present survey aims at investigating how different specialists approach asthmatic patients. A web anonymous questionnaire was randomly administered to 604 General Practitioners (GPs), 241 Pneumologists and 131 Allergists. It concerned: epidemiology, diagnostic workup, follow-up and risk factors, treatment and future risk. A general agreement emerges about asthma diagnostic work-up. All categories are aware of the impact of comorbidities on asthma. LABA/inhaled steroids combination is considered the first choice treatment. Surprisingly, depot steroids and long-acting beta2 agonists (LABA) alone are still prescribed by GPs. Concerning monitoring tools, Allergists rely on inflammation biomarkers, whereas reduction of rescue medication is more relevant for GPs. Asthma Control Test (ACT) is considered time consuming by more than 50% of all physicians and is not known by most of GPs. Adherence is considered a crucial problem in asthma management. All categories seem to have a good knowledge about asthma. The cultural background may account for mild differences in asthma control tools and treatment options. GPs have a pivotal role in discriminating patients who need specific assessment by specialists. It is thus important that GPs and specialists share common tools for recognizing and managing those patients.

### Introduction

Asthma affects more than 300 million persons worldwide and causes substantial morbidity. In developed countries its prevalence is estimated to be between 8% and 12% in adults and 10-15% in children (1). In Italy the overall estimate is 2.5 mil-

lions. Despite being not associated with high mortality, asthma can cause sensitive limitations in daily life, in terms of reduced productivity at work or school and frequent inability to perform normal activities. According to recent European data, more than 50% of treated patients have not well-controlled asthma (2). As there is currently no cure for asthma, the cornerstone of

its management is the achievement and maintenance of an optimal control (3). Different specialists should contribute to this goal, such as Allergists (ALL), Pneumologists (PNE) and general practitioners (GPs), as GINA guidelines suggest.

The present survey aims at investigating how Italian specialists and GPs approach patients with asthma, in order to point out pitfalls and unmet needs concerning real-life management of the disease.

## Materials and methods

A board of experts belonging to AIPO (Associazione Italiana Pneumologi Ospedalieri – Italian Association of Hospital Pulmonologists) and IFIACI (Federazione delle Società Italiane di Immunologia, Allergologia ed Immunologia Clinica – Federation of Italian Societies of Allergy and Clinical Immunology) developed a questionnaire composed of 24 multiple choice questions covering epidemiological (number and type of asthma patients assisted) and clinical (presence of comorbidities or risk factors) aspects about asthma, and explored the overall management strategies (diagnosis, monitoring, treatment, counseling, treatment, adherence) adopted by the Italian physicians.

Between 9<sup>th</sup> of December 2010 and 28<sup>th</sup> of January 2011, a self-administered anonymous questionnaire was e-mailed to a sample of GPs, Pneumologists and Allergists randomly selected from the national registers of Physicians. The online questionnaire could only be answered once. It was e-mailed two more

times to non-responders 2 and 4 months after the first invitation. In respect to the total number of contacted physicians, 20% of GPs (n. 604), 25% of Pneumologists (n. 241) and 30% of Allergists (n. 131) belonging to all Italian regions effectively participated in the survey.

The sample (n. 976 Italian physicians) was representative of the medical population considered, with a standard error (95% confidence level) of 4.0% for GPs, 6.1% for Pulmonologists and 8.1% for Allergists.

The answers provided by the three groups were compared and analyzed. Student's t-test was used to detect significant differences in the means of quantitative variables for independent samples. The statistical cut-off  $\alpha = 0.05$  was chosen.

## **Results and comments**

## Study population

64% of GPs declare that among their patients at least 20 people have asthma. Considering that the number of patients for each GP is around 1000, the perception of at least 2% of asthmatic patients is rather far from epidemiological data on the general population, indicating that the proportion of patients with a diagnosis of asthma is around 5%. The possibility that some patients with intermittent asthma or with seasonal symptoms do not visit the GP's office and self-administer bronchodilators on demand may explain that underestimation.



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Figure 1



# Figure 2

As far as Allergists and Pneumologists are concerned, one in three specialists reports seeing more than 20 asthmatic patients per week. This proportion is slightly higher for Allergists (36%) than Pneumologists (34%). This might depend on the different types of respiratory diseases treated by Pneumologists, which could reduce the time selectively dedicated to asthmatics. However, these data might also suggest that Allergists are today aware of the frequent involvement of lower airways in patients with allergic rhinitis, and therefore regularly assess both upper and lower airway involvement (4).

According to GPs perception, patients with seasonal symptoms seem to have a higher prevalence than patients with chronic symptoms (56% vs. 44%, respectively), probably because pollenosis exacerbations are evaluated as a first step in a primary care setting (**figure 1**). Pneumologists report a higher number of asthmatic patients with chronic symptoms (presumably more severe patients), whereas Allergists refer an equal distribution of both kinds of patients.

## Diagnostic work-up

No significant differences are detectable among the three types of physicians concerning the relevance of symptoms suggestive for asthma (data not shown). However, cough and chest tightness are regarded as less important by GPs, presumably because these symptoms are shared by other diseases and are not considered asthma-specific in daily practice. Wheezing and night

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awakenings are relevant for all physicians as well as the role of triggers (smoke, allergens, physical exercise). Rhinorrhea is less relevant for Allergists, probably because it is not considered a specific symptom of asthma. Also phlegm is not considered suggestive for asthma, presumably because it is mainly related to acute bronchitis or COPD.

As far as diagnosis according to the survey there is a general agreement on the importance of spirometry, reversibility test, bronchial challenge with metacholine and evaluation of the atopic status (**figure 2**), as indicated in international guidelines (5). It is worth of note the discrepancy between the importance attributed to spirometry as a diagnostic tool and its use in clinical practice (only around 30% of asthmatic patients (6)). On the other hand, in the analysis of the data from a questionnaire it should be taken into account that results could be influenced by predefined answers, as well as by the tendency to give "desirable" more than "real" responding.

Concerning the role of chest X-ray, there is a significant difference between GPs and specialists: not surprisingly, GPs take into consideration chest X-ray evaluation too, since asthma symptoms are not so specific. Inflammation assessment (FeNO) seems to be important for Pneumologists and Allergists, but it is significantly quite neglected by GPs. Actually, according to published data and guidelines, the role of FeNO measurement in routine asthma diagnosis is yet unclear (7,8), even if its correlation with bronchial eosinophilic inflammation has been proven (9,10).

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# Figure 3

### Follow-up and risk factors for asthma severity

According to our data, one in three patients (31.6-36.6%) is followed-up at least twice yearly, without significant differences among the three categories.

As shown in **figure 3**, there is a general agreement about the importance of spirometry, the use of rescue short acting beta2 bronchodilators, night awakenings, wheezing and exacerbations as markers for monitoring asthma, as reported by recently published data (11). In this context, it is important to note that according to international guidelines, the regular use of reliever is one of the elements defining uncontrolled asthma and that reducing or eliminating the need for reliever treatment is both an important goal and a measure of successful treatment (3). Exacerbations are less relevant for GPs: presumably, the lack of a standardized definition of exacerbation may account for this finding. Chest tightness and cough are also regarded as less important, being non-specific symptoms.

Another question addressed in the survey concerns the use of Asthma Control Test (ACT), a validated questionnaire reflecting the multidimensional nature of asthma control in the follow up of asthmatic patients. As shown in **figure 4**, more than 50% of GPs never use ACT and only 5% use it often. By contrast, a significant proportion of specialists (37%) report that they often use this tool in the assessment of their patients and only 17% never used it. Surprisingly, by analysing the reasons of poor/no use, more than 50% of all physicians declare that ACT is time consuming (**figure 4**). One in four GPs does not know this questionnaire, whereas two in

ten specialists consider it not reliable or not useful in daily practice. However, ACT is a brief, simple, questionnaire for patient self-evaluation, with demonstrated effectiveness and reliability (12-14). It can be easily performed in the waiting room before the visit without waste of time for the physician, thus improving the assessment of asthma control in a busy clinical practice setting.

Consistently with international reports (15-18), all physicians are aware that risk factors such as smoking and comorbidities (rhinitis, gastro-esophageal reflux, sleep apnea, obesity) may impact on the natural history of asthma, being responsible for clinical exacerbations as well as for a reduction in treatment efficacy (**figure 5**).

Small differences are observed among categories, probably reflecting their different cultural background. GPs are particularly sensitive to smoking as a risk factor also for other morbid conditions treated in everyday practice (cardiovascular, metabolic diseases). Rhinitis is mainly taken into consideration by Allergists, as a consequence of the implementation of ARIA guidelines (4,17), based on a global approach of the respiratory tract. Gastro-esophageal reflux is a more significant risk factor for Pneumologists and sleep apnea for GPs. Despite increasing evidence of a strong link between asthma and obesity (15,16) it seems a less relevant comorbidity for all physicians, mainly related to metabolic and cardiovascular diseases.

Thus, comorbidities may contribute to identify patients with increased risk of severe asthma and susceptibility to exacerbations (different phenotypes?), needing a more careful and strict monitoring to maintain control.

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# Treatment and future risk

For all physicians the main goals of pharmacologic therapy are the prevention of symptoms and exacerbations with a regular treatment, the control of inflammation and the reduction in reliever use (**figure 6**), suggesting that the message of international guidelines seems to be at least partially accepted. Specialists are significantly more focused on the role of inflammation, whereas for GPs achieving bronchodilation is also a relatively important target.

For all physicians the combination of LABA and inhaled steroids is the first choice of the treatment for seasonal asthma (**figure** 7).

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tion therapy fulfils both a sustained and safe bronchoprotection and an adequate control of inflammation, in order to prevent the long-term adverse consequences of airway remodeling (20).

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The higher dosage of inhaled steroid used by Pneumologists suggests that they usually treat more severe asthma. Moreover, most patients are visited for worsening of symptoms, indicating the need

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for a therapy at the step 3 or 4 of GINA guidelines (3). Anti-histamines are also prescribed, presumably for concomitant rhinitis. Surprisingly, depot steroid are still prescribed as well as long-acting beta2 agonists (LABA) alone, despite the recent warnings against their use without inhaled steroids (21). Pneumologists use more leukotriene antagonists, Allergists more immunotherapy. Also in perennial asthma the combination of LABA and inhaled steroids (at medium or higher doses) is the first choice; only slight differences are observed with respect to seasonal asthma (**figure 8**), such as a wider use of leukotriene antagonists in all categories, probably used in association with inhaled steroids or with the combination of inhaled steroids and LABA.

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International guidelines report that, in addition to clinical manifestations, asthma control should include the control of the expected future risk of the patient, such as exacerbations, accelerated decline in lung function and side effects of treatment. In this respect, all categories share key points in the management of the future risk, as the need of a chronic treatment (82% Pneumologists, 85% Allergists and 90% GPs) and the crucial role of adherence to treatment (76% Pneumologists, 76% Allergists and 67% GPs).

Like in every chronic disease, adherence to therapy is of fundamental importance to achieve and maintain asthma control (22). In this context, all physicians report that only 50% of patients are able to manage their treatment autonomously.

Two main aspects of adherence have been taken into account: treatment continuity and compliance to the therapeutic regimen, including the correct use of inhaler.

In regards to the first aspect, in patients with seasonal symptoms the type of sensitization and the pollen count of the causative allergen drive 63% of Allergists' choice about the length of the treatment (vs. 41% of Pneumologists and 30% of GPs); 34% of GPs vs. 17% of specialists suggests a therapy of at least two months starting before the pollen season. A high proportion of all physicians (48% of Allergists, 59% of Pneumologists, 44% of GPs) declare to treat patients before the pollen season.

This perspective is intriguing. In fact, most of patients are treated with a combination therapy, as before mentioned. This choice agrees with a step 3 of severity according to GINA Guidelines (3). So, do GPs start this treatment before the beginning of pollen season in asymptomatic patients?

In the case of chronic symptoms of asthma, 40% of GPs and 30% of Pneumologists report to start a long-term treatment without clear indication about follow-up schedule. This behavior is therefore far from the step up and step down approach suggested by GINA Guidelines<sup>3</sup>.

In regards to the factors or behaviors that may improve patient adherence and compliance, GPs are less prone than specialists to counseling, patient's education, scheduling regular visits (**figure 9**), possibly due to a lack of time. Furthermore, the routine use of PEF or questionnaires (like ACT) is generally less accepted. Pneumologists are more interested in technical progress, considering the role of the type of device in patient adherence and compliance. Along this line, the Task Force of the European Respiratory Society has delivered a consensus statement for pulmonary specialists focused on the patient-use aspects of the aerosol delivery devices that are currently available (23). Since the dose delivered to the lungs is dependent on the correct use of the delivery system, prescribers should ensure that patients can and will use devices correctly (23). Moreover, once a patient is familiar and stabilized on one type of inhaler, he should not be switched to new devices without his involvement and without follow-up education on how to use the device properly. A recent study has shown that patient compliance and asthma control deteriorates if an inhaler is substituted with a different device at the prescribing or dispensing stage without involving the patient (24). In patients with persistent asthma, adherence is much more important if we consider that a regular use of treatment at a stable dose is necessary in order to prevent exacerbations (25).

Despite the importance attributed to treatment continuity, a recent population-based retrospective study conducted in Italy showed that patients with asthma received only 1.54 prescribed packages of controller medication per patient per year. Asthma guidelines suggest that the large majority of people with a diagnosis of asthma should be given an anti-inflammatory controller medication for regular use, but the small number of prescriptions of controller medications/patient/year clearly indicates that patients were not being treated on a regular basis (26).

## Conclusions

According to the results of this survey, all physicians seem to have a good knowledge about asthma and share a common disease management goal from a theoretical point of view: to prevent symptoms and exacerbations and to control airway inflammation, thus reducing the future risk of disease progression. All physicians are aware that risk factors and comorbidities may identify patients with increased risk of poorly controlled asthma and susceptibility to exacerbations, needing a more careful and strict follow-up for treatment continuity. Interest and expertise may account for small differences across the physician types, such as the importance attributed to risk factors and comorbidities for asthma severity or the focus of Allergists for the immunological pathogenesis and the immunomodulator treatment (immunotherapy).

Although the combination of LABA and inhaled steroids is the first choice in the treatment of asthma, in line with published data showing that this regimen is more effective in preventing clinical manifestations and more rapid in gaining asthma control, it is concerning to find a high percentage of physicians (mainly GPs) still prescribing depot steroids or LABA monotherapy.

In regard to follow-up, there is general agreement that not many patients are able to manage their treatment autonomously. Scheduling regular visits and patient's education may improve adherence especially for specialists. However, there is no a common acceptance of a simple tool like ACT to monitor asthma control. Finally, all physicians share the need of more time to dedicate to asthma plan management in daily practice.

Since patients are often evaluated in a primary care setting as a first line approach, GPs have a pivotal role in discriminating patients who need specific assessment by specialists. It is thus important that GPs and specialists share common tools for recognizing those patients.

# References

- Baïz N, Annesi-Maesano I. Is the asthma epidemic still ascending? Clin Chest Med. 2012;33(3):419-29.
- Demoly P, Annunziata K, Gubba E, Adamek L. Repeated cross-sectional survey of patient-reported asthma control in Europe in the past 5 years. Eur Respir Rev. 2012;21(123):66-74.
- GINA report. Global strategy for asthma management and prevention. Revised 2010. Available at: www.ginasthma.org
- Bousquet J, Schünemann HJ, Samolinski B et al., World Health Organization Collaborating Center for Asthma and Rhinitis. Allergic Rhinitis and its Impact on Asthma (ARIA): Achievements in 10 years and future needs. J Allergy Clin Immunol. 2012;130(5):1049-62.
- Tepper RS, Wise RS, Covar R et al. Asthma outcomes: pulmonary physiology. J Allergy Clin Immunol. 2012;129(3) Suppl:S65-87.
- Cazzola M, Bettoncelli G, Sessa E, Cricelli C. Primary care of the patient with chronic obstructive pulmonary disease in Italy. Respir Med. 2009;103:582-8.
- Bahna SL. Should exhaled nitric oxide measurement be part of routine asthma management? Ann Allergy Asthma Immunol. 2012;109(5):289-91.
- Schleich FN, Asandei R, Manise M, Sele J, Seidel L, Louis R. Is FENO50 useful diagnostic tool in suspected asthma? Int J Clin Pract. 2012;66(2):158-65.
- Dweik RA, Boggs PB, Erzurum SC et al. An official ATS clinical practice guideline: interpretation of exhaled nitric oxide levels (FENO) for clinical applications. Am J Respir Crit Care Med. 2011;184(5):602-15.
- Volbeda F, Broekema M, Lodewijk ME et al. Clinical control of asthma associates with measures of airway inflammation. Thorax. 2013;68(1):19-24.
- Calhoun WJ, Ameredes BT, King TS et al. Comparison of physician-, biomarker-, and symptom-based strategies for adjustment of inhaled corticosteroid therapy in adults with asthma: the BASALT randomized controlled trial. JAMA. 2012;308(10):987-97.
- Nathan RA, Sorkness CA, Kosinski M et al. Development of the Asthma Control Test: A survey for assessing asthma control. J Allergy Clin Immunol. 2004;113(1):59-65.

- 13. Miedinger D, Neukomm E, Chhajed PN, Schnyder A, Naef M, Ackermann M, Leuppi JD. The use of the Asthma Control Test in general practice and its correlation with asthma control according to the GINA guidelines. Curr Med Res Opin. 2011;27(12):2301-8.
- Jia CE, Zhang HP, Lv Y et al. The Asthma Control Test and Asthma Control Questionnaire for assessing asthma control: Systematic review and meta-analysis. J Allergy Clin Immunol. 2013;131(3):695-703.
- Boulet LP, Boulay MÈ. Asthma-related comorbidities. Expert Rev Respir Med. 2011;5(3):377-93.
- Gershon AS, Guan J, Wang C, Victor JC, To T. Describing and quantifying asthma comorbidity: a population study. PLoS One. 2012;7(5):e34967.
- Braido F, Baiardini I, Menoni S et al. Patients with asthma and comorbid allergic rhinitis: is optimal quality of life achievable in real life? PLoS One. 2012;7(2):e31178.
- Cazzola M, Calzetta L, Bettoncelli G et al. Asthma and comorbid medical illness. Eur Respir J. 2011;38(1):42-9.
- Bateman ED, Boushey HA, Bousquet J, Busse WW, Clark TJ, Pauwels RA, Pedersen SE. GOAL Investigators Group. Can guideline-defined asthma control be achieved? The Gaining Optimal Asthma ControL study. Am J Respir Crit Care Med. 2004;170(8):836-44.
- Grainge CL, Lau LC, Ward JA et al. Effect of bronchoconstriction on airway remodeling in asthma. N Engl J Med. 2011;364(21):2006-15.
- Chowdhury BA, Dal Pan G. The FDA and Safe Use of Long-Acting Beta-Agonists in the Treatment of Asthma. N Engl J Med. 2010;362(13):1169-71.
- 22. Sumino K, Cabana MD. Medication adherence in asthma patients. Curr Opin Pulm Med. 2013;19(1):49-53.
- Laube BL, Janssens HM, de Jongh FH et al. What the pulmonary specialist should know about the new inhalation therapies. Eur Respir J. 2011;37(6):1308-31.
- 24. Thomas M, Price D, Chrystyn H, et al. Inhaled corticosteroids for asthma: impact of practice level device switching on asthma control. BMC Pulm Med. 2009;9:1.
- 25. Bateman ED, Bousquet J, Busse WW, Clark TJ, Gul N, Gibbs M, Pedersen S. Stability of asthma control with regular treatment: an analysis of the Gaining Optimal Asthma controL (GOAL) study. Allergy. 2008;63(7):932-8.
- Cazzola M, Segretia A, Bettoncelli G et al. Change in asthma and COPD prescribing by Italian general practitioners between 2006 and 2008. Prim Care Respir J. 2011;20(3):291-298.