



## Original Article

## Factors Associated with Asthma Control in Primary Care Patients in Spain: The CHAS study

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## ARTICLE INFO

## Article history:

Received November 6, 2009

Accepted January 18, 2010

## Keywords:

Asthma  
Epidemiology  
Primary care  
Risk factors

## ABSTRACT

**Introduction:** Asthma control has been found to be inadequate in all populations studied to date and accounts for the majority of costs for this disease. The objective of our study was to evaluate the prevalence of poorly-controlled asthma in primary care patients and to identify some of the factors associated with this situation.

**Methods:** We conducted a transversal study that included asthmatic patients over 18 years of age who were monitored in primary care visits (n = 2159). Asthma control was evaluated using the Asthma Control Questionnaire. The demographic variables and the adherence to therapy were evaluated using a questionnaire. The OR for poorly controlled asthma was calculated using logistic regression using asthma control as the dependent variable, which was assessed using the ACQ score.

**Results:** The prevalence of uncontrolled asthma was 63.8%. Risk factors for poorly-controlled asthma were treatment with oral corticosteroids (OR = 6.55), greater severity of asthma (OR = 3.11), the presence of a recent stressful event (OR = 2.44), a lesser importance given to compliance with therapy (OR = 1.66) and living in rural areas (OR = 1.29). In contrast, sex, age, obesity, smoking, alcohol consumption and educational level did not show any influence over asthma control.

**Conclusions:** Asthma remains poorly controlled in Spain but some of the factors related to this situation could be changed by the healthcare system.

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### Factores asociados con el control del asma en pacientes de atención primaria en España: el estudio CHAS

## RESUMEN

**Introducción:** El control del asma es inadecuado en todas las poblaciones estudiadas hasta el momento actual, generando la mayor parte de los costes de la enfermedad. El objetivo de nuestro estudio fue evaluar la prevalencia de asma mal controlada en pacientes de atención primaria, e identificar algunos factores asociados con este hecho.

**Métodos:** Llevamos a cabo un estudio transversal, incluyendo pacientes asmáticos mayores de 18 años, seguidos en consultas de atención primaria (n = 2159). El control del asma se evaluó con el cuestionario "Asthma Control Questionnaire". Las variables sociodemográficas y el cumplimiento terapéutico se evaluaron mediante un cuestionario. Mediante regresión logística se calcularon los OR de asma mal controlada; utilizando como variable dependiente el control del asma, valorado de acuerdo a la puntuación ACQ.

**Resultados:** La prevalencia de asma no controlada fue del 63,9%. El tratamiento con corticoides orales (OR = 6,55), la mayor gravedad del asma (OR = 3,11), la presencia de un evento estresante reciente (OR = 2,44), una menor importancia otorgada al cumplimiento terapéutico (OR = 1,66) y vivir en un medio rural (OR =

## Palabras clave:

Asma  
Epidemiología  
Atención Primaria  
Factores de riesgo

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1,29) fueron factores de riesgo para asma mal controlada. Por el contrario, el sexo, la edad, la obesidad, el tabaquismo, el consumo de alcohol y el nivel educacional no mostraron ninguna influencia sobre el control del asma.

**Conclusiones:** En España el asma permanece mal controlada, y algunos de los factores relacionados con esta situación podrían ser modificables desde el sistema sanitario.

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## Introduction

Asthma control is considered a fundamental objective in the management of these patients<sup>1</sup> since it results in a major part of the high costs of this disease, which in Spain is close to 1,500 million euros annually.<sup>2</sup> However, the results obtained by various authors show that it remains insufficient in all populations studied.<sup>3-5</sup>

Furthermore, the wide variability in levels of control of this disease, even in neighbouring countries, is well known. In the European Community Respiratory Health Survey, the percentage of poorly-controlled asthmatics in some countries exceeds almost triple that of other countries, for example, 20% in Iceland versus 67% in Italy.<sup>6</sup>

In the INSPIRE study,<sup>7</sup> which included data from various European countries including Spain, the number of patients with uncontrolled asthma reached 72%, evaluated according to the Asthma Control Questionnaire (ACQ), defining well-controlled patients as those with a score less than 0.75.<sup>8</sup>

Significant differences were also observed in the factors associated with poor control of the disease since factors such as age, sex or educational level may be associated with better control of asthma for some authors, worse control for others or not have any influence in other populations.<sup>6,9-12</sup>

Additionally, asthmatic patients tend to overestimate their control of the disease, believing that a situation is under control when actually it is not.<sup>7</sup>

Various authors have created validated questionnaires for evaluating asthma control, among them the ACQ, which is one of the most frequently used.<sup>8</sup>

The objective of the *Control and Handling of Asthma in Spain* (CHAS) study was to evaluate the prevalence of uncontrolled asthma in primary care patients as well as to identify the factors associated with this situation.

## Patients and Methods

We conducted a transversal study of Spain's asthmatic population who were over 18 years of age and treated in primary care. Although the primary objective of the study is of an analytical nature (to establish the relationship between exposure and effect), a transversal study was chosen because: 1) the simultaneous determination of independent and dependent variables is as valid as the determination at two different times when the independent variables show great stability over time; 2) the characteristics of the independent and dependent variables minimise the risk of reverse causality.

Under these conditions, the results of a transversal design have similar validity as those of a longitudinal study.

The inclusion of patients was performed by multistage sampling in all of the autonomous communities of Spain. General practitioners were the sample unit in the first stage (n = 182) and 12 patients from each of these doctors were randomly included, up to n = 2,230.

Inclusion criteria were as follows: 1) older than 18 years of age; 2) diagnosed with asthma at least one year earlier through medical history and the necessary complementary examinations for confirmation; 3) had attended a visit at their Primary Care Centre in the previous two years; 4) and had signed the informed consent for

participating in the study. Exclusion criteria were as follows: 1) inability to read or understand the questionnaires, in the opinion of the researcher; 2) COPD diagnosis.

Each doctor contacted their patients by telephone. Those that refused to participate were considered non-responders.

The collection of data was performed through personal interviews in the doctor's office (between November 2007 and March 2008).

Asthma control was evaluated using the ACQ.<sup>8</sup> For this study, we used the abbreviated version, which has been used in population studies without loss of validity.<sup>13</sup> The patient and doctor were also asked about the degree of asthma control. Quality of life was evaluated using the EuroQuol<sup>14</sup> questionnaire. Demographic variables and treatment compliance were measured using a questionnaire specifically designed for this study.

The study was approved by the Clinical Research Ethics Committee of the Hospital Clínico San Carlos of Madrid.

## Variables

### Dependent Variable

Asthma control was assessed as a dichotomous variable, according to the ACQ score, defining well-controlled patients as those with an ACQ score of less than 0.75 and "not well controlled" as those with ACQ  $\geq$  0.75. The positive and negative predictive values for this cut-off point were 0.75 and 0.81, respectively.<sup>8</sup>

### Independent Variables

Demographic variables included were age, sex, place of residence (rural/urban) and educational level (primary, secondary and university studies).

The presence or not of allergies was recorded from what was reported by the patient.

In terms of smoking, the patients were classified as active smokers, ex-smokers or never smokers. Three groups were established based on BMI (<25 kg/m<sup>2</sup>;  $\geq$  25 kg/m<sup>2</sup>-30 kg/m<sup>2</sup>;  $\geq$  30 kg/m<sup>2</sup>).

Patients were asked about the incidence of any stressful event that may have occurred in the last 15 days, according to their own estimation (yes/no).

Treatment compliance was evaluated through 3 variables: 1) treatment compliance according to the doctor; 2) frequency of forgetting medication according to the patient; 3) the importance of compliance according to the patient. This last variable was obtained by asking the patient about their degree of agreement (from 0 = completely disagree, to 10 = completely agree) with the statement "Strict compliance with the medication prescribed by my doctor will improve my asthma symptoms", and was categorised, by research staff consensus, into two settings: < 8 y  $\geq$  8.

Asthma severity was determined according to the criteria of the GINA 2006 guide, which is based on the patient situation before initiating any treatment.<sup>15</sup>

The base treatment was classified into four mutually exclusive categories: 1) those that took oral corticosteroids the previous year; 2) those that were treated with a combination of long-acting beta-2 agonists and inhaled corticosteroids with any other drug except for oral corticosteroids (OCS); 3) those treated with inhaled corticosteroids without long-acting beta agonists on a continuous basis, although

**Table 1**  
Description of the included population

	n (%)
Age, years	
18-39 years	799 (37.0)
40-59 years	716 (33.2%)
≥ 60 years	644 (29.8%)
Sex	
Male	911 (42.2%)
Female	1,248 (57.8%)
BMI (kg/m <sup>2</sup> )	
< 25	844 (39.1%)
≥ 25-30	880 (40.8%)
≥ 30	433 (20.1%)
Educational level	
No schooling	173 (8.03%)
Primary education	916 (42.5%)
Secondary education	715 (33.2%)
University	351 (16.3%)
Occupation	
Active worker	1,114 (51.6%)
Housework	408 (18.9%)
Unemployed	39 (1.81%)
Disability	66 (3.06%)
Retired	393 (18.2%)
Student	137 (6.35%)
Cohabitation	
Lives alone	242 (11.2%)
With other people	1,914 (88.8%)
Place of residence	
Small town	404 (18.7%)
Large town	470 (21.8%)
City	1,284 (59.5%)
Family history of asthma	
None	1,162 (53.8%)
Parents	696 (32.2%)
Grandparents	258 (11.9%)
Uncles and aunts	168 (7.78%)
Asthma severity	
Intermittent	564 (26.1%)
Persistent mild	789 (36.6%)
Persistent moderate	714 (33.1%)
Persistent severe	91 (4.22%)
Smoking	
Never smoker	1,359 (63%)
Former smoker	451 (20.9%)
Active smoker	347 (16.09%)
Alcohol consumption (g)	
≤ 22.5 g	956 (50.0%)
>22.5 g	956 (50.0%)
Pets at home	
Yes	639 (29.6%)
No	1,518 (70.4%)
Allergies	
Yes	943 (43.7%)
No	1,216 (56.3%)
Stressful event in the last 15 days	
Yes	312 (14.5%)
No	1,839 (85.5%)
Adherence to treatment (doctor's opinion)	
Very poor	41 (1.9%)
Poor	321 (14.9%)
Acceptable	814 (37.7%)
Good	756 (35.0%)
Very good	227 (10.5%)
How often did they forget to take their medicine?	
Never	837 (38.8%)
1-5/month	1,016 (47.1%)
6-10/month	229 (10.6%)
> 10/month	77 (3.57%)
Importance of compliance (patient's opinion)	
< 8	544 (25.2%)
≥ 8	1,612 (74.8%)
Treatment for asthma	
Oral corticosteroids	159 (7.5%)
LABA+Inhaled corticosteroids	1,499 (70.3%)
Inhaled corticosteroids	214 (10.0%)
SABA or LABA	259 (12.2%)
ACQ Score	
< 0.75	779 (36.1%)
0.75-1.50	573 (26.5%)
> 1.5	807 (37.4%)

Table 1 (continued)

	n (%)
Asthma control (doctor's opinion):	
Very poorly controlled	83 (3.85%)
Poorly controlled	329 (15.3%)
Controlled	734 (34.0%)
Completely controlled	1,011 (46.9%)
Asthma control (patient's opinion):	
Very poorly controlled	43 (2.0%)
Poorly controlled	193 (8.98%)
Controlled	675 (31.4%)
Completely controlled	1,238 (57.6%)

ACQ: Asthma Control Questionnaire; BMI: body mass index; LABA: long-acting beta-agonists; N: number; SABA: Short-acting beta-agonists; %: percentage.

they could take beta agonists on demand; and 4) only beta-2 agonists.

### Statistical analysis

Statistical analysis was performed using SAS software v8.2. 2. For the continuous variables, we calculated the mean, median, standard deviation, and maximum and minimum values. For the categorical variables, we calculated the absolute and relative frequencies.

Using logistic regression, we obtained the OR and its CI of 95%. In the logistic regression, we included as independent variables all those with a statistical significance of  $p < 0.2$  in the univariate analysis.

### Results

A total of 182 primary care doctors participated in the recruitment process. The analysis included 2159 patients (96.9% of the recruits), the majority of whom were women (58%), with a mean age of 48 years, and with a median time from diagnosis of asthma of 15.1 years (table 1). The prevalence of uncontrolled asthma was 63.9% (CI of 95%: 61.9-65.9%).

Independent determinants of poorly-controlled asthma were treatment with OCS, baseline asthma severity, the presence of a recent stressful event, the importance given to therapy compliance, and living in a rural area (table 2). In contrast, sex, age, obesity, smoking, alcohol consumption and educational level did not show any influence over asthma control (table 2).

### Discussion

The results of this study show an unsatisfactory state of asthma control in Spain since a large percentage of its population is not well controlled, as in other countries.<sup>6,9,10,16,17</sup> The use of the ACQ as an instrument for measuring asthma control reinforces the validity of the results since the questionnaire has been widely validated.<sup>8</sup>

In a previous study also performed in Spain in 2004 with primary-care and specialised medical consultation patients, 74% were not adequately controlled.<sup>18</sup>

In addition to poor control of the disease, patients often overestimate their degree of control, which could be one of the conditioning factors for poor therapy compliance and, therefore, may increase the individual, economic and social costs of the disease.<sup>9</sup>

The finding of worse control in patients that require OCS is consistent with the findings of other authors.<sup>11,12</sup> Since this type of treatment may be indicated in severe exacerbations, a determining factor of poor control of the disease, this association seems reasonable.<sup>6</sup> Other factors may be implicated in this association, such as failure of treatment adherence, which may reach 45% in patients

with OCS treatment,<sup>19</sup> and resistance to corticosteroids, which may affect around 10% of asthmatics.<sup>20</sup>

The baseline severity of the disease is the second most important factor in terms of influence on the lack of asthma control. Patients with moderate-severe asthma are more than three times more likely to be poorly controlled as compared to those with mild-intermittent asthma. This same effect has been referred to by other European studies with a high number of patients<sup>9,17</sup> and also in an original prospective study performed in France.<sup>21</sup> In contrast, a study performed on a Spanish population showed no influence of baseline severity on the degree of control of the disease.<sup>18</sup> In this case, patients came in almost equal amounts from medical specialists and general

practitioners. This fact may have caused differences in the results of the disease management since it is known that management under specialists improves results.<sup>22</sup>

The perception that asthmatic patients have of the disease seems far removed from reality given that between 45% and 85% of the patients with uncontrolled asthma believe that they have good control of the disease.<sup>10,16,17</sup> Furthermore, this poor perception is associated with poorer therapy compliance.<sup>23</sup> In our study, we evaluated the importance that patients attached to adherence, which could be considered an indicator of the perception of asthma, associating those who were less perceptive with a poorer control of the disease.

**Table 2**

Factors associated with poorly controlled asthma, univariate and multivariate analysis\*

	Uncontrolled asthma (%)	OR (95% CI), %	
		Univariate	Adjusted*
<b>Sex</b>			
Male	62.24	1	
Female	65.14	1.13 (0.95-1.35)	
<b>Age, years</b>			
18-39 years	55.82	1	1
40-59 years	67.04	1.61 (1.31-1.98)	1.26 (0.98-1.60)
≥ 60 years	70.50	1.89 (1.52-2.35)	1.29 (0.97-1.72)
<b>BMI (kg/m<sup>2</sup>)</b>			
< 25	59.12	1	1
≥ 25-30	64.89	1.28 (1.05-1.55)	1.07 (0.85-1.34)
≥ 30	71.13	1.70 (1.33-2.18)	1.14 (0.84-1.53)
<b>Smoking</b>			
Never smoker	62.03	1	1
Former smoker	68.96	1.36 (1.08-1.71)	1.11 (0.86-1.43)
Active smoker	64.55	1.12 (0.87-1.43)	1.16 (0.88-1.54)
<b>How often did they forget to take their medicine?</b>			
Never	55.56	1	1
Sometimes	69.21	1.80 (1.50-2.15)	1.62 (1.31-2.00)
<b>Alcohol consumption</b>			
≤ 22.5 g	63.18	1	
> 22.5 g	64.44	1.06 (0.88-1.27)	
<b>Educational level</b>			
Secondary or higher	58.04	1	1
None or primary school	70.93	1.61 (1.35-1.93)	1.18 (0.94-1.46)
<b>Place of residence</b>			
City	60.90	1	1
Town	68.31	1.38 (1.15-1.66)	1.29 (1.05-1.58)
<b>Stressful event in the last 15 days</b>			
No	61.34	1	1
Yes	78.53	2.31 (1.73-3.07)	2.44 (1.77-3.35)
<b>Adherence to treatment (doctor's opinion)</b>			
Acceptable, good or very good	61.66	1	1
Poor or very poor	75.14	1.88 (1.45-2.43)	1.47 (1.09-1.98)
<b>Importance of adherence (patient's opinion)</b>			
≥ 8	60.67	1	1
< 8	73.35	1.78 (1.44-2.21)	1.66 (1.30-2.12)
<b>Baseline severity of asthma</b>			
Intermittent or mild persistent	53.14	1	1
Moderate or severe	82.11	4.05 (3.28-4.99)	3.11 (2.48-3.90)
<b>Treatment for asthma</b>			
SABA or LABA	39.77	1	1
Inhaled corticosteroids	51.87	1.63 (1.13-2.35)	1.49 (1.00-2.20)
LABA+Inhaled corticosteroids	67.58	3.16 (2.41-4.14)	2.09 (1.56-2.81)
Oral corticosteroids	89.94	13.54 (7.63-24.02)	6.55 (3.54-12.12)

ACQ: Asthma Control Questionnaire; BMI: body mass index; LABA: long lasting beta-agonists; OR: odds ratio related with the other categories of each variable; SABA: Short-acting beta-agonists.

\* Adjusted for the variables included in the table.

The history of a stressful event increases by more than double the probability of poor asthma control. Although this was a transversal study, the question was whether there was a previous stressful event, which seems to indicate that the psychological phenomenon contributes to the worsening of the respiratory disease and not the other way round. Various psychological factors have been related to poor asthma control, but there is no clearly defined psychopathology associated with worse control of this disease.<sup>24</sup> It is known that anxiety and depression are twice as frequent in asthmatics than in the general population.<sup>25</sup> Nevertheless, the effect on asthma control is different for each type of disorder. Depression is associated with poorer control of the disease, but anxiety is not.<sup>25,26</sup> In addition to the change in behaviour that a person's mood may cause, common psychological mechanisms have been suggested in which inflammatory cytokines or the cholinergic reactivity of the airways may be involved.<sup>25,26</sup> Also both anxiety and depression are associated with negative attitudes towards medication, which could lead to poor treatment compliance.<sup>27</sup>

Compliance was evaluated using various tools, although no one method of measurement is considered the Gold Standard.<sup>28</sup> In this study we evaluated compliance in terms of the frequency of forgetting to take medication as reported by the patient as well as the subjective perception of the doctor, in a similar fashion as other authors.<sup>29</sup> Generally, in chronic diseases such as with asthma, compliance is often suboptimal.<sup>24</sup> Even in clinical trials with chronic patients, where patient care is standardised, the rates of compliance vary between 43-78%,<sup>28,30</sup> despite the knowledge that therapy compliance according to guidelines reduces the morbidity and mortality of asthma.<sup>31</sup>

Furthermore, the fact that asthma progresses with episodic exacerbations makes many patients think of not being sick when there is an absence of symptoms, and therefore making them believe that they do not need treatment.<sup>32</sup> This lack of compliance causes poorer asthma control in our patients, as has been reported by other authors.<sup>9,33</sup>

The difference in the degree of control between patients who live in an urban environment as compared to those who live in a rural environment is not surprising. In various diseases, a different behaviour has been observed among those who live in rural settings versus those who live in urban settings, which is probably due to the interaction of various elements not analysed in this study.<sup>34,35</sup> In asthma, the influence of environmental factors plays an especially relevant role. Furthermore, other interrelated factors may be associated with the place of residence such as differences in access to health care, socioeconomic status, occupational differences and the level of compliance with health recommendations.<sup>38-40</sup>

One limitation of this study is that, as a transversal study, the validity of the conclusions may be limited by the difficulty in differentiating between cause and effect. However, it is unlikely that the factors associated with asthma control change during the period in which the dependent variable is measured. In these cases, the results of a transversal study are similar to those obtained from longitudinal studies.<sup>41</sup>

The lack of association between asthma control and factors such as smoking and obesity was initially surprising. We believe, as other authors do, that the "healthy smoker" effect may affect these results. This is consistent with the observation in the univariate analysis that being an ex-smoker increases the risk of poor asthma control by 36%, while this effect is not observed among active smokers nor in the multivariate analysis.<sup>42</sup> As for obesity, some recent studies also did not observe a significant relationship with poor asthma control, pointing to the possibility of common pathophysiological mechanisms as confounding factors in this association.<sup>43,44</sup>

Another limitation was that the doctors who participated were not included randomly. However, given the high number of individuals included and the distribution among primary care

doctors from all over the country, it is likely that these results constitute the actual situation of asthma control in Spain, at least among those patients who attend primary care offices. Furthermore, it is known that almost 80% of the Spanish population visits their primary care doctor at least once a year.<sup>45</sup>

Regarding variables included, one can also consider certain limitations such as the lack of spirometry when carrying out fieldwork and various factors that could change asthma control such as rhinitis and gastroesophageal reflux. However, the inclusion of all variables, which in some previous studies showed an influence over asthma control, seemed untenable for a study with such a wide geographical distribution and such a high number of patients.

In conclusion, asthma remains poorly controlled in Spain but some of the factors related to this situation could be modified through the healthcare system. Furthermore, the need for a deep study on the health education aspects seems especially important.

### Conflicts of Interest

Javier Nuevo and Mónica Tafalla are employed by AstraZeneca Farmacéutica Spain S.A.

### Funding

The CHAS study was financed by AstraZeneca Farmacéutica Spain S.A.

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