

Original article

Asthma control in Europe: A real-world evaluation based on an international population-based study

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Background: Epidemiologic evidence related to asthma control in patients from the general population is scanty.

Objectives: We sought to assess asthma control in several European centers according to the Global Initiative for Asthma (GINA) guidelines and to investigate its determinants.

Methods: In the European Community Respiratory Health Survey II (1999-2002), 1241 adults with asthma were identified and classified into inhaled corticosteroid (ICS) users and non-ICS users in the last year. Control was assessed in both groups

by using the GINA proposal (controlled, partly controlled, and uncontrolled asthma), and it was related to potential determinants.

Results: Only 15% (95% CI, 12% to 19%) of subjects who had used ICSs in the last year and 45% (95% CI, 41% to 50%) of non-ICS users had their asthma under control; individuals with uncontrolled asthma accounted for 49% (95% CI, 44% to 53%) and 18% (95% CI, 15% to 21%), respectively. Among ICS users, the prevalence of uncontrolled asthma showed great variability across Europe, ranging from 20% (95% CI, 7% to 41%; Iceland) to 67% (95% CI, 35% to 90%; Italy).

Overweight status, chronic cough and phlegm, and sensitization to *Cladosporium* species were associated with poor control in ICS users. About 65% and 87% of ICS users with uncontrolled and partly controlled asthma, respectively, were on a medication regimen that was less than recommended by the GINA guidelines.

Conclusion: Six of 7 European asthmatic adults using ICSs in the last year did not achieve good disease control. The large majority of subjects with poorly controlled asthma were using anti asthma drugs in a suboptimal way. A wide variability in asthma control emerged across Europe.

Clinical implications: Greater attention should be paid to asthma management and to the implementation of the GINA guidelines. (J Allergy Clin Immunol ■■■■;■■■:■■■-■■■.)

Key words: Asthma control, inhaled corticosteroids, Global Initiative for Asthma, predictors of uncontrolled asthma, *Cladosporium* species, total IgE, body mass index, European Community Respiratory Health Survey, population-based study, cross-sectional study

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Achieving and maintaining optimal asthma control is a major goal of asthma management. Although the results of clinical trials advocate that asthma control can be reached in most patients,¹ the epidemiologic evidence suggests that many subjects with asthma have poorly controlled disease and that there is a significant gap between the treatment goals and the current level

Abbreviations used

BMI: Body mass index
 ECRHS: European Community Respiratory Health Survey
 GINA: Global Initiative for Asthma
 ICS: Inhaled corticosteroid

of asthma control achieved in the general population.²⁻⁵ Therefore the challenge that remains is to find the best way to assess asthma control and define management strategies to ensure that this control is achieved and maintained.⁶ Accordingly, the new update of the Global Initiative for Asthma (GINA) guidelines 2006⁷ is based on the control of the disease and attempts to quantify and graduate the level of control by using a classification of asthmatic subjects into “controlled,” “partly controlled,” and “uncontrolled” groups.

This newly introduced asthma management approach based on the monitoring of disease control is expected to facilitate acceptance and use of asthma guidelines in clinical practice. However, the practical implementation of the asthma guidelines can only be improved when all clinicians and general practitioners are well aware of the level of asthma control that their population has reached and of the consequences of uncontrolled asthma in terms of morbidity, quality of life, and economic burden.

The major aims of this study were to assess the prevalence of uncontrolled and partly controlled asthma in Europe, according to the GINA definition, and to investigate the determinants of asthma control in subjects with different levels of asthma severity who were identified in the frame of the European Community Respiratory Health Survey (ECRHS) II, which is an international population-based survey.

METHODS

Study design

The ECRHS⁸ is a multicenter study on the prevalence, determinants, and management of asthma performed in 48 centers during 1991 through 1993. The design of the survey involved 2 stages. In the first stage a screening questionnaire on respiratory symptoms was mailed to a community-based probability sample of 20- to 44-year-old persons. In the second stage a 20% random sample of responders to stage 1, with the addition of subjects who reported symptoms of waking with shortness of breath or asthma attacks in the last 12 months or who were using asthma medication in stage 1 at the screening questionnaire (symptomatic sample), was invited to a local chest clinic to undergo a standardized clinical interview and allergologic and lung function tests. The ECRHS II⁹ is a follow-up study of the participants in the second stage of ECRHS performed between 1999 and 2002. The following analyses consider data from 25 centers that took part in the ECRHS II.

Ethics approval

Local ethics committees at each center approved the study protocols.

Questionnaires and clinical tests

In the ECRHS II the subjects were administered a structured clinical interview, which included questions on the presence of asthma or respiratory symptoms and therapy (the full questionnaire can be found at <http://www.ecrhs.org/quests.htm>). Pack-years smoked over the subject's lifetime were calculated, combining information on smoking habits obtained in the ECRHS I and II.¹⁰ The subject's weight and height were measured according to a standard procedure. Weight was recorded to the nearest kilogram. Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters. In a few centers participants were asked their height and weight. FEV₁ was measured in all subjects who agreed according to a standardized protocol.¹¹ FEV₁ percent predicted was computed on the basis of sex, age, and height.¹² Blood samples were collected, and specific IgE levels against house dust mite (*Dermatophagoides pteronyssinus*), cat dander, timothy grass, and *Cladosporium* species were measured. A subject was considered sensitized to an allergen if the assay result for that allergen was greater than 0.35 kU/L, the detection limit of the assay.

Definition of physician-diagnosed current asthma

In the ECRHS II a subject who reported a physician's diagnosis of asthma and who had respiratory symptoms (wheeze; nocturnal chest tightness; attack of breathlessness after activity, at rest, or at night; or 1 asthma attack) or had used asthma medications in the previous 12 months was considered a subject with current asthma. All individuals with physician-diagnosed current asthma in the ECRHS II were eligible for this analysis.

Asthma control

According to the GINA guidelines,⁷ asthma was considered controlled if all these features were present: diurnal symptoms less than once a week and no asthma attacks in the last 3 months, no activity (work and other activities) limitations in the last 12 months, no nocturnal symptoms in the last 3 months, short-acting β_2 -agonists twice or less per week in the last 3 months and no use of oral steroids in the last 12 months, and FEV₁ of 80% of predicted value or greater. Asthma was considered partly controlled if 1 or 2 of the above features were absent. Asthma was considered uncontrolled if more than 2 features were absent or if asthma, shortness of breath, or wheezing had caused hospital/emergency department admissions in the last 12 months; oral steroids were used in short courses or continuously in the last 12 months; or the subject had more than 12 asthma attacks (1 per week or more) in the last 3 months.

Potential determinants of asthma control

The following factors were examined: sex; age; educational level (low level indicated by having completed full-time education before the age of 16 years and high level indicated otherwise); age at asthma onset; allergic rhinitis (present if a subject reported having nasal allergies, including hay fever); chronic cough and phlegm; nonseasonal asthma (present if a subject reported usually having asthma attacks for >6 months a year); parental asthma (present if a subject reported that his or her mother or father had ever had asthma); lifetime number of 10 pack-years' smoking history; BMI (BMI <25, BMI $\geq$ 25); and sensitization to house dust mite, cat, timothy grass, or *Cladosporium* species.

Treatment

The classification of treatment followed the indications of the last version of the GINA guidelines.⁷ Treatment was classified in one of 5 steps, according to the reported daily medication use in the last 3

months, except for oral steroids; subjects using oral steroids (in short courses or continuously) in the last 12 months were classified in step 5. For a detailed description of the treatment classification, see the [Methods](#) section of the Online Repository at www.jacionline.org.

Statistical analysis

Data were summarized as medians with interquartile ranges for continuous variables and as percentages for categorical variables. Comparison of variables across strata was performed by using the χ^2 test for categorical variables and the Kruskal-Wallis test for continuous variables. The conventional 5% level of statistical significance was used.

Estimates from different countries were examined for heterogeneity by using the test statistic Q .¹³

A multinomial regression model was fitted to the data by using asthma control (controlled, partly controlled, and uncontrolled) as the dependent variable to identify the factors associated with asthma control. The model identified centers as the clustering factors, and the Huber/White sandwich estimate of variance was used to adjust for within-center correlation.¹⁴ Multivariate associations of potential determinants with asthma control were expressed by relative risk ratios (using controlled asthma as the reference category) and their 95% CIs. All the variables considered for the univariate analysis were included in the multinomial regression model.

All the analyses were stratified by any use of inhaled corticosteroids (ICSs) in the last 12 months (ie, ICS users vs non-ICS users).

The statistical analysis was performed with STATA software, release 9 (StataCorp, College Station, Tex).

RESULTS

Participants and nonparticipants

Of the 15,705 subjects participating in the ECRHS I from 25 centers, 9580 took part in the ECRHS II (response rate, 61%). Participants were slightly older than nonparticipants (median, 34 [interquartile range, 7] years vs 33 [interquartile range, 7] years; $P < .001$), and the proportion of subjects who reported that they were smokers in the ECRHS I was significantly smaller in subjects participating in the ECRHS II with respect to subjects not participating (36% vs 44%, $P < .001$).

Asthmatic sample

In the ECRHS II 1241 adults with current asthma from 25 centers in 11 countries were identified. About 52% of the subjects came from the strictly random sample (see further information in the Results section and [Table E1](#) in the Online Repository at www.jacionline.org).

Subjects from the symptomatic sample were more likely to report nocturnal symptoms (33% vs 26%, $P = .008$) and short-acting β_2 -agonist use more than twice a week (34% vs 24%, $P < .001$) in the last 3 months and emergency department visits (8% vs 5%, $P = .013$) and hospital admissions (2.4% vs 0.6%, $P = .011$) in the last 12 months than subjects from the random sample. The proportions of subjects reporting diurnal symptoms in the last 3 months and of subjects with FEV₁ of less than 80% of predicted value were similar in the 2 groups.

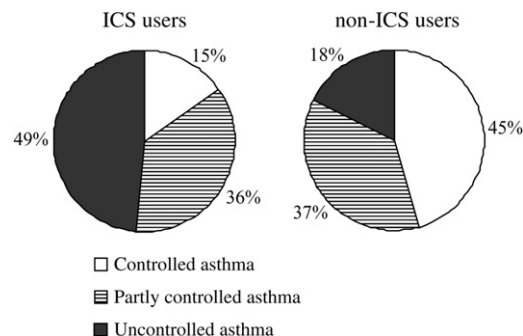


FIG 1. Distribution of asthma control based on ICS use in the last 12 months.

ICS users and non-ICS users

About 43% of the subjects in the sample had used ICSs in the last 12 months ($n = 521$). Of the 690 non-ICS users, only 26 (4%) had used theophylline, a cromone, or a leukotriene modifier in the last 12 months. ICS users and non-ICS users were statistically significantly different with regard to the percentages of women (62% and 56%, respectively; $P = .025$) and of subjects reporting chronic cough and phlegm (32% and 22%, respectively; $P < .001$), nonseasonal asthma (47% and 36%, respectively; $P < .001$), sensitization to cat (41% and 32%, respectively; $P = .003$), and sensitization to *Cladosporium* species (8% and 4%, respectively; $P = .004$).

ICS users were more likely to report diurnal symptoms (once a week or more; 37% vs 15%, $P < .001$) and nocturnal symptoms (43% vs 19%, $P < .001$), and they also had a poorer lung function (proportion of subjects with FEV₁ <80% of predicted value, 20% vs 10%; $P < .001$) than non-ICS users.

Among subjects who had used ICSs in the last 12 months, 54% reported they had used ICSs continuously in the last 3 months. The remaining 46% reported having used ICSs when needed or in short courses or not having used ICSs in the last 3 months.

Asthma control

Sufficient data to classify asthma control were available for 1042 individuals with asthma (1025 had data on ICS use in the last 12 months: 468 ICS users and 557 non-ICS users), and 524 (50%) of them belonged to the random sample. Overall, 32% (95% CI, 29% to 34%) of the asthmatic subjects had completely controlled symptoms: 15% (95% CI, 12% to 19%) in the group who used ICSs in the last 12 months and 45% (95% CI, 41% to 50%) in the group of non-ICS users ([Fig 1](#)). The prevalence of uncontrolled asthma in the overall sample was 32% (95% CI, 29% to 35%), 49% (95% CI, 44% to 53%) in ICS users and 18% (95% CI, 15% to 21%) in non-ICS users. A significant between-country variation ($P < .001$) in the percentage of uncontrolled asthma was found in ICS users: the prevalence ranged from 20% (95% CI, 7% to 41%; Iceland) to 67% (95% CI, 35% to 90%; Italy; [Fig 2](#)). No geographic heterogeneity was detected in subjects not using ICSs.

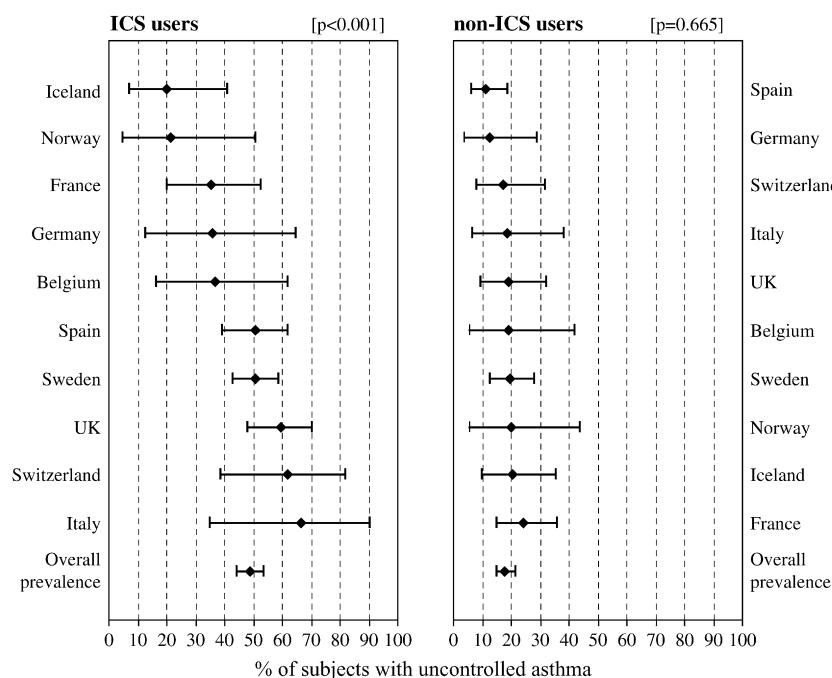


FIG 2. Prevalence of subjects with uncontrolled asthma among ICS users and non-ICS users, according to the country. Estonia was not considered because of the small number of ICS users ($n = 3$). The P value for heterogeneity between countries is reported in brackets.

Determinants of asthma control: Univariate analysis

Among ICS users, the presence of chronic cough and phlegm and nonseasonal asthma was associated with the lack of control (Table I); overweight or obese subjects were more frequent among the uncontrolled (56%) or partly controlled (55%) group than among the controlled group (38%, $P = .030$). The proportion of ICS users reporting sensitization to *Cladosporium* species ranged from 2% in subjects with controlled asthma to 5% in subjects with partly controlled asthma and up to 12% in subjects with uncontrolled asthma ($P = .005$), whereas the percentage of subjects sensitized to grass pollen was higher in subjects with controlled asthma.

In the case of non-ICS users, the proportion of subjects reporting chronic cough and phlegm and nonseasonal asthma and the proportion of subjects having total IgE levels of greater than 100 kU/L significantly increased as asthma control decreased (Table II).

Determinants of asthma control: Multivariate analysis

In ICS users, when all the variables were considered simultaneously (Table III), the risk of having partly controlled and uncontrolled asthma decreased with age, and it was more than 3-fold greater in obese or overweight subjects than in normal-weight or underweight subjects. The risk of having a lack in asthma control was particularly high in subjects reporting chronic cough and phlegm and in those sensitized to *Cladosporium* species. Sensitization

to grass pollen was inversely associated with partly controlled asthma.

In the case of non-ICS users, subjects with nonseasonal asthma and subjects with total IgE levels of greater than 100 kU/L had a higher risk of having partly controlled or uncontrolled asthma. Subjects with a greater number of pack-years smoked, chronic cough and phlegm, or an older age at asthma onset had a significantly greater risk of having uncontrolled asthma.

Asthma management in ICS users

Among asthmatic subjects who had used ICSs in the last year, 30% reported that they had received a written personalized asthma action plan from their physician, 43% reported to own a peak flowmeter, and 22% reported that they had undergone spirometry in the last 12 months. The prevalence of uncontrolled asthma was significantly higher in subjects who reported that they had been given a written plan from their physician in comparison with subjects who did not (58% vs 45%, $P = .030$), as well as in subjects who owned a peak flowmeter in comparison with subjects who did not possess a peak flowmeter (55% vs 43%, $P = .025$, see Table E2 in the Online Repository at www.jacionline.org).

The proportion of subjects in the 5 steps of asthma treatment of the GINA guidelines 2006 is reported in Fig 3. It is interesting to note that about 39% of the subjects with uncontrolled asthma and 53% of those with partly controlled asthma had not taken any daily anti-inflammatory therapy in the last 3 months (step 1). Oral steroids

TABLE I. Distribution of the main sociodemographic and clinical characteristics in subjects with current asthma using ICSs in the last 12 months (ICS users), according to the level of asthma control

	Controlled asthma (n = 72)	Partly controlled asthma (n = 168)	Uncontrolled asthma (n = 228)	Total	P value
Female sex (%)	65.3	59.5	64.5	62.8	.539
Median age (y; IQR)	44.0 (12.2)	42.5 (13.4)	42.7 (12.1)	42.8 (12.5)	.903
Low educational level (%)	9.7	13.9	16.0	14.3	.408
BMI ≥ 25 kg/m ² (%)	38.0	54.6	55.7	52.3	.030
Median lifetime smoking (no. of 10 pack-years; IQR)	0.00 (0.60)	0.00 (1.04)	0.09 (1.38)	0.00 (1.13)	.129
Parental asthma (%)	22.4	26.6	31.9	28.5	.258
Median age at onset (y; IQR)	20.0 (17.0)	20.0 (21.0)	18.0 (22.0)	20.0 (20.0)	.067
Nonseasonal asthma (%)	47.1	38.4	53.5	47.2	.013
Allergic rhinitis (%)	65.3	69.6	68.0	68.2	.799
Chronic cough and phlegm (%)	16.7	28.6	39.5	32.1	.001
Total IgE >100 kU/L (%)	48.5	42.7	53.2	48.6	.165
Sensitization to HDM (%)	29.4	37.8	39.6	37.2	.327
Sensitization to cat (%)	44.1	40.6	38.5	40.2	.717
Sensitization to grass pollen (%)	50.0	28.7	38.0	36.7	.010
Sensitization to <i>Cladosporium</i> species (%)	1.5	4.9	12.3	7.8	.005

Statistically significant results are shown in bold.
IQR, Interquartile range; HDM, house dust mite.

TABLE II. Distribution of the main sociodemographic and clinical characteristics in subjects with current asthma not using ICSs in the last 12 months (non-ICS users), according to the level of asthma control

	Controlled asthma (n = 253)	Partly controlled asthma (n = 205)	Uncontrolled asthma (n = 99)	Total	P value
Female sex (%)	59.3	54.6	55.6	56.9	.580
Median age (y; IQR)	41.5 (12.4)	42.7 (13.7)	41.8 (12.7)	41.9 (12.7)	.590
Low educational level (%)	13.8	15.2	11.1	13.9	.627
BMI ≥ 25 kg/m ² (%)	50.8	50.0	56.5	51.4	.589
Median lifetime smoke (no. of 10 pack-years; IQR)	0.09 (1.43)	0.04 (1.38)	0.00 (1.61)	0.05 (1.49)	.841
Parental asthma (%)	23.9	26.0	21.9	24.3	.726
Median age at onset (y; IQR)	20.0 (23.0)	19.0 (23.0)	19.0 (20.0)	19.0 (23.0)	.780
Nonseasonal asthma (%)	27.5	39.2	45.6	35.2	.003
Allergic rhinitis (%)	60.7	68.8	66.7	64.8	.181
Chronic cough and phlegm (%)	18.6	22.9	32.7	22.7	.018
Total IgE >100 kU/L (%)	40.8	53.3	61.5	48.9	.002
Sensitization to HDM (%)	35.1	38.5	33.7	36.1	.690
Sensitization to cat (%)	27.6	32.4	33.7	30.4	.447
Sensitization to grass pollen (%)	38.3	42.9	41.0	40.5	.647
Sensitization to <i>Cladosporium</i> species (%)	3.5	4.4	3.6	3.9	.894

Statistically significant results are shown in bold.
IQR, Interquartile range; HDM, house dust mite.

(step 5) were used in short courses or daily by 22% of ICS users with uncontrolled asthma.

DISCUSSION

Our study showed that 85% of the European asthmatic adults from the ECRHS II who had used ICSs in the last 12 months were not able to achieve total control of the disease: 49% of them had uncontrolled asthma, and 36% had partly controlled asthma. Among those who had not used ICSs in the last 12 months, 18% had uncontrolled and

36% had partly controlled asthma. These results confirm the evidence that asthma control is suboptimal in a remarkable proportion of patients, according to previous studies.^{2,3}

We used a composite measure of asthma control, according to the scheme based on the current opinion and proposed in the last update of the GINA guidelines.⁷ This measure has not been formally validated. However, it jointly takes several markers of uncontrolled asthma into account (diurnal and nocturnal symptoms, limitation of activities, the need for reliever or rescue treatment, lung function, and exacerbations) that have usually been

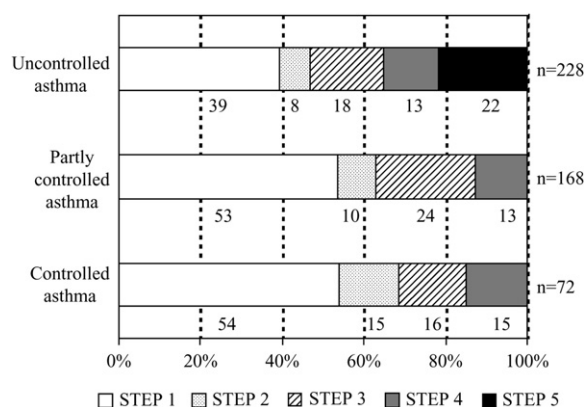
TABLE III. Adjusted* relative risk ratios† (95% CI) for the association between asthma control and risk factors

	ICS use in the last 12 mo			
	Yes		No	
	Partly controlled asthma	Uncontrolled asthma	Partly controlled asthma	Uncontrolled asthma
Sex (female vs male)	0.87 (0.37-2.05)	1.21 (0.62-2.37)	0.67 (0.44-1.00)	0.91 (0.49-1.69)
Age	0.94 (0.88-0.99)	0.96 (0.92-1.00)	1.01 (0.97-1.05)	0.99 (0.95-1.03)
Educational level (low vs high)	1.01 (0.24-4.17)	0.81 (0.22-3.05)	1.06 (0.48-2.31)	1.93 (0.81-4.62)
BMI (≥ 25 kg/m ²)	3.53 (1.77-7.06)	3.22 (1.57-6.59)	0.93 (0.54-1.59)	1.83 (0.75-4.46)
Lifetime no. of 10 pack-years	1.30 (0.88-1.93)	1.33 (0.88-2.03)	0.95 (0.78-1.14)	1.23 (1.00-1.52)
Parental asthma	1.59 (0.75-3.40)	1.95 (0.83-4.55)	1.03 (0.51-2.06)	0.51 (0.22-1.17)
Age at onset	1.02 (0.98-1.05)	0.99 (0.96-1.03)	1.02 (0.99-1.05)	1.03 (1.00-1.05)
Nonseasonal asthma	0.79 (0.41-1.54)	1.33 (0.58-3.05)	1.90 (1.23-2.95)	2.49 (1.51-4.11)
Allergic rhinitis	2.16 (0.80-5.82)	1.86 (0.81-4.31)	1.24 (0.79-1.95)	1.20 (0.60-2.40)
Chronic cough and phlegm	2.21 (0.78-6.24)	3.55 (1.31-9.60)	1.32 (0.81-2.14)	2.64 (1.35-5.16)
Total IgE >100 kU/L	0.58 (0.31-1.10)	1.07 (0.47-2.48)	1.69 (1.02-2.79)	3.67 (1.76-7.67)
Sensitization to HDM	2.08 (0.80-5.41)	1.57 (0.54-4.51)	0.99 (0.53-1.87)	0.64 (0.32-1.31)
Sensitization to cat	1.48 (0.79-2.75)	0.60 (0.20-1.80)	1.11 (0.58-2.11)	1.24 (0.54-2.81)
Sensitization to grass pollen	0.19 (0.08-0.43)	0.42 (0.12-1.46)	0.99 (0.53-1.84)	0.78 (0.37-1.63)
Sensitization to <i>Cladosporium</i> species	4.73 (0.39-56.6)	13.6 (1.25-148.28)	1.30 (0.57-2.96)	1.49 (0.35-6.30)

HDM, House dust mite.

*Also adjusted for type of sample (random vs symptomatic).

†Obtained through a multinomial logistic regression model, with the controlled group as the reference category. Relative risk ratios that are significantly different from 1 at the 5% level are shown in bold.

**FIG 3.** GINA treatment steps according to controlled, partly controlled, and uncontrolled asthma among ICS users. The numbers close to each bar section are percentages. *Step 1*, No daily controller; *step 2*, low-dose ICS, or leukotriene modifier, or theophylline, or cromones; *step 3*, low-dose ICS combined with leukotriene modifier, or with theophylline, or with long-acting β_2 -agonist, or medium/high-dose ICS alone; *step 4*, medium/high-dose ICS combined with leukotriene modifier or with long-acting β_2 -agonist; *step 5*, oral steroids.

considered separately in the past but that should be considered together to define the global health status of subjects with asthma.¹⁵

We chose to analyze ICS users and non-ICS users separately because ICS use can be considered a proxy of asthma severity. This choice is in agreement with other articles on asthma control.^{3,16} In our study ICS users were more likely to report diurnal and nocturnal symptoms and had poorer lung function than non-ICS users. However, ICS users are likely to constitute only a subset of subjects with persistent asthma, which also includes non-ICS users

with frequent symptoms, poor lung function, or both. On the other hand, non-ICS users are likely to be a mixture of subjects with intermittent asthma (no symptoms and normal lung function) who do not require ICSs and subjects with persistent asthma (frequent symptoms, poor lung function, or both) who are inadequately treated and should be taking ICSs.⁷

Although some countries are represented by only 1 center, there is evidence of a wide geographic variability in asthma control among ICS users. In fact, we found that the proportion of uncontrolled asthma in ICS users was significantly heterogeneous between countries in Europe, ranging from 20% (Iceland) to 67% (Italy). The geographic variability in asthma control could be due to different levels of implementation of the guidelines for asthma treatment, to a different use of drugs, or to a geographic variation in asthma severity across Europe. In a previous study on antiasthma medication in the ECRHS, the authors found that there was a wide variation in the use of inhaled anti-inflammatory medication, mainly steroid inhalers.¹⁷ Ten years later, in the same cohort a general increase in the use of ICSs was found, even if the geographic variability in ICS use was still apparent.¹⁸ It is worth noting that the country with the highest percentage of subjects with uncontrolled asthma in our study (Italy) was also the country with the lowest percentage of ICS daily use (29%).¹⁸

In our study subjects with chronic cough and phlegm were more likely to have their symptoms partly controlled or uncontrolled than subjects without chronic cough and phlegm, and this association was stronger in ICS users. Among ICS users, subjects who were younger, overweight, or sensitized to *Cladosporium* species were more likely to have partly controlled or uncontrolled asthma; subjects sensitized to grass pollen were more likely to

have controlled asthma. Among non-ICS users, a high level of total IgE, nonseasonal asthma, lifetime pack-years of smoking, and a later age at asthma onset were associated with poorly controlled asthma.

It has been hypothesized that in subjects with asthma the underlying severity of the disease is inversely associated with the level of control and that its effect on control is modulated by different factors.¹⁹ Therefore the association between poorly controlled asthma and chronic cough and phlegm, BMI, or sensitization to *Cladosporium* species found in our analysis, mainly or only in ICS users, could be explained by the underlying association between asthma severity and the above risk factors, which have been previously described.²⁰⁻²³

High serum total IgE levels are strongly associated with asthma severity,²⁰ and they are an independent predictor of immediate treatment response to ICSs.²⁴ A low decrease in lung function in long-term steroid users was observed in asthmatic subjects with increased (>100 kU/L) total IgE levels, whereas subjects with low IgE levels seemed to be less responsive.²⁵ In our study we have described a strong association between total IgE levels and poorly controlled asthma in non-ICS users. The lack of a similar association in subjects taking ICSs is probably due to the beneficial results that steroids yield in atopic subjects with asthma.

We considered subjects with asthma who received a physician's diagnosis and could consequently have been prescribed optimal treatment. Among the subjects who had used ICSs in the last year (ie, who had been prescribed ICSs by their physician), however, 65% and 87% of ICS users with uncontrolled and partly controlled asthma, respectively, were taking a medication step that was lower than the one recommended by the GINA guidelines (steps 1, 2, or 3). Our data support the hypothesis that the poor control of asthma is at least in part due to the inadequacy of the treatment regimen to the subject's current level of control. In contrast, subjects with uncontrolled asthma and on treatment steps 4 and 5 are likely to have difficult-to-treat or steroid-resistant asthma.

Among asthmatic individuals who had used ICSs in the last year, only 30% reported ever having received a personalized written action plan from their physician, and only 22% of them had undergone spirometry in the last 12 months. These findings are in agreement with previous studies³ and indicate an inadequate monitoring of disease progression. Asthma control was significantly poorer for subjects who had received a written action plan or who owned a peak flowmeter. These associations are likely to be confounded by severity; that is, patients with more severe asthma whose symptoms are less controlled are probably followed up more carefully by physicians who tend to pay more precise attention to disease management.

To our knowledge, this is one of the few population-based studies describing asthma control and its potential determinants in a relatively large sample of adults with asthma in Europe, which has used a composite measure of asthma control.

This study has some potential limitations. It is a cross-sectional study, and therefore it is not possible to establish the temporal sequence between the determinants studied and asthma control. Furthermore, the centers were not selected with the intention of being representative of the countries. Hence our results must be interpreted with caution.

In conclusion, our study found that a major proportion of European adults with asthma are poorly controlled and that the majority of them were receiving suboptimal antiasthma therapy. Among subjects who had used ICSs in the last 12 months, the level of control seems to be highly variable across the European centers involved. Our findings highlight that greater attention should be paid to disease management in subjects with poorly controlled asthma.

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Professor Paul Vermeire was one of the earlier members of the ECRHS, joining the study from its beginning in the early 1990s. He was principal investigator in the 2 Belgian centers and a member of the Steering Committee. With his extensive clinical knowledge and experience, he made important contributions to the work of the Therapy and Health Economics Working Group. He died in early August during the final preparation of this paper and will be much missed by his colleagues and friends in the ECRHS.

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METHODS

The classification of treatment followed the indications of the last version of the GINA guidelines^{E1}; treatment was classified in one of 5 steps, according to the reported daily medication use in the last 3 months, except for oral steroids (use in the last 12 months): step 1, no daily controller medication; step 2, beclomethasone dipropionate (BDP) of 500 µg or less (or an equipotent dose of another ICS) or leukotriene modifiers, or theophylline, or cromones; step 3, BDP of 500 µg or less (or equivalent) plus long-acting inhaled β_2 -agonist, or BDP of 500 µg or less (or equivalent) plus leukotriene modifiers, or BDP of 500 µg or less (or equivalent) plus theophylline, or BDP of greater than 500 µg (or equivalent); step 4, BDP of greater than 500 µg (or equivalent) plus long-acting inhaled β_2 -agonist or plus leukotriene modifiers; step 5, oral steroids in short courses or continuously.

RESULTS

Table E1 shows the numbers and percentages of subjects in the random sample by center and the total number of subjects with asthma considered in the analysis when subjects from the symptomatic sample were included. The sample composition (ie, the percentage of individuals from the random sample) significantly varied in the different centers ($P < .001$).

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TABLE E1. Number of subjects from the random sample, number (percentage) of subjects with current asthma from the random sample, and number of subjects with current asthma when subjects from the symptomatic sample were included in each center

Country	Center	Subjects from the random sample	Subjects with asthma from the random sample (%)	Total no. of subjects with asthma (random and symptomatic samples)
Belgium	South Antwerp	339	11 (3.2)	23
	Antwerp City	298	18 (6.0)	28
Germany	Hamburg	303	25 (8.3)	25
	Erfurt	287	23 (8.0)	23
Spain	Barcelona	271	14 (5.2)	46
	Galdakao	360	13 (3.6)	46
	Albacete	307	18 (5.9)	53
	Oviedo	242	13 (5.4)	34
France	Huelva	204	12 (5.9)	30
	Pessac	165	23 (13.9)	23
	Grenoble	384	34 (8.9)	58
	Montpellier	201	23 (11.4)	23
Italy	Paris	433	45 (10.4)	45
	Pavia	192	7 (3.7)	7
	Torino	123	8 (6.5)	17
	Verona	204	14 (6.9)	18
United Kingdom	Ipswich	297	40 (13.5)	83
	Norwich	257	39 (15.2)	77
Iceland	Gardabaer	457	39 (8.5)	77
Norway	Bergen	595	63 (10.6)	63
Sweden	Göteborg	491	42 (8.6)	95
	Umeå	421	43 (10.2)	121
	Uppsala	513	41 (8.0)	131
Switzerland	Basel	458	33 (7.2)	82
Estonia	Tartu	259	4 (1.5)	13
Total		8061	645 (8.0)	1241

TABLE E2. Distribution of asthma control according to some features of disease management in subjects using ICSs in the last 12 months

	n*	Controlled asthma	Partly controlled asthma	Uncontrolled asthma	Total	P value
Ever received a written action plan from physician (%)						.030
No	322	17.1	37.6	45.3	100.0	
Yes	137	11.0	30.6	58.4	100.0	
Owning a peak flowmeter (%)						.025
No	265	15.9	40.7	43.4	100.0	
Yes	202	14.9	29.7	55.4	100.0	
Spirometry in the last 12 mo (%)						.862
No	363	15.7	36.4	47.9	100.0	
Yes	102	14.7	34.3	51.0	100.0	
Daily use of ICS in the last 3 mo (%)						.093
No	227	16.3	40.1	43.6	100.0	
Yes	241	14.5	32.0	53.5	100.0	

Statistically significant results are reported in boldface.

*Numbers might not sum up to the total of ICS users (n = 468) because of missing data.