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 antiasthma 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 2007;120:1360-7.)

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*

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 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

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

Global Initiative for Asthma (GINA) guidelines 2006[7] 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 ECRHS[8] 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 II[9] 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. FEV_1 was measured in all subjects who agreed according to a standardized protocol.[11] FEV_1 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 FEV_1 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.