

Clinical management of asthma in 1999: the Asthma Insights and Reality in Europe (AIRE) study

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ABSTRACT: Asthma management guidelines provide recommendations for the optimum control of asthma. This survey assessed the current levels of asthma control as reported by patients, which partly reflect the extent to which guideline recommendations are implemented.

Current asthma patients were identified by telephone by screening 73,880 households in seven European countries. Designated respondents were interviewed on healthcare utilization, symptom severity, activity limitations and asthma control.

Current asthma patients were identified in 3,488 households, and 2,803 patients (80.4%) completed the survey. Forty-six per cent of patients reported daytime symptoms and 30% reported asthma-related sleep disturbances, at least once a week. In the past 12 months, 25% of patients reported an unscheduled urgent care visit, 10% reported one or more emergency room visits and 7% reported overnight hospitalization due to asthma. In the past 4 weeks, more patients had used prescription quick-relief medication (63%) than inhaled corticosteroids (23%). Patient perception of asthma control did not match their symptom severity; approximately 50% of patients reporting severe persistent symptoms also considered their asthma to be completely or well controlled.

The current level of asthma control in Europe falls far short of the goals for long-term asthma management. Patients' perception of asthma control is different from their actual asthma control.

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Asthma is a severe and sometimes fatal chronic disease affecting a large proportion of the population. Western Europe has some of the highest prevalence rates of asthma in the world [1–3]. Among children, the regional average is 13.0%; there is a lower overall prevalence in adults (8.4%). Furthermore, according to data from population-based surveys there has been a 2–4% annual increase in asthma prevalence rates in most European countries over the past 15 yrs [4].

The primary mechanism for combating this well-recognized increase in the prevalence of asthma has been the development of guidelines to promote standardized methods of diagnosis and treatment. In 1993 the National Heart, Lung and Blood Institute, and the World Health Organization convened a working group to develop a global strategy for asthma management and prevention which was subsequently published as the Global Initiative for Asthma (GINA) [5]. The GINA guidelines specify eight goals for the long-term management of asthma: minimal chronic symptoms; minimal exacerbations; no emergency visits; minimum need for as-required β_2 -agonists; no limitations to daily activities; near normal peak expiratory flow (PEF); PEF circadian variation <20%; and minimal adverse effects from asthma medication.

Research published since the release of the GINA guidelines indicates that in many countries patients with asthma are inadequately treated [3, 6] and that adherence

to asthma treatment guidelines is generally poor. As a consequence of poor adherence, there is a general failure to achieve the set guideline goals [7, 8]. In a survey of respiratory specialists, considerable differences between an international consensus and asthma management were reported [9]. This problem was highlighted further in a more recent survey of respiratory physicians from five European countries who reported that although they accepted the recommendations in asthma guidelines, only a small proportion of patients were treated according to the guidelines [10]. Evidence also suggests that in the USA current asthma practice falls short of the GINA guideline goals [11].

The Asthma Insights and Reality in Europe (AIRE) survey is the first comprehensive, multinational survey assessing the level of asthma control among current asthmatics in Western Europe from the patient's perspective and provides the best estimate currently available of how well the goals of the GINA guidelines are being met in Europe.

Methods

Selection of subjects

The AIRE survey was conducted February 25–April 21 1999. A sample of asthma patients was identified by

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systematically screening 73,880 households in seven European countries (France, Germany, Italy, the Netherlands, Spain, Sweden, UK) by telephone. Collectively, the population of these seven countries represents approximately 73% of the total population of Western Europe. The AIRE survey was conducted by telephone in order to permit systematic screening of a national sample of households in order to identify a national probability sample of persons who had been diagnosed with asthma. The estimated landline telephone coverage in Sweden, France, the Netherlands, the United Kingdom, and Germany is over 90% of all households. The estimated landline telephone coverage is only slightly lower in Italy and Spain, with over 80% of households in these countries having at least one phone line [12].

The sampling method used telephone numbers (listed and unlisted) randomly generated by a truncated list-assisted random-digit dialling (RDD) sampling procedure [13–15]. Sampling by random-digit dialling, selected households with unlisted numbers are at an equal probability relative to households with listed numbers. The proportion of numbers screened out as businesses ranged from 1% in the United Kingdom to 6% in Italy, and they were excluded to calculate the final response rate of 80%. Mobile phone numbers were not screened with the RDD process used. The influence of this effect was likely to be minimal within the sample because less than one percent of all households in Europe have a mobile phone and no other landline connection [12].

Patients with current asthma were identified as those with asthma diagnosed by a physician who were currently taking medication for their asthma or had asthma attacks and symptoms during the past year. If a household had more than one current asthma patient, one designated respondent was randomly selected by computer for interview. If the respondent was younger than 16 yrs, the interview was conducted with a proxy who was the parent or guardian most knowledgeable about the child's treatment. The designated respondents were assured of the voluntary nature of the survey and the confidentiality of all survey responses.

Telephone interviews

Telephone interviews (average duration 25 min) were performed using a structured questionnaire. All telephone interviews were conducted from a single, telephone-interviewing facility using computer-assisted telephone-interviewing. Interviews were conducted by experienced interviewers in the mother tongue of the designated respondent. Initial contacts were made on weekday evenings and weekends, since these were the times that persons were most likely to be at home. Interviewers attempted a minimum of 10 calls to each sampled number before treating it as a permanent non-responding household. These interview attempts were made at different times, on different days over a three-week period. Numbers, where busy signals were encountered, were redialled 15 min after an initial contact attempt. If an eligible respondent was identified but could not be interviewed at that time, then an interview appointment was scheduled at the respondent's convenience. There was an unlimited number of callbacks for eligible respondents.

Questionnaire

The survey questionnaire was based on the American Thoracic Society (ATS) questionnaire [16] with additional questions on healthcare use and activity limitation. Respondents were questioned on symptom severity, sleep disruption, overnight hospitalization, emergency room visits, unscheduled urgent care visit (defined as an unexpected visit to the doctor's office, clinic or hospital), activity limitations due to asthma, use of asthma therapy and perceived asthma control. The asthma symptoms section of the questionnaire was identical to both the ATS and European Community Respiratory Health Survey (ECRHS) questionnaires. Previous research has demonstrated that the ATS questionnaire is a valid tool for the measurement of asthma symptoms in the general population [17] and is highly reliable when administered by telephone [18]. The healthcare utilization questions were similar to questions used in previous research at an International Study of Asthma and Allergies in Childhood (ISAAC) study site in the USA [19]. Using a subsample of 54 children identified from a USA pulmonology practice and tested twice over a four-week period, the authors found excellent reliability ($\kappa > 0.75$) for the questions on hospitalizations (1.0) and emergency room visits (0.83) in the past 12 months and good reliability ($\kappa > 0.40$) for the question on physician office visits in the past year (0.50). The English version of the questionnaire was translated and back-translated into Dutch, French, German, Italian, Spanish and Swedish by translators experienced in the use of health surveys. Review by a pulmonologist found no evidence of any significant difference between the original and the back-translated instrument.

Data management and analysis

The study design required approximately 400 interviews with current asthma patients in each of the seven countries. This allowed for equal sample precision in the population estimates with an error of 5% and a power of 80%. The sample was stratified by region within each country and sampled proportionately. Since existing asthma treatment guidelines recommend different management practices for children and adults and responses for children were obtained by proxy, data on asthma morbidity and asthma management practices were stratified by age (children: aged < 16 yrs; adults: aged ≥ 16 yrs). The frequency and severity of day- and night-time symptoms, exercise-induced symptoms and severe episodes, and total symptom frequency were used to develop a symptom severity index similar to the GINA asthma severity scale (table 1). This method has been validated by recent evidence of a correlation between increases in several inflammatory markers in sputum and more severe asthma using the GINA asthma severity classification [20].

Patient demographic and asthma severity characteristics were compared using Chi-squared analysis to identify factors that might account for differences in asthma management across countries. All statistical tests were two-sided and comparisons with $< 5\%$ probability of error were considered statistically significant.

Table 1. – Symptom severity index developed according to frequency and severity of asthma symptoms (cough, wheeze, shortness of breath or chest tightness)

Frequency of asthma symptoms	Severe persistent	Moderate persistent	Mild persistent	Mild intermittent
Daytime	3 times·day ⁻¹	everyday (≤ 2 times·day ⁻¹)	at least 2 times·week ⁻¹	<2 times·week ⁻¹
Night-time	every night/most nights	at least 2 times·week ⁻¹	at least 2 times·month ⁻¹	<2 times·month ⁻¹
Severe episodes in the past 12 months		everyday	at least 2 times·week ⁻¹	≤ 1 time·week ⁻¹
Exercise-induced symptoms in the past 12 months		everyday	at least 2 times·week ⁻¹	≤ 1 time·week ⁻¹
During a typical week	21 times·week ⁻¹	7 times·week ⁻¹	3–6 times·week ⁻¹	≤ 2 times·week ⁻¹

Results

Sample population

Of the 73,880 households screened, one or more current asthma patients were identified in 3,488 households. Full interviews were completed by 2,803 (80.4%) respondents. Reasons for noncompletion of the interview included: refusal to conduct the interview (n=254), premature termination of the interview (n=154) and awaiting call-back from an interviewer when the survey ended (n=277). Twenty-seven percent of the study population were children represented by proxy and over 70% of proxy responses were by the child's mother.

The seven national samples of asthmatics showed similar age and sex distributions, significant differences between national and pooled samples were only observed for age in German children (9.6 versus 8.6 yrs overall, $p < 0.05$) and French adults (39.9 versus 42.8 yrs overall, $p < 0.05$), and for gender in German children (28.8% female versus 40.6% overall, Chi-squared $p < 0.05$). Demographic and asthma-related variables for paediatric and adult populations are summarized in table 2. Using the symptom severity index, slightly more children were classified as having intermittent asthma (54.1%) than persistent asthma (45.9%), whereas more adults had persistent (63.0%) than intermittent disease (37.0%).

Table 2. – Demographic and asthma-related variables in children and adults

	Children	Adults
Current asthma patients n	753	2050
Mean age \pm SD yrs	8.8 \pm 4.1	42.7 \pm 18.5
Male %	56.0	39.1
Mean age \pm SD at diagnosis of asthma yrs	3.5 \pm 3.3	25.1 \pm 20.2
Mean duration of asthma \pm SD yrs	5.3 \pm 3.6	17.6 \pm 14.7
Current smoker %	ND	17.5
Current symptom severity* %		
Mild intermittent	54.1	37.0
Mild persistent	17.9	19.3
Moderate persistent	12.9	23.2
Severe persistent	15.1	20.5
Self-assessed asthma severity %		
None	40.2	27.4
Mild	36.3	38.5
Moderate	18.7	26.2
Severe	4.6	7.7

ND: not determined; SD: standard deviation. *: assessed using the symptom severity index.

Asthma control

According to the definition of asthma control in the GINA guidelines, a large proportion of the population surveyed were poorly controlled (table 3). Overall, only 5.3% of all patients (5.1% of adults and 5.8% of children) met all the criteria for asthma control. Over one-third of children and half of the adults reported daytime symptoms at least once a week. Furthermore, 28.0% of children and 30.5% of adults reported asthma-related sleep disturbances at least once a week. Sleep disruption every night was reported by 6.7% of children and 5.3% of adults. Episodes of cough, wheezing, chest tightness and shortness of breath were common, occurring in 51.5% and 57.2% of children and adults, respectively, at least once a month. A total of 36.0% of children and 27.9% of adults required an unscheduled urgent care visit in the past 12 months. One or more emergency room visits due to asthma were reported for 18% of children and 11% of adults in the past year. Overnight hospitalization was necessary for 7% of all patients in the past 12 months. A high proportion of patients surveyed also experienced limitations to their normal daily activities (table 3).

One of the GINA goals is to achieve normal or near normal lung function; however, 60.5% of children and 45.0% of adults reported that their doctor had never performed a lung function test. Furthermore, only 30.1% of children and 29.0% of adults used a peak flow meter at least once a week.

Although the GINA guidelines stipulate minimal use of as-required β_2 -agonists, in the AIRE study nearly two-thirds of adults and children had used quick-relief medication in the past month. Forty-one percent of patients had used a prescription anti-inflammatory drug and approximately 23% had taken an inhaled corticosteroid (ICS) in the past 4 weeks for asthma. There was no correlation between the use of ICS and disease severity. Thus, ICS were being used by 25.8% of children with severe persistent asthma, 32.7% with moderate persistent disease and 33.5% with mild persistent disease. The corresponding adult data for severe, moderate and mild persistent asthma were 25.4%, 22.7% and 27.6%, respectively (fig. 1).

Despite the high frequency of asthma symptoms, acute healthcare visits and activity limitations reported in the survey, 76.5% of children and 65.9% of adults said they had no asthma symptoms or only mild asthma during the past 4 weeks. Furthermore, patient perception of asthma control differed markedly from that based on a more objective assessment of symptom severity (fig. 2).

Table 3. – The Global Initiative for Asthma (GINA) recommendations and the Asthma Insights and Reality in Europe (AIRE) results

GINA recommendation	AIRE result	Symptoms %	
		Children	Adults
Minimal chronic symptoms	Daytime symptoms once a week	38.2	50.1
	Sleep disturbances at least once a week	28.0	30.5
Minimal episodes	Reported episodes of coughing, wheezing, chest tightness or shortness of breath in the last month	51.5	57.2
	Unscheduled urgent care visits during last year	36.0	27.9
No emergency visits	Emergency visits during last year	18	11
	Used as-required β_2 -agonists during the last month	61.0	63.6
Minimal need for β_2 -agonists	Limitation of activities		
	Sports	29.5	47.1
No limitations on activities	Normal physical activity	19.1	37.9
	Choice of jobs/career	–	23.0
	Social activities	13.8	25.5
	Sleep	31.2	36.2
	Lifestyle	18.6	33.0
	Housekeeping chores	10.9	34.1
	School/work absence	42.7	17.1
	Never had a lung function test	60.5	45.0

Discussion

The AIRE survey provides direct evidence that despite the availability of effective therapies, asthma control is suboptimal for many of the current patients in Western Europe, with long-term management falling far short of the goals in the GINA guidelines [5]. Only 5.3% of the population surveyed met all the goals of the GINA guidelines. The most significant findings were the high levels of both unscheduled emergency visits and hospitalization experienced by these current asthma patients. A novel and disturbing finding was the high level of as-required use of bronchodilator medications and the low level (26%) use of anti-inflammatory medications among patients with severe and moderate persistent asthma. Together, these findings suggest that asthma may be dangerously under-treated in some patients.

The AIRE results are supported by data from two other large asthma surveys, the ECRHS [3] and the Asthma In America (AIA) survey [11]. In the AIA survey, 9% of

patients were hospitalized and 23% visited an emergency room because of their asthma in the past year, 30% of patients experienced weekly sleep disruption and 48% said that asthma restricted their sport or recreational activities [11]. In the ECRHS, 25–60% of patients had consulted a physician in the past year because of their asthma and sleep disturbance was reported by 24–52% of patients [3]. In a previous study of asthma severity, the most important symptoms identified were frequency of bronchodilator use and nocturnal attacks [21], both of which were high among the patients in this survey.

AIRE is the largest multinational survey of asthma patients conducted in Western Europe to date. It provides an unparalleled resource for understanding the current state of asthma management and treatment in Europe from the patients' perspective, representing a major advance for future directions in asthma policy and education. With approximately 400 asthma patients from each of the seven countries, the population surveyed was larger than that

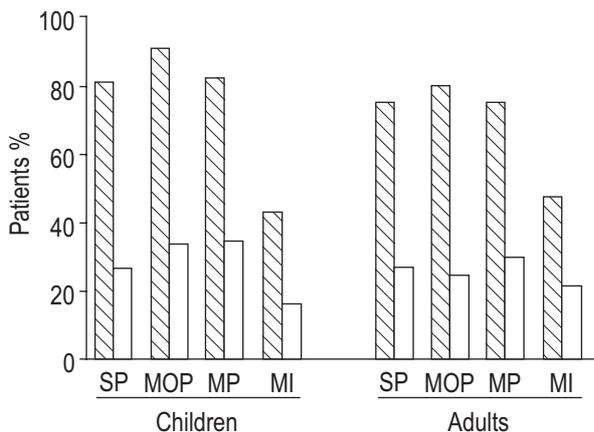


Fig. 1. – β_2 -agonist use and current use of inhaled corticosteroid therapy according to symptom severity. SP: severe persistent; MOP: moderate persistent; MP: mild persistent; MI: mild intermittent; ▨: β_2 -agonist; □: inhaled corticosteroid.

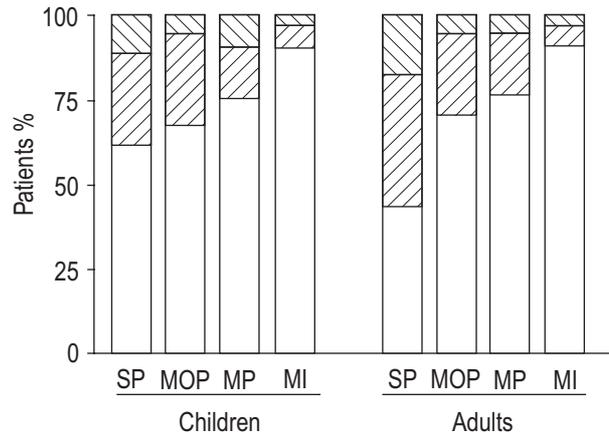


Fig. 2. – Symptom severity index by self-classification of asthma control. SP: severe persistent; MOP: moderate persistent; MP: mild persistent; MI: mild intermittent; □: well/completely controlled; ▨: somewhat controlled; ▩: poorly/not controlled.

identified from the European sections of the ECRHS and the ISAAC [1–3].

The sample obtained in the present study was comparable (*e.g.* in mean age and gender ratios) across all of the seven European countries surveyed. Although the AIRE study was not an asthma prevalence study, to ensure that the sample obtained represented a population-based sample of asthmatics within a country, asthma prevalence using the responses to the screening process and population weights for each country were estimated. The overall population prevalence of asthma was estimated as being 3.6% and differences in asthma population prevalence were comparable with between-country differences reported in the ISAAC survey and the ECRHS [1, 3]. The countries sampled were also relatively homogeneous with respect to asthma management practices. Given that this study sampled for current asthmatics, the prevalence estimate indicates that the sampling process obtained a representative sample of these patients.

Some potential limitations of this survey require consideration. Firstly, although telephone sampling is a powerful epidemiological tool, it excludes households with no telephone (most commonly rural areas and low-income households) which may have higher rates of asthma. This potential limitation is shared with the ECRHS and ISAAC study methods. The sampling units in ECRHS were a limited number of areas within each country and the ISAAC sampling units were schools also within a few cities in each country surveyed. Both sampling frames would tend to exclude subjects from poorer and more rural areas. Previous research in the USA [22–25] and Europe [26] indicates that lower socioeconomic status may reduce access to asthma-related medical care and increase the risk of asthma morbidity. Given the very low proportion of potential subjects with a mobile phone but no household landline, and the high likelihood that these people would be young adults, it is unlikely that the lack of phones among these individuals was a strong influence on the results of the study. As a result, the problem of poor asthma control in Europe may be worse than identified because of the exclusion of patients with a higher burden of illness due to lower socioeconomic status. Secondly, only patients with current asthma were questioned in the survey. Since this excluded untreated and undiagnosed patients, who generally have mild disease, the distribution of asthma severity was skewed toward more severe disease. However, patients with current asthma were targeted to improve response and minimize misclassification of patient behaviour and asthma related healthcare use resulting from poor recall, because such patients were expected to have both a better understanding of asthma terminology and memory for their asthma experience. Thirdly, although data on children with asthma were obtained by proxy, this was determined from the parent or guardian who knew the child's disease best. The resulting sample was homogeneous across all seven countries indicating bias due to poor proxy response was not significant in this study.

A key finding of the AIRE survey was the major discrepancy between patients' perceived control of asthma and reported symptom severity. Patients tended to underestimate the severity of their condition and overestimate control, tolerating, as an acceptable degree of control, a much higher rate of symptoms than recommended by

medical professionals. It is a cause for concern that 50% of patients with severe disease perceived their asthma to be well controlled given the relatively poor quality of life and high level of healthcare utilization reported in this study. The reasons for this are unclear but may be related to both patient adaptation to their condition and a poor understanding by their physician of the severity of their underlying disease. Thus, it appears that many patients often settle for a quality of life considerably less than that achievable if recommended management practices and asthma treatments are used. Improving patients' and physicians' expectations of what can be achieved with asthma therapy may lead to improved overall asthma control.

The under-utilization of ICS among patients with severe asthma is a novel finding at variance with generally accepted usage levels of these agents in this population. Despite possible under-reporting of medication use due to questioning by telephone, the consistently low ICS use regardless of asthma severity indicates that potential bias, due to more accurate recollection and reporting of drug use by patients with severe disease, was not a problem. Thus, the trend of poor ICS utilization among patients with severe asthma is probably real, suggesting substantial under-treatment of these patients. This implies an immediate need to improve communication and awareness among patients and physicians regarding the reasons underlying the use of anti-inflammatory medications, and the imperative need for the appropriate use of such agents, to improve compliance and prevent the severe consequences of poor asthma control.

The survey also revealed insufficient monitoring of asthma and its treatment. A large percentage of patients reported never having had a lung function test. Previous research indicates that lung function testing can provide a substantial insight into the outcome of asthma [27]. A clear finding of the survey is that focusing on a single dimension of patient experience will significantly underestimate asthma severity.

To conclude, the Asthma Insights and Reality in Europe study highlights the gap between the long-term goals of asthma management, as stipulated by the Global Initiative for Asthma guidelines, and reality in Western Europe. The Global Initiative for Asthma goals are not currently being met, and patients and their doctors may be complacent about the level of asthma control being achieved. It is imperative that public health resources and educational efforts are targeted to improve asthma control and reduce the disease burden on both the healthcare system and society.

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