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International variations in asthma treatment compliance

The results of the European Community Respiratory Health Survey (ECRHS)

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International variations in asthma treatment compliance. The results of the European Community Respiratory Health Survey (ECRHS). I. Cerveri, F. Locatelli, M.C. Zoia, A. Corsico, S. Accordini, R. de Marco, on behalf of the ECRHS. ©ERS Journals Ltd 1999.
ABSTRACT: Noncompliance to medication is a major barrier to effective asthma management. Its real extent and geographical variation throughout the world are not yet known.

The data on compliance, collected in the framework of the European Community Respiratory Health Survey (ECRHS) on 1771 subjects (aged 20–44 yrs) with current asthma identified in 14 countries, offer a unique opportunity to assess the extent of noncompliance and its variation across countries.

The median percentage of current asthmatics who had received a medical prescription at least once was 95%. The compliance of those patients who had received a medical prescription was found to be low in all countries (median 67%) but with wide variations, the rate ranging from 40% (USA) to 78% (Iceland). During exacerbations patients′ rate of compliance increased to 72%. Age was the only variable which influenced compliance to treatment. A significant, although weak, negative correlation was found between patients′ compliance and rate of hospital casualty department or emergency room admissions.

This study documents that compliance to the treatment of asthma is poor worldwide and that there are large variations between countries. These results emphasize the necessity for further efforts to improve patients′ education and to promulgate the international guidelines.
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Despite improvements in the understanding of the pathophysiology of asthma and in the availability of many effective drugs, during the last few decades, the frequency and severity of asthma seem to have increased in several countries both in children and in adults [1–3]. There are two major reasons why the management of a disease may be unsuccessful: 1) reasonable treatment and an action plan are not prescribed by the caregiver; 2) the patient does not follow the adequate treatment prescribed by the caregiver. To improve the management of asthma, in 1991 the National Asthma Education Program (NAEP) Expert Panel, sponsored by the National Heart, Lung, and Blood Institute, published guidelines for the diagnosis and management of asthma [4, 5]. Unfortunately, compliance to these guidelines has been recently reported to be low in the USA [6]. Poor compliance to asthma medication regimens has been repeatedly demonstrated in both children and adults [7–11]. Decades of research on adherence have demonstrated that patient compliance in both clinical and research settings is a serious problem across all diseases but particularly in the treatment of chronic diseases with frequent periods of remission and complex medication regimens, such as asthma [8].

The real extent, causes and implications of noncompliance have not been completely established [9]. In particular no comparative data from different countries have been reported.

The European Community Respiratory Health Survey (ECRHS), a multicentre study of the variation in the prevalence, risk factors and management of asthma throughout the European Union and elsewhere [12], included a structured interview with a series of questions concerning patient adherence to treatment. One of the important results of this survey [13] was that there were differences in treatment practices between countries; further analyses in France and Italy documented that antiasthmatic drugs were underused [14, 15]. The problem of noncompliance was not specifically addressed.

The aim of this study was to evaluate the extent of noncompliance in different countries and its geographical variations by means of an analysis of all the cases of current asthma identified in 14 countries which provided usable data.

Methods

Subjects and study design

Data presented in this study were collected in the framework of stage 2 of the ECRHS and come from 34 centres in 14 countries (table 1). The methods used in the

Table 1. – Number of participants, response rates and number of current asthmatics in stage 2

Country	Centre	Random sample n	Response rate %	Symptomatic sample n	Reponse rate %	Current asthmatics (total) n
Belgium	South Antwerp	577	72.1	76	69.7	21
	Antwerp City	562	64.8	87	49.2	42
Germany	Hamburg	1252	37.8			35
	Erfurt	731	67.9			3
Spain	Barcelona	393	73.6	123	84.2	36
	Galdakao	486	84.4	106	91.4	33
	Albacete	435	66.1	191	68.7	28
	Oviedo	355	68.3	167	74.2	19
	Huelva	271	56.7	132	49.6	17
France	Bordeaux	544	18.5			51
	Grenoble	473	40.6	49	44.5	32
	Montpellier	456	12.2			45
	Paris	652	20.9			29
Ireland	Dublin	437	73.0	127	85.2	51
Italy	Pavia	309	38.0			11
	Turin	244	47.1	111	30.2	23
	Verona	340	67.5	18	3.7	13
Netherlands	Groningen	380	63.4			11
	Bergen-op-Zoom	452	70.8			15
	Geleen	413	61.8			7
UK	Cambridge	277	52.6	58	45.0	57
	Caerphilly	377	71.6	138	57.0	86
	Ipswich	420	61.6	111	70.3	82
	Norwich	473	72.1	108	71.1	93
Iceland	Reykjavik	559	83.2	84	93.3	50
Norway	Bergen	835	87.1			26
Sweden	Göteborg	682	88.3	184	81.8	87
	Umea	552	90.3	156	60.9	119
	Upsala	622	87.7	201	93.1	104
New Zealand	Wellington	481	64.9	138	73.4	136
	Christchurch	455	63.7	129	70.5	114
	Hawkes Bay	316	57.6	86	59.7	71
USA	Portland	549	34.3	116	45.3	57
Australia	Melbourne	669	40.7	207	47.2	167

study have been described previously [12]. Participating centres selected areas for study which were defined by pre-existing administrative boundaries, had populations of at least 150,000 inhabitants and, where possible, had up-to-date sampling frames for subjects aged 20–44 yrs.

Stage 1. In the first phase of the study, randomly selected samples of at least 1,500 people of each sex were sent questionnaires enquiring about respiratory symptoms, attacks of asthma, use of asthma medications and hay fever or nasal allergies, together with questions checking age and sex of the respondents.

Stage 2. In the second part of the study, a random sample of those selected for the first stage were invited to come for a structured interview, blood tests, skin tests and an assessment of lung function by spirometry and airway challenge with methacholine. Detailed information on medication use to help breathing, compliance and use of health care services because of breathing problems was collected during the interview. In many of the centres, an additional sample of all individuals who in the screening questionnaire reported: 1) having been woken by an attack of shortness of breath at any time in the last 12 months; 2) having had an attack of asthma in the last 12 months; and, or 3) currently taking medicine for asthma, were invited to participate in the second stage of the study. For the purpose of the present analysis all current asthmatics identified in stage 2 of the ECRHS were considered.

Case identification and compliance related variables

All subjects who answered "yes" to the question "Have you ever had asthma? If yes, was this confirmed by a family doctor?" and who reported having had at least one asthma attack in the last 12 months or of being on anti-asthmatic treatment at the time of the study were considered as being current asthmatics.

Owing to the difficulty in categorizing the severity of asthma by epidemiological tools, this study considered only two levels of severity: the most severe being subjects who had had >10 asthma attacks in the preceding 12 months.

For evaluation of medical prescriptions and patient compliance the questions: "Have you ever been prescribed medicines for your breathing?", "If you are prescribed medicines for your breathing, do you normally take all the medicines?", "When your breathing gets worse, and you are prescribed medicines for your breathing, do you normally take all of the medicines?" were used.

For the evaluation of health care resources the questions: "Have you ever visited a hospital casualty department or emergency room because of breathing problems?" and "Have you ever spent at least a night in hospital because of breathing problems?" were used.

For the evaluation of the subjective impressions of the patients about their therapy the questions: "Do you think it

Table 2. – Number of current asthmatics, number (%) of subjects who received medical prescription and number (%) of subjects with severe asthma by countries

Country	No.	Medical prescription (%)	Severe asthma* (%)
Belgium	63	59 (93.7)	18 (29.0)
Germany	38	38 (100.0)	12 (32.4)
Spain	133	116 (87.2)	18 (13.5)
France	157	141 (96.6)	48 (32.2)
Ireland	51	45 (88.2)	5 (10.2)
Italy	47	44 (93.6)	12 (28.6)
Netherlands	33	31 (93.9)	2 (6.5)
UK	318	311 (97.8)	55 (18.5)
Iceland	50	46 (92.0)	11 (24.4)
Norway	26	26 (100.0)	3 (13.0)
Sweden	310	307 (99.0)	72 (24.7)
New Zealand	321	297 (96.7)	77 (26.7)
USA	57	47 (83.9)	22 (40.7)
Australia	167	161 (96.4)	65 (39.9)
Total	1771	1669 (95)	420 (25)

Percentages were computed excluding subjects with missing values. *: >10 asthma attacks in the preceding 12 months.

is bad for you to take medicines all the time to help your breathing" and "Do you think you should take as much medicine as you need to get rid of all your breathing problems?" were used.

Statistical analysis

Results were reported as percentages with 95% confidence intervals (CI). When extreme values of a percentage (0 or 1) were observed, CI were computed by means of tail intervals [13]. Age was coded in two levels, using the median value of current asthmatics as the threshold value (33 yrs). The effect of sex, age and severity on compliance was assessed by a meta-analytic approach (fixed effect model), estimating the common odds ratio (OR) *via* Mantel-Haenzel analysis and testing homogeneity of effects across centres by the Chi-squared (χ^2) test [17], using Stata Statistical Software (Release number 5, 1997; Stata Corp., College Station, TX, USA). Multiple logistic regression was used when adjusting the effect of a single factor for the others. Analyses were carried out by country when estimating the single OR; the common OR was computed with a model in which country was an additional factor.

Linear regression was used when correlating the rate of compliance in each country with the rate of casualty or emergency room admissions.

Since question nonresponse affected all of the variables used in the present analysis to some extent, the estimates computed on data from only responders were compared with those obtained assuming that all nonresponders answered affirmatively or negatively to the questions studied. The variation in the prevalence estimated by the three models was <5% for all of the questions except for asthma severity. The estimated prevalence of severe asthma depended heavily upon the nonresponse assumption. However the estimates of the association between asthma severity and compliance were less influenced by nonresponse.

Results

The total number of participants in the random sample (table 1) was 17,029 (52% female, mean age 34 yrs, range 20–48 yrs). The participation rate varied from 90% in Umea to 12% in Montpellier. The total number of participants in the symptomatic sample was 2,903 (57% female, mean age 34 yrs, range 20–47 yrs). Overall, the total number of current asthmatics (random plus symptomatic sample) was 1,771 (58% female, mean age 33 yrs, range 21–47 yrs). The percentage of those with severe asthma was 25% (ranging from 24–30% according to the nonresponse models); Australia and the USA were

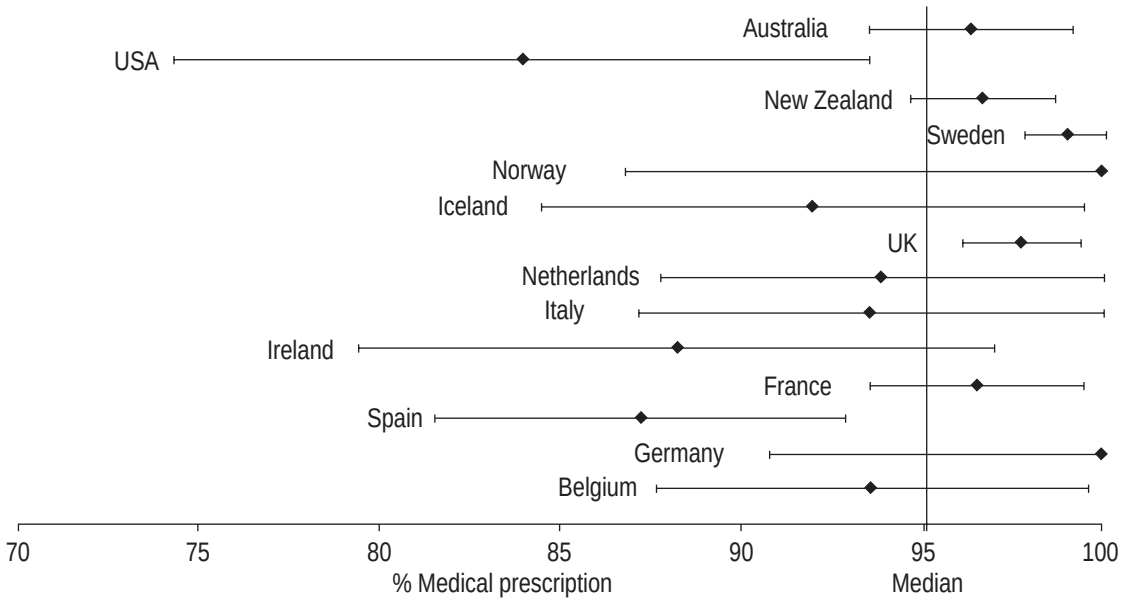

Fig. 1. – Prevalence (%) (♦) (95% confidence intervals (CI)) (——) of medical prescription by country. A prevalence significantly different from the median is present when the 95% CI does not fit the vertical line of the median value.

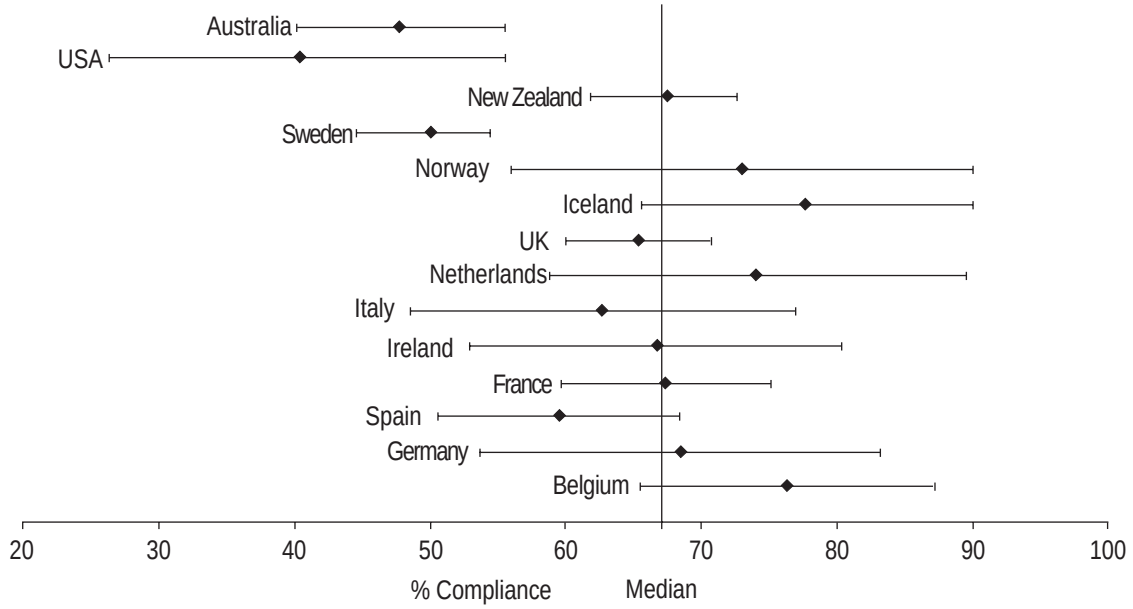

Fig. 2. – Prevalence (%) (♦) (95% confidence intervals (CI)) (——) of compliance between subjects with indications for treatment by country. A prevalence significantly different from the median is present when the 95% CI does not fit the vertical line of the median value.

the countries with the highest percentage (40%) of severe asthmatics (table 2).

The median percentage of subjects who had received, at least once, a medical prescription for their breathing was 95%; the percentage was significantly higher in Sweden and the UK and significantly lower in the USA and Spain (fig. 1).

The compliance of those patients who had received a medical prescription was found to be low in all countries (median 67%) but with wide variations, the rate ranging from 40% (USA) to 78% (Iceland) (fig. 2). The USA, Australia and Sweden had significantly lower rates. During exacerbations patients′ rate of compliance increased to 72% (fig. 3); the rate in the USA improved to 66% but those in Australia and Sweden remained significantly lower than the median.

The meta-analysis by centre (table 3) on the effect of sex, age and severity showed no heterogeneity across centres for all the studied factors. Age was the only variable which influenced compliance to treatment (p= 0.002). In particular, patients >33 yrs old showed a higher adherence to treatment (OR=1.4; 95% CI: 1.1–1.7). Even when all of the covariates have been adjusted for, the results did not change. Figure 4 shows the OR for the effect of severity on compliance adjusted for sex and age. Overall there was no significant heterogeneity across

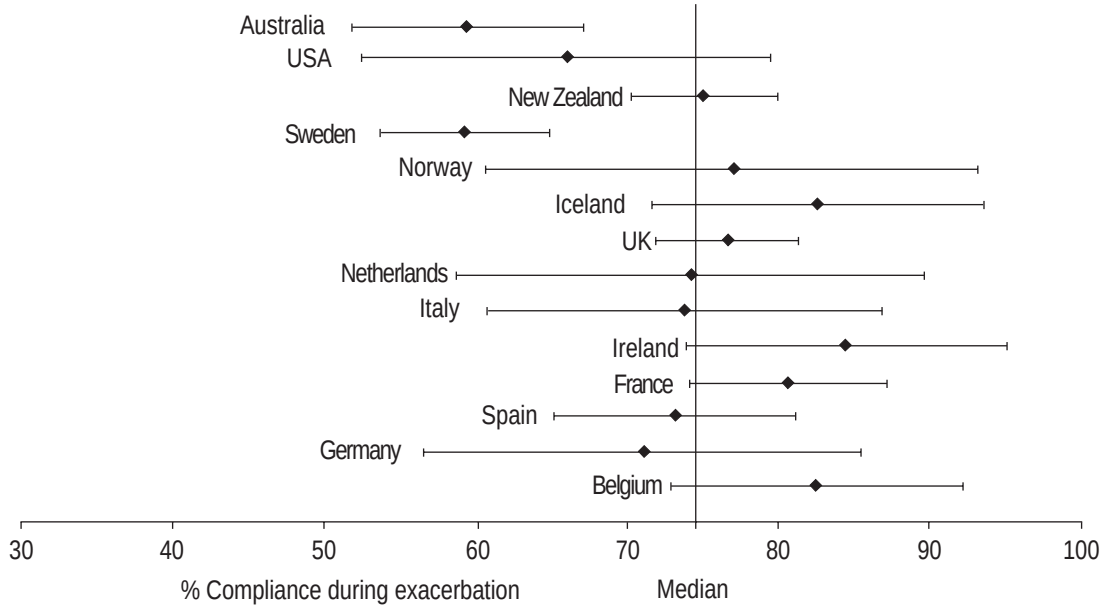

Fig. 3. – Prevalence (%) (♦) (95% confidence intervals (CI)) (——) of compliance during exacerbations between subjects with indications for treatment by country. A prevalence significantly different from the median is present when the 95% CI does not fit the vertical line of the median value.

Table 3. – Pooled odds ratios (ORp), 95% confidence interval (CI), Chi-squared (χ^2) for heterogeneity of the effect of sex, age and severe asthma on compliance

	Sex	Age	Severity
ORp (95% CI)	1.12 (0.92–1.38)	1.39 (1.13–1.70)	1.04 (0.82–1.33)
Test for heterogeneity χ^2 (p-value)*	14.52 (0.34)	11.57 (0.56)	15.1 (0.30)

*: 13 degrees of freedom.

countries and the common OR (OR=1.1; 95% CI: 0.8–1.4) was not significant, with the sole exception of that in the USA (OR=6.3; 95% CI: 1.6–25.5).

A significant, although weak, ecological negative correlation (r= -0.55; p<0.05) was found between the rate of patients' compliance and rate of hospital casualty department or emergency room admissions with the USA having one of the highest uses of these settings (51%) and the lowest compliance (40%) (fig. 5).

Only 25% of patients thought that they should take as much medicine as they need to remove all of their breathing problems and that it is not bad to take medicines all the time to help their breathing. Thirty-five per cent of patients thought that they should take as much medicine as they need but they are afraid to take medicines all of the time. Twenty eight per cent of patients even think that drugs are bad and not necessary. Twelve per cent of patients think that drugs are not bad but are not necessary.

Discussion

This study documents that compliance to the treatment of asthma is poor worldwide and that there are large variations between countries. Poor adherence to asthma medication regimens is already well known [8]; however, this comparison between countries is the first based upon the same questions directly addressing asthma medication use. Another important finding of this study is that severity of disease does not significantly influence the compliance rate.

In an attempt to understand the reasons for noncompliance the subjects were asked what they thought about the consumption of antiasthmatic drugs. Surprisingly only ~60% of them considered that they needed to take all of their medicines to remove all of their breathing problems. Unfortunately more than a half of them were afraid to take the medicines, probably because of side effects. More than 10% of the patients thought that drugs are dangerous and unnecessary.

Looking at differences between countries, a very high percentage of asthmatics had received an asthma medication prescription, at least once in their life, in almost all countries but the USA and Spain. In these two countries, the percentage of subjects who had never received a prescription for asthma seems to be particularly substantial, taking into account that the diagnosis of asthma was made by doctors. Another interesting result relates to the peculiar pattern of patient compliance in the USA and Australia: in these two countries, in fact, there is the lowest compliance with the highest prevalence of severe asthmatics. Asthma mortality represents a major problem in both countries [18]; low compliance has been documented to be a risk factor for adult and childhood asthma deaths [10, 19]. Many studies have speculated about the possible determinants of this situation in the USA and Australia [6, 14, 20] referring to difficulties in access to health care resources because of social, economic and geographical barriers. Considering all of the countries, a significant negative correlation was found between patient compliance and

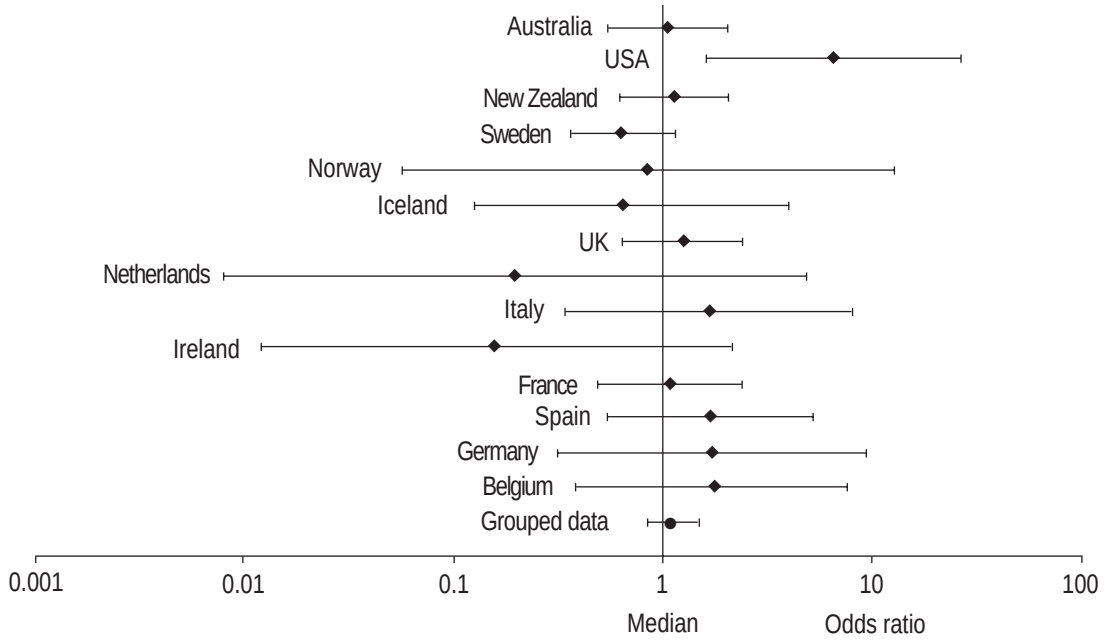

Fig. 4. – Estimated odds ratios (OR) (♦) and 95% confidence intervals (CI) (——) of the effect of severe asthma on compliance by country adjusted for sex and age. —●— : grouped data, OR and CI. The OR and the 95% CI are plotted on a logarithmic scale. A significant OR is present when the 95% CI does not fit the vertical line.

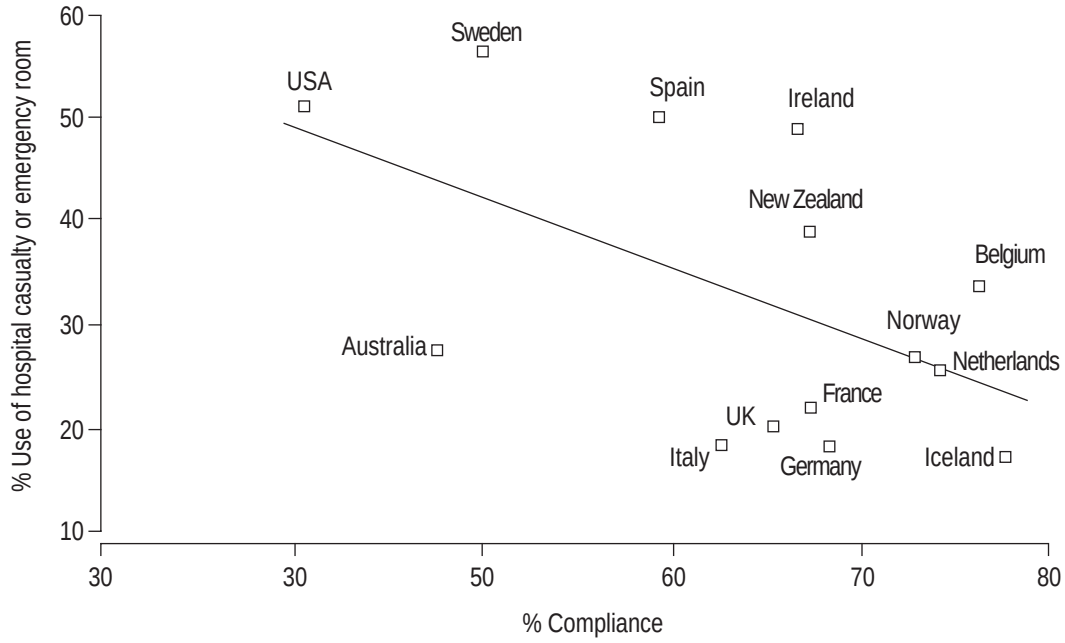

Fig. 5. – Relationship between compliance rate (%) and utilization of hospital casualty departments or emergency rooms by country (the solid line represents estimated linear regression). r=-0.55, p<0.05.

rate of hospital casualty department or emergency room attendances. It was observed that. subjects suffering from more severe asthma did not show better compliance to antiasthmatic treatment than those with milder asthma. Although the data do not allow the confirmation of a cause-effect relationship, it is reasonable to suppose that poor adherence to treatment may result in increased disease severity and in unnecessary hospitalizations. Use of health services might have been avoided if the management of the disease had been correct. Other factors could, however, be considered as accounting for the negative correlation between patient compliance and rate of hospital casualty department or emergency room attendances: one of which is the possible bias introduced by differently organized respiratory health care systems in various countries.

In this analysis the variations, by country, of self-reported compliance to treatment in current asthmatics have been described. The limitations of self-reported data have been described by many researchers [8, 21] and no validated instruments were available at the time of the survey to measure asthma medication compliance. In all the countries the same questions were asked (which had undergone a back translation procedure) directly addressing the patients′ compliance to the prescribed regimen. Thus, the estimates should have been affected by the same degree of inaccuracy, although the effect of cultural factors in explaining some of the differences observed across countries could not be ruled out. Overestimation in self-reporting is well known and probably due to a desire to please [21, 22]: of course this possible overestimation emphasizes the importance of the phenomenon of non-compliance that was observed. Thus the importance of this report lies not only in the absolute values of compliance, which are likely to be significantly overestimated in all cases, but predominantly in the pattern across countries always assuming that the pattern of "being choosy with the truth" is the same across countries.

The main problem in interpreting the reported variations is related to the different precision of the estimates, due to the large difference across countries in the number of current asthmatics included in the study, mainly reflecting differences in the number of centres participating in the study in each country and the size of the initial samples [3]. Given the absence of comparable data at an international level, the authors preferred to publish all of the data coming from the ECRHS international database, rather than selecting the countries which guarantee the highest stability of the estimates. The analysis does not, in any case, allow evaluation of the causes of the variations across countries.

Overall, the results emphasize the need for further efforts to improve patient education and communication in all of the countries that were investigated in the European Community Respiratory Health Survey and to promulgate the international guidelines.

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