

Changes in the Prevalence of Asthma in the Spanish Cohort of the European Community Respiratory Health Survey (ECRHS-II)

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OBJETIVE: The rise in the prevalence of asthma in the second half of the 20th century has not been evenly distributed according to recent surveys. We assessed changes in the prevalence of asthma after a period of 9 to 10 years in a cohort of young adults in the Spanish arm of the European Community Respiratory Health Survey (ECRHS).

MATERIAL AND METHODS: The ECRHS-II is a multicenter cohort study taking place in 27 centers around Europe, with Spanish centers located in Albacete, Barcelona, Galdakao, Huelva, and Oviedo. The ECRHS questionnaire was administered to individuals who had participated in the first phase of the survey; spirometry and methacholine challenge tests were also performed according to the published protocol.

RESULTS: Among new smokers, the prevalence of wheezing in the last 12 months increased from 10% to 33%, while the frequency of phlegm production rose from 8% to 22% ($P < .05$). In ex-smokers, the prevalences of wheezing and phlegm production decreased from 21% to 12% and from 15% to 8%, respectively ($P < .05$). Symptom prevalences remained similar for never smokers, although the frequency of diagnosed asthma rose from 4% to 7% ($P < .05$). After adjusting for smoking, age, sex, and center, we found no significant differences in the frequency of symptoms or asthma, even when the phrase bronchial hyperreactivity was included in the definition. However, the rate of reported asthma rose annually by 0.34% (95% confidence interval [CI], 0.20%-0.48%), while diagnosed asthma rose by 0.26% (95% CI, 0.13%-0.39%) and treated asthma by 0.16% (95% CI, 0.07%-0.25%).

CONCLUSIONS: Increased prevalence rates of asthma diagnosis and treatment have been detected, but the rates of reported symptoms have remained similar, consistent with the assumption that more persons are being classified as asthmatics.

Key words: Prevalence. Asthma. Cohort study.

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Cambios en la prevalencia de asma en la población española del Estudio de Salud Respiratoria de la Comunidad Europea (ECRHS-II)

OBJETIVO: El aumento de la frecuencia de asma ocurrido en la segunda mitad del siglo XX no es homogéneo entre los estudios más recientes. Hemos evaluado los cambios en la prevalencia de asma después de un seguimiento de 9-10 años en la población de adultos jóvenes del grupo español del Estudio de Salud Respiratoria de la Comunidad Europea (ECRHS).

MATERIAL Y MÉTODOS: El ECRHS-II es un estudio multicéntrico de seguimiento en 27 centros de Europa. Los centros españoles participantes se hallan en las ciudades de Albacete, Barcelona, Galdakao, Huelva y Oviedo. Se ha estudiado a los participantes del ECRHS-I mediante la utilización del cuestionario ECRHS y la realización de espirometría y test de metacolina según el protocolo ya publicado en trabajos anteriores.

RESULTADOS: La prevalencia de sibilancias en los últimos 12 meses en los nuevos fumadores aumenta del 10 al 33%, y la de expectoración, del 8 al 22%, mientras que entre quienes han abandonado el tabaco descienden del 21 al 12% y del 15 al 8%, respectivamente ($p < 0,05$). Entre los que nunca han fumado no se observan cambios en la prevalencia de síntomas, pero sí un aumento en la de asma diagnosticada (del 4 al 7%) ($p < 0,05$). Ajustando por hábito tabáquico, edad, sexo y centro no se observan cambios en los síntomas ni al introducir la hiperreactividad bronquial en la definición de asma, pero sí en el asma comunicada (un aumento del 0,34%; intervalo de confianza [IC] del 95%, 0,20-0,48%) por año, el asma diagnosticada (0,26%; IC del 95%, 0,13-0,39%) y el asma tratada (0,16%; IC del 95%, 0,07-0,25%).

CONCLUSIONES: Se aprecia un aumento de la prevalencia del diagnóstico de asma y del tratamiento del asma, que no se acompaña de un aumento de síntomas, lo que puede ser congruente con la idea de que hay una mayor clasificación de personas como asmáticas.

Palabras clave: Prevalencia. Asma. Estudio de seguimiento.

Introduction

Asthma is found worldwide, among persons of all ages and it ranks among the most prevalent diseases. The social and occupational impact of asthma on the individual is great and the economic costs are high. Although many studies have analyzed the prevalence of asthma in manifestly different populations, the difficulty in defining this disease complicates the reliability of comparisons between different populations around the world. Some epidemiological studies carried out in recent decades have reported that the prevalence of asthma seems to be rising.^{1,2} However, a recent review of the literature on trends in adults found evidence that a plateau may have been reached in some countries while in others the rates seem to have declined after decades of rising prevalence.³

Incidence is less often investigated than prevalence. A longitudinal cohort study in Finland found that while the prevalence of asthma increased slightly between 1975 (2% in men and 2.2% in women) and 1990 (2.9% in men and 3.1% in women) the incidence was similar in both men (2.3%) and women (2.6%) during follow-up between 1976 and 1990.⁴ Another cohort study in Nordic countries found an incidence rate of 2.2 per 1000 person-years.⁵ A recent review of the most important cohort studies estimated a rate of 5.9 and 4.4 per 1000 person-years in men and women, respectively.⁶

The European Community Respiratory Health Survey (ECRHS-II), carried out in 28 European health care centers, found that asthma medication and crises have increased in the cohort of young adults studied, but not to the same degree as the rise in symptoms suggestive of asthma. The results revealed considerable geographic variability.⁷ However, bronchial hyperreactivity was not measured in the ECRHS-II study. Given the observed variability and the possibility that specific patterns might differ between areas and countries partly because asthma was defined only by reported symptoms, we carried out a specific analysis for Spanish areas.

In 1995 the Spanish ECRHS-I group reported the prevalence of asthma and bronchial hyperreactivity in young adults in 5 parts of the country.⁸ The present aim is to report changes in asthma prevalence in this cohort after 9 years.

Material and Methods

The ECRHS is a multicenter cohort study carried out in 28 centers around Europe. The following 5 Spanish cities are represented: Albacete, Barcelona, Galdakao, Huelva, and Oviedo. The participants in the ECRHS-I carried out in 1991 and 1992 also took part in the present study. Details of the selection and data collection processes have been reported elsewhere.⁹

The second stage of the study was undertaken between 1998 and 2001. The persons who had participated in ECRHS-I were invited to come to the referral hospital in their geographic area to participate in the second phase.

Questionnaire

The questionnaire contained the same items as the instrument used in the ECRHS-I, plus 21 questions about occupation,

exposure to environmental pollution, and for women, questions about the menstrual cycle. An individual was considered to have asthma symptoms if he or she responded affirmatively to the 3 following questions: 1) Have you been woken by an attack of shortness of breath at any time in the last 12 months? 2) Have you had an attack of asthma in the last 12 months? and 3) Are you currently taking any medicines for asthma? A trained interviewer administered the questionnaire in a room free of distractions. All interviews were recorded.

Smoking Habit

An individual was considered a nonsmoker if he or she had never smoked or had smoked fewer than 20 packs ever. A current smoker was a person who had started smoking at least a month earlier and continued smoking. An ex-smoker was a person who had smoked more than 20 packs ever but was not currently smoking. Smoking was recorded as described by Chinn,⁷ according to whether there were changes in habit between the first and the second ECRHS phases: nonsmoker in the ECRHS-I and the ECRHS-II; any category in the first study and ex-smoker in the second; nonsmoker or ex-smoker in the ECRHS-I and current smoker at the end of the present study; and current smoker in both studies. A final category was comprised of individuals whose responses about their past smoking habits while being interviewed for the ECRHS-II were different from what they originally reported in the ECRHS-I; these were classified as discrepancies.

Lung Function and Bronchial Hyperreactivity

Lung function tests were performed and followed by a methacholine challenge test of bronchial hyperreactivity. If a participant's baseline forced expiratory volume in 1 second (FEV₁) was 70% of predicted, that subject did not undergo the challenge test. Bell spirometers (Biomedin 9000, Papua, Italy), as were used in the ECRHS-I phase, were also used in the second phase. The equipment and technique complied with the criteria of the European Community for Steel and Coal¹⁰ and the American Thoracic Society.¹¹

Individuals with an FEV₁ over 70% of predicted performed maneuvers again after inhaling the diluent of the methacholine solution. If the postdiluent FEV₁ was less than 90% of the best baseline FEV₁, the methacholine provocation test was abandoned and constriction was reversed with salbutamol. If FEV₁ after the diluent step was greater than 90% of baseline, the test continued.

The methacholine solutions (Hoffman La Roche, Basel, Switzerland) were prepared at a central location (Pharmacy Department, Hospital Clínic i Provincial, Barcelona, Spain). Methacholine was administered during a maximal inspiratory effort to total lung capacity, with increasing doses from a pressurized dosimeter (Mefar MB3, Bovezzo, Italy) connected to a nebulizer.

The protocol for performing the tests has been previously described in detail.⁸ Individuals were considered hyperreactive if their FEV₁ declined 20% or more in comparison with the best postdiluent FEV₁. The maximum allowed cumulative dose was 5.117 μmol of inhaled methacholine. Alternatively, a response was predicted by extrapolation to a dose of 8 μmol of inhaled methacholine.

Quality Assurance

A quality assurance plan was designed for field work at all the participating centers. Throughout the data collection period

an experienced technician collected spirometric curves randomly every month for the center coordinator. Methacholine weights were also checked. At least 2 on-site audits were conducted during the course of the study.

The protocol also contemplated strict quality control of methacholine nebulizer flow as well as monitoring the quality of recorded responses to the questionnaire.

Statistical Analysis

Overall results were expressed as absolute frequency and percentage for qualitative variables and as mean (SD) for numerical data. Length of follow-up was expressed as median and interquartile range.

Differences in ECRHS-II participation between centers according to respiratory symptoms reported in the ECRHS-I phase and the prevalence of those symptoms between centers in this study were compared. First, a χ^2 test was applied to assess differences in ECRHS-II participation according to symptom reporting in the first phase. Then the same test was used to assess the statistical significance of differences in smoking prevalence between the participating centers.

Generalized estimation equations were used to assess annual changes in the prevalence of respiratory symptoms adjusted for center, sex, age, and smoking habit; results were expressed as percentage and 95% confidence interval.

Statistical analyses were performed with the SAS statistical program, version 8.02 (SAS Institute, Cary, North Carolina, USA) and Stata 8 (Stata Corp, College Station, Texas, USA). Results were considered significant at $P < .05$.

Results

We studied a population of 1386 subjects (655 men and 731 women) with a mean age of 41 years. The population was distributed geographically as follows: 308 (22%) in Albacete, 272 (20%) in Barcelona, 360 (26%) in Galdakao, 204 (15%) in Huelva, and 242 (17%) in Oviedo. A total of 1115 individuals underwent spirometry and 999 completed a methacholine challenge test.

The 594 (43%) smokers in the cohort were distributed geographically as follows: 144 (47%) in Albacete, 105 (39%) in Barcelona, 144 (40%) in Galdakao, 94 (46%) in Huelva, and 107 (44%) in Oviedo. There were more smokers among the men (46%) than among the women (40%) in all centers, and the difference was significant in Albacete (55% of men and 39% of women were smokers).

Table 1 shows the participation in the second phase of the study according to geographic area and whether or not subjects presented respiratory or asthma symptoms in the ECRHS-I phase. We detected no significant difference in ECRHS-II participation according to whether subjects did or did not report symptoms in the ECRHS-I ($P > .05$).

Table 2 shows the characteristics of participants in each geographic area (mean age, sex, median follow-up time) as well as smoking status in the ECRHS-II in relation to the ECRHS-I phase. There were no significant differences between areas with regard to smoking.

Table 3 presents the prevalence of symptoms in the ECRHS-I and ECRHS-II, adjusted for age, sex, and geographic area according to relative change in smoking status between the first and second phase. Among smokers, the prevalence of certain asthma symptoms increased between phase I and phase II. Among ex-smokers, on the other hand, wheezing, cough, and expectoration during the winter decreased overall, although these symptoms increased among those who reported having had asthma at some time. Among new smokers (nonsmokers or ex-smokers in the ECRHS-I who were current smokers in the second phase), there was a significant increase in the prevalence of wheezing and expectoration in winter. Finally, in the group of individuals who were smokers in both surveys, we observed a significant increase in the prevalence of wheezing and in reports of the diagnosis and treatment of asthma.

Table 4 shows the prevalences of symptoms in the ECRHS-I and the adjusted annual change in prevalences since then. When a change in prevalence in an area differed from that of other areas, the change for the other areas is also shown. After adjustment for center, sex, age, and smoking, significant increases in wheezing and shortness of breath were evident in Huelva. In Albacete cough and expectoration were significantly less common than in other areas.

In all areas there were significant increases in physician-diagnosed asthma and taking medication for asthma. However, there was no annual increase in the prevalence of asthma defined as asthma symptoms plus bronchial hyperreactivity.

TABLE 1
Participation of Subjects at Each Spanish ECRHS-II Center, by Presence of Respiratory Symptoms in the ECRHS-I

	Albacete	Barcelona	Galdakao	Huelva	Oviedo	Total
No respiratory symptom in the ECRHS-I						
Participants in the ECRHS-II	120 (71%)	167 (68%)	188 (74%)	94 (73%)	109 (68%)	678 (71%)
Not participants in the ECRHS-II	48 (29%)	79 (32%)	67 (26%)	34 (27%)	51 (32%)	279 (29%)
At least 1 respiratory symptom in the ECRHS-I						
Participants in the ECRHS-II	143 (70%)	81 (71%)	143 (73%)	75 (77%)	103 (67%)	545 (71%)
Not participants in the ECRHS-II	61 (30%)	33 (29%)	52 (27%)	22 (23%)	50 (33%)	218 (29%)
Asthma symptoms in the ECRHS-I						
Participants in the ECRHS-II	29 (64%)	13 (81%)	17 (85%)	16 (64%)	16 (67%)	91 (70%)
Not participants in the ECRHS-II	16 (36%)	3 (19%)	3 (15%)	9 (36%)	8 (33%)	39 (30%)

TABLE 2
Prevalence of Smoking in the 5 Areas of the Spanish ECRHS-II Study (n=1386)*

	Albacete	Barcelona	Galdakao	Huelva	Oviedo	Total
Age, mean (SD), y	40.56 (7.40)	41.47 (6.98)	40.60 (7.11)	41.16 (7.27)		
Women, n (%)	163 (53%)	157 (58%)	182 (51%)	105 (51%)		
Duration of follow-up, median, mo	8.62	88.9	8.66	8.45		
Smoking						
Nonsmoker in the ECRHS-I and -II, n (%)	105 (34%)	92 (34%)	119 (33%)	60 (29%)	64 (26%)	440 (32%)
Any category in the ECRHS-I and ex-smoker in ECRHS-II, n (%)	49 (16%)	58 (21%)	71 (18%)	36 (18%)	54 (22%)	268 (19%)
Never smoker or ex-smoker in the ECRHS-I and current smoker in ECRHS-II, n (%)	15 (5%)	12 (4%)	11 (3%)	5 (2%)	8 (3%)	51 (4%)
Current smoker in the ECRHS-I and ECRHS-II, n (%)	128 (41%)	92 (34%)	131 (36%)	80 (39%)	97 (40%)	528 (38%)
Discrepancies†, n (%)	11 (4%)	18 (7%)	28 (8%)	23 (11%)	19 (8%)	99 (7%)

*Differences in smoking between areas were not statistically significant ($P=0.08$).

†Discrepancies refer to cases in which responses about past smoking habits were different from what had originally been reported by the individual in the ECRHS-I.

TABLE 3
Prevalence (Percentage) of Respiratory Symptoms in the ECRHS-I and ECRHS-II, by Change in Smoking Habit*

	NS-NS		ES-II		N/ES-S		S-S	
	I	II	I	II	I	II	I	II
Wheezing	9.3	13.2	20.9	12.0†	9.8	33.3†	34.8	42.2†
Wheezing, not during a cold	5.0	5.0	9.7	4.9†	7.8	11.8	18.9	22.6
Shortness of breath	5.5	7.7	4.5	6.4	3.9	7.8	5.7	7.6
Waking up at night with shortness of breath	4.8	5.9	6.7	9.0	5.9	7.8	7.0	10.1
Cough in winter	8.6	7.3	11.6	6.0†	11.8	17.6	23.1	22.8
Expectoration	6.6	7.1	14.9	8.3†	7.8	21.6†	17.0	18.1
Asthma at some time	4.8	8.0†	3.4	7.8†	3.9	9.8	2.8	5.1
Asthma diagnosis	4.5	7.3†	3.0	6.0	3.9	9.8	2.3	4.0
Asthma attack in the past 12 months	3.0	3.0	1.5	3.0	2.0	2.0	0.6	1.5
Asthma medicines	2.3	3.4	1.1	3.0	0.0	3.9	0.0	1.0†
Asthma symptoms	6.6	8.7	7.1	11.7	5.9	13.7	7.2	11.2†
Asthma+bronchial hyperreactivity	3.1	2.9	2.0	3.6	2.9	2.6	1.3	2.6

*ES-II indicates ex-smoker in the second phase of the study; S-S, smoker in both phases of the study; N/ES-S, never smoker or ex-smoker in the first phase and smoker in the second; NS-NS, nonsmoker in both phases of the study.

†Significant increases or decreases ($P<0.05$) in the prevalence of smoking, adjusted for age, sex, and center.

Discussion

The results of this cohort study in a population of young adults from 5 areas of Spain indicate that the diagnosis of asthma and its treatment have increased in prevalence. Although we detected a greater prevalence of wheezing in Huelva, there was no significant difference between this center and the others. The only symptom without the word *asthma* that increased in all areas was waking up at night because of shortness of breath. Given that other symptoms did not increase and that the combination of a diagnosis of asthma plus bronchial hyperreactivity did not increase, this rise in the prevalence of shortness of breath at night might be mainly attributable to the increase in the number of diagnoses, with a consequent effect of classification on the questionnaire items that included the word *asthma*. The effect could be explained by better diagnosis and treatment on a population level, therefore leading to better monitoring of recent symptoms. Or it could also be explained by overdiagnosis of poorly defined respiratory processes that in the past were not classified

as asthma. The lack of an observed increase in the frequency of asthma attacks in the last 12 months (Table 4) would point to the first explanation, although it is very likely that this was not the only factor.

As expected, we found an association between smoking and the prevalence of respiratory symptoms, such that quitting smoking had a beneficial effect and continuing or starting to smoke had a negative impact, particularly on cough, phlegm, and wheezing. These results are consistent with the findings of a study in which quitting smoking was a significant predictor of cough remission (odds ratio, 2.2; 95% confidence interval, 1.3-3.7) and wheezing (odds ratio, 6.2; 95% confidence interval, 3.5-11.2).¹²

Our findings are also consistent with results from 2 cross-sectional surveys carried out in Norway in 1972 and 1999 in individuals aged 15 to 70 years. In those studies it was observed that the rate of asthma diagnosed by a physician rose from 3.4% to 9.3% and that the prevalence of symptoms increased less according to Pekkanen and Pearce.¹³ In a recent study of young adults in Melbourne

TABLE 4
Changes in the Prevalence of Respiratory Symptoms, Adjusted for Center, Sex, Age, and Smoking Habit*

	Baseline (ECRHS-I) Prevalence, %					Annual Change in Prevalence, 95% CI	P (Between Centers)
	Albacete	Barcelona	Galdakao	Huelva	Oviedo		
Wheezing	19.9	17.5	17.3	19.1	16.7	0.24 (−0.03 to 0.51)	.35
Wheezing, not during a cold							
Huelva				9.7		0.55 (−0.04 to 1.14)	.060
Others	9.7	11.0	8.8	11.9	–	0.10 (−0.3 to 0.09)	
Shortness of breath							
Huelva				1.6		0.94† (0.38 to 1.51)	.032
Others	8.5	1.9	0.2		3.7	0.13 (−0.05 to 0.30)	
Woken up at night with shortness of breath	6.7	2.7	2.6	8.0	5.3	0.24† (0.05 to 0.43)	.661
Cough							
Albacete	8.4					−0.97 (−1.48 to −0.45)	.079
Others		0.3	0.2	14.8	6.5	−0.17 (−0.41 to 0.06)	
Expectoration							
Albacete	16.9					−0.57† (−1.08 to −0.05)	.078
Others		10.8	9.6	16.3	12.6	0.09 (−0.16 to 0.34)	
Asthma at some time	2.8	3.2	1.0	2.3	2.9	0.34† (0.20 to 0.48)	.348
Asthma diagnosis	2.2	3.0	0.9	2.8	2.1	0.26† (0.13 to 0.39)	.870
Asthma attack in the past 12 months	0.8	1.2	0.0	0.7	0.9	0.05 (−0.04 to 0.14)	.482
Asthma medicines	1.1	1.1	1.1	1.1	1.1	0.16† (0.07 to 0.25)	.431
Asthma symptoms	9.2	5.6	5.4	9.9	8.1	0.41† (0.21 to 0.61)	.715
Asthma + bronchial hyperreactivity	1.3	2.4	1.0	1.6	2.3	0.06 (−0.07 to 0.18)	.630

*CI indicates confidence interval.
†P<.05.

comparing the results of 3 postal surveys using a method similar to that of the ECRHS, it was shown that asthma symptoms increased between 1990 and 1992 but later decreased after 1998.¹⁴ That study also showed a rise in current use of medicines for asthma, a finding also reported in a study carried out in peripheral city districts in Italy.¹⁵ A recent study of changes occurring over a 15-year period, undertaken in a population sample that was different from these last studies, found that the prevalence of asthma in children aged 12 years had risen and that it was counterbalanced by increased use of antiasthma medications.¹⁶

These results and ours may indicate that the introduction of international guidelines on asthma has led to more widespread recognition of symptoms among clinicians and, as a result, the diagnosis of asthma and initiation of early treatment has become more common. In fact, the period between the 2 phases of our study saw the development and introduction of guidelines for the diagnosis and management of asthma by both the National Heart, Lung, and Blood Institute¹⁷ and the British Thoracic Society.¹⁸ The availability of these guidelines during the last decade, along with a campaign to build awareness of

new antiasthma agents such as leukotriene antagonists, new inhaler devices for corticosteroids, and long-acting β -agonists, may have led to a rise in physician-diagnosed asthma and the prescription of treatment. A report from Estonia after a study in a population aged 15 to 64 years supports that hypothesis.¹⁹ The authors reported that the 2% prevalence of physician-diagnosed asthma, 2.7% prevalence of having had asthma at some time, and 2.4% prevalence of the use of antiasthma medications were clearly lower than the rates they saw had been reported for Sweden and Finland. In those more highly developed neighboring countries the rate of physician-diagnosed asthma ranges from 5% to 9%, according to the Estonian authors, who attributed the differences to the application of different diagnostic criteria.

It is unknown why the rising prevalence of asthma is related to physicians' knowledge and greater willingness to establish the diagnosis. The rise in the rate of treatment, but not of symptoms, may indicate that the increased use of effective medications has attenuated morbidity in asthmatics, although this interpretation is not consistent with recent studies on control of asthma that have reported very disheartening findings in this respect.²⁰

The finding that the prevalence of asthma does not increase when the definition includes both symptoms of asthma and bronchial hyperreactivity is consistent with the fact that there is no increase in the prevalence of respiratory symptoms that include the word *asthma*. As is well known, bronchial hyperreactivity is a feature of asthma that is strictly related to pathophysiologic abnormality in this disease. For that reason it is extremely useful and objective, as it is not influenced by variability in the perception of symptoms or diagnostic trends. However, it is not the perfect marker of asthma²¹; it is a complement to information from symptoms questionnaires rather than a substitute for it.

The first limitation of our study pertains to any long-term investigation that inevitably undergoes changes in protocols and improvements in knowledge and technological resources. More questions were included in the ECRHS-II than were present in the first phase of the study, but we have maintained a number of the original questions and have based our analysis on them. The same equipment used to measure lung function in the first phase was also used in the second and in nearly all centers the test maneuvers were the same. Another limitation of such studies is failure to respond. In our study the response rate ranged from 66% in Oviedo to 78% in Huelva, and we felt the number of responses received permitted analysis. With regard to selection bias, we did not find there were differences in the rate of participation in the second phase between subjects who had respiratory symptoms in the first phase and those who did not.

In conclusion, this cohort study of young Spanish adults demonstrates an increase in the prevalence and treatment of asthma, with no increase in respiratory symptoms. This pattern remains the same even if bronchial hyperreactivity is included in the definition. These results agree with the analysis of the European section of the ECRHS-II⁷ and are consistent with the notion that the current increase in awareness of asthma symptoms, diagnosis, and treatment of adults is largely a consequence of education, greater understanding of symptoms, and/or more prompt prescription of medications as well as to a greater willingness of physicians to make the diagnosis and treat the disease.

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