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Original article

Factors associated with poorly controlled asthma among adults in France

Facteurs associés à un mauvais contrôle de l'asthme en France

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Abstract

Objectives. – To describe the level of asthma control using the Asthma Control Test (ACT) in real life, and to identify factors associated with poorly controlled asthma (ACT score <20).

Methods. – Participating GPs and specialists had to include the first two consecutive patients with a diagnosis of asthma ≥ 12 months at a consultation for asthma.

Results. – Of the 5508 adult patients screened by 987 physicians, 2165 were included in the cohort. They were 47% overweight, 81% non-smokers, 66% with an asthma diagnosis ≥ 10 years, and a median ACT score of 18 [5–25]. Asthma was poorly controlled in 62% of patients. Independent factors associated with poorly controlled asthma were: emergency visit for exacerbation of asthma during the past three months (odds ratio [OR]: 4.3; 95% confidence interval [95% CI] [2.9–6.3]), use of short-acting beta2-agonist (OR: 2.8; 95% CI [2.2–3.4]) or theophyllin (OR: 2.6; 95% CI [1.2–5.4]), being a current (OR: 2.1; 95% CI [1.6–2.8]) or a former smoker (OR: 1.4; 95% CI [1.1–1.7]), professionally inactive (OR: 1.9; 95% CI [1.3–2.8]), unemployed (OR: 1.9; 95% CI [0.9–4.0]) or retired (OR: 1.7; 95% CI [1.3–2.2]), being obese (OR: 1.7; 95% CI [1.2–2.2]), no use of combinations of long-acting beta2-agonist and corticosteroid (OR: 1.5; 95% CI [1.2–1.9]), being a woman (OR: 1.4; 95% CI [1.1–1.7]), and presenting an atopic dermatitis (OR: 1.4; 95% CI [1.1–1.8]).

Conclusion. – Treated asthma patients are still poorly controlled. Data are useful for patient care as they allow identifying high-risk patients with most prominent factor of having emergency visit for the exacerbation of asthma in the previous 3 months.

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Keywords: Asthma; Control; Asthma Control Test; Management

Résumé

Objectifs. – Décrire le niveau de contrôle de l'asthme avec le test de contrôle de l'asthme (ACT) en pratique courante et identifier les facteurs associés à un mauvais contrôle (score ACT < 20).

Méthodes. – MG et spécialistes devaient inclure lors d'une consultation pour l'asthme les deux premiers patients ayant un diagnostic d'asthme ≥ 12 mois.

Résultats. – Cinq mille cinq cent huit patients adultes ciblés par 987 médecins, 2165 inclus dans la cohorte : 47 % en surpoids, 81 % de non-fumeurs, 66 % avec un diagnostic d'asthme ≥ 10 ans, score ACT médian de 18 [5–25]. L'asthme était mal contrôlé chez 62 % des patients. Les

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facteurs indépendants associés au mauvais contrôle étaient : visite d'urgence pour exacerbation de l'asthme au cours des 3 derniers mois (OR : 4,3 ; IC 95 % [2,9–6,3]), utilisation d'un bêta2-agoniste de courte durée d'action (OR : 2,8 ; IC 95 % [2,2–3,4]) ou théophylline (OR : 2,6 ; IC 95 % [1,2–5,4]), fumeur (OR : 2,1 ; IC 95 % [1,6–2,8]), ancien fumeur (OR : 1,4 ; IC 95 % [1,1–1,7]), professionnellement inactif (OR : 1,9 ; IC 95 % [1,3–2,8]), chômeurs (OR : 1,9 ; IC 95 % [0,9–4,0]) ou à la retraite (OR : 1,7 ; IC 95 % [1,3–2,2]), obèse (OR : 1,7 ; IC 95 % [1,2–2,2]), sans combinaison de bêta2-agoniste à long terme et corticoides (OR : 1,5 ; IC 95 % [1,2–1,9]), être une femme (OR : 1,4 ; IC 95 % [1,1–1,7]), présentant une dermatite atopique (OR : 1,4 ; IC 95 % [1,1–1,8]).

Conclusion. – Les patients asthmatiques traités sont encore mal contrôlés. Ces données permettent d'identifier les patients à haut risque, l'exacerbation de l'asthme au cours des 3 derniers mois influençant principalement la visite d'urgence.

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Mots clés : Asthme ; Contrôle ; Test de contrôle de l'asthme ; Prise en charge

1. Introduction

Asthma is a chronic inflammatory disease of the airways affecting 235 million people in the world [1]. There has been a sharp increase in the prevalence of asthma over the last few decades in all the industrialized countries [2]. In 2006, 10.2% of people reported having suffered from asthma at least once during their lifetime [2]. The prevalence of asthma in the French population whatever the gender was estimated to be 6.7% in 2006 (i.e. 4.15 million of asthmatics in France) [2]. The prevalence varied with age, decreasing among individuals aged from 20 to 50 years, and increasing to reach 7% in those 60 of age and over [2]. Additionally, the prevalence of asthma among smokers was higher in women than in men (7.8 versus 5.2%), but similar among former (6%) or non-smokers (7%) [2].

In France, hospitalizations for asthma have decreased since 1998 in adults but increased among very young children [2]. Regarding mortality, asthma death rates have steadily declined since 2000, reflecting a better management of asthmatics [2]. Nevertheless, asthma is still insufficiently controlled in real life despite efficacy of the available current therapeutic arsenal [3], and poor asthma control is the main risk factor of exacerbation of asthma [5]. In the French ER'Asthma study, general practitioners (GPs) found that asthma control was unacceptable in 72% of patients [4]. More recently, in 2006, the French Health, Health Care and Insurance survey (ESPS) carried out on the general population showed that only 39% of asthmatics were controlled, 46% partly controlled and 15% uncontrolled according to the GINA 2006 [2,6].

The national (HAS 2004) and international asthma guidelines (GINA) have emphasized the importance of focusing on asthma control rather than severity of asthma in clinical practice for good asthma control [6–8]. In the French ER'Asthma survey, normal BMI, non-smoker status, age under 50 years, use of fixed combination therapy (inhaled corticoids and long-acting β_2 -adrenergic agonists), and good compliance to anti-asthmatic treatment were associated with optimal control of asthma [4]. In 2006, it was shown that inadequately controlled French asthmatics were more likely to be overweight or obese, age of 65 and over, with allergy (rhinitis, atopic dermatitis), and to belong to a disadvantaged social group [1,2]. Additionally, an asthmatic with obesity or with a current smoking status had a higher risk to be poorly controlled than an asthmatic with a

normal weight or with a non-smoker status, respectively [1]. Many papers have shown a positive link between asthma and two risk factors, namely obesity and smoking, and also with many comorbid conditions, such as depression, anxiety, eczema, gastro-esophageal reflux disease or cardiovascular diseases [9].

The ATHMOS study was conducted in a large cohort of French patients with asthma in order to better understand factors associated with poorly controlled asthma that should help physicians to determine more efficiently the preventive measures with the greatest impact on asthma control and prevent the complications of the disease. The objectives of the present study were to describe the level of asthma control using the Asthma Control Test (ACT) in real life [10,11] and identify factors associated with poorly controlled asthma at inclusion and after a 3-month follow-up. This paper focuses on the cohort at inclusion and factors associated with poorly controlled asthma. The 3-month follow-up data and predictive factors of poorly controlled asthma will be presented in another paper.

2. Design, methods and participants

2.1. Study design

ATHMOS was a transversal and longitudinal epidemiological study of a large cohort of French asthmatic adult patients. The investigation was based on a sample of 1500 French physicians with private practice drawn at random from the CEGEDIM database (www.cegedim.com) and distributed as follows: 2/3 general practitioners (GPs) and 1/3 of allergists or chest physicians, as it was estimated that around 1/3 asthmatic patients had a follow-up with a specialist for asthma.

Each physician had to include the first two consecutive patients fulfilling required eligible criteria at a regular outpatient consultation for asthma throughout a period of 3 months. Enrollment was between September 2006 and September 2007.

2.2. Selection criteria

Adult patients were eligible if they had a physician diagnosis of asthma for at least 12 months made at the discretion of each participating physician.

Eligible patients who gave their informed consent to participate in the study and were not participating in other

clinical studies at the time of enrollment were included in the study cohort. Those who did not want to participate to the study were not included in the study cohort but were listed in a patient register in order to obtain a reference population from which the representativeness of the study cohort was checked.

Patients, who were judged unable to fulfill alone a questionnaire by the practitioner, aged under 18 years, had a pathology that could interfere with the interpretation of the results, and participated in other clinical studies were excluded.

2.3. Data collection

Participating physicians completed a short questionnaire concerning their socio-demographic data and their own professional activity.

For each patient included in the cohort, physicians had to fill out a questionnaire with socio-demographic characteristics, history of asthma, history of smoking, presence or absence of co-morbidities (allergic rhinitis, food allergies, atopic dermatitis, allergic conjunctivitis, and others should be cited), reason of consultation, number of admissions to hospital and loss of work hours due to asthma in the past 3 months, current anti-asthmatic treatment, spirometry testing [if Yes: PEF value (peak expiratory flow), if No: reason], and lung function investigation at inclusion [if Yes: FEV₁ value (forced expiratory volume in one second), FVC value (forced vital capacity) and FEV₁/FVC ratio]. In France, some GPs have a spirometer to measure PEF values; however, lung function (FEV₁, FVC values) is only investigated by chest physicians.

Likewise, for each eligible but not included patients in the study cohort (up to 8 patients per physician), physicians were asked to collect all data (socio-demographic characteristics, history of asthma, FEV₁, PEF, current anti-asthmatic treatment and reason of non-inclusion) in a patient register.

2.4. Asthma control

The level of asthma control was assessed using a patient-based tool for identifying patients with poorly controlled asthma, the ACT (Asthma Control Test is a trademark of QualityMetric Incorporated; Copyright 2002 by QualityMetric Incorporated) with 5 items assessing asthma symptoms in its French validated version [10,11]. Each patient completed an ACT questionnaire.

For each patient, ACT score was calculated by summing up scores obtained for each item with response options corresponding to a 5-point Likert-type rating scale. ACT scores ranged from 5 (poor control of asthma) to 25 (complete control of asthma) [10].

Patients were categorized into 2 groups according to ACT scores towards the cutoff score of 19 suggested by Schatz as ACT <20 (poorly controlled) or ACT ≥20 (well-controlled) [12].

2.5. Statistical analysis

The statistical analysis of the collected data was performed using SAS software, version 8.2 (SAS Institute, North Carolina,

US). The representativeness of the physicians and the patients were analyzed.

Taking into account a high hypothesis with a frequency of 50% for each level (controlled, not controlled), we estimated that a sample size of 2654 subjects would be sufficient to obtain a precision of 2.5% with a 99% confidence interval (CI). In order to account for 12% of non-responses to ACT questionnaire, a total of 3000 subjects were planned to be enrolled in the study.

Patients over 18 years old for whom fulfilled inclusion criteria and ACT questionnaire at inclusion were available composed the analyzable study population.

The primary variable was ACT score and all other parameters were considered as secondary variables. Quantitative variables were described by mean, standard deviation, median, minimum and maximum and qualitative variables by the number and frequency. For comparison of quantitative parameters (analysis of variance) the normality hypotheses for variables was controlled by a Shapiro-Wilks test. If these hypotheses were not fulfilled, a non-parametric approach using Kruskal-Wallis test was considered. For comparison of qualitative parameters, Chi² or Fisher exact tests were used. The type I error (α) was set at 5% in a bilateral approach.

Two distinct models were built in order to identify factors associated with poorly controlled asthma at inclusion, regarding ACT <20 (binary variables) or the level of asthma control expressed with ACT score (continuous quantitative variables). First of all, each factor was evaluated independently using univariate analysis. Then, all the 20% significant variables were entered into a multivariate logistic regression (binary model) or a multivariate linear regression (continuous model). The final models were built using stepwise selection factors method with a 5% significance level.

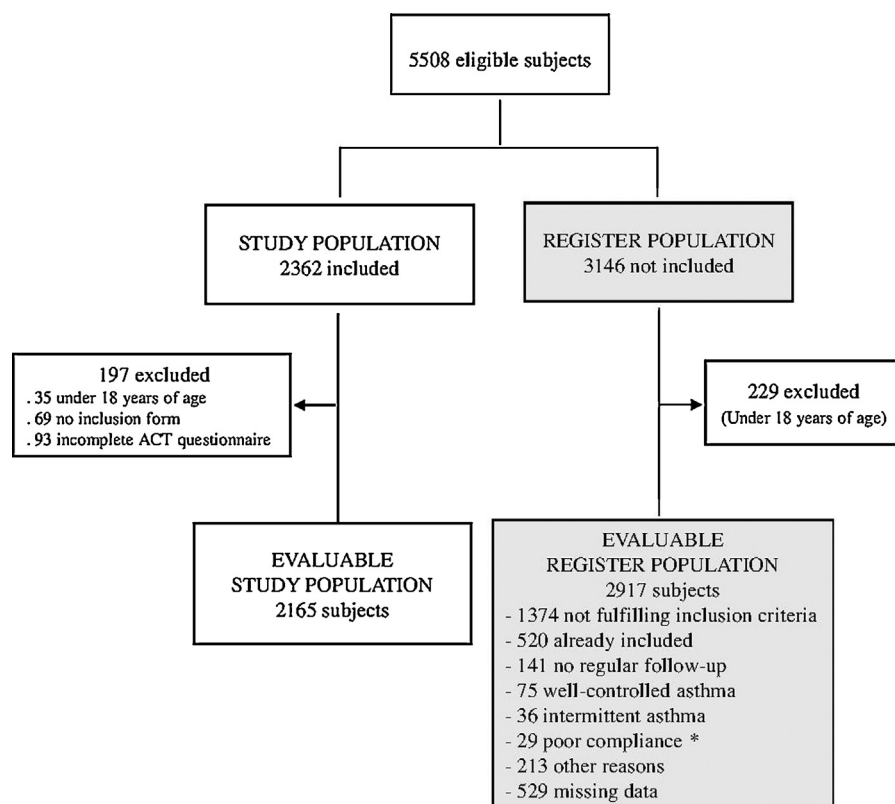
3. Results

Of the 1500 physicians who were drawn at random, 1213 accepted to participate in the ATHMOS study. Finally, 987 physicians including 749 GPs, 118 chest physicians and 120 allergists screened 5508 patients. Men accounted for 68% of chest physicians and 28% of allergists, and were overrepresented in GPs compared with French population of GPs (80% versus 71%; $P < 0.001$). The geographic distribution of participating physicians was slightly different from the one observed nationally. The study was based on a relatively representative sample of French physicians.

3.1. Study population

A total of 5508 subjects were eligible for the study as they had a physician diagnosis of asthma for at least one year. Among them, 3146 subjects not fulfilling inclusion criteria were not included in the cohort study and listed in the patient register as shown in Fig. 1. As 29 patients were under 18 years of age, the evaluable register population included a total of 2917 adults (Fig. 1).

The study cohort included 2362 subjects who fulfilled inclusion criteria, but the evaluable cohort was comprised of 2165 included subjects as shown in Fig. 1. The baseline



* At the discretion of physicians

Fig. 1. Disposition of patients.

characteristics of the study population are presented in Table 1. The population was homogenous in terms of gender (female: 52%). The mean age was 46.1 (S.D.: 16.5) years. The mean BMI was 25.3 (S.D.: 4.6) kg/m² and 47% were overweight. The mean duration of asthma was 18.2 (S.D.: 12.9) years and 66% of patients were diagnosed more than 10 years ago. During the past three months, 13% of patients had 1.5 (S.D.: 1.0) emergency visits because of an exacerbation of their asthma. More than half of the patients were non-smokers. Among professionally active patients, 10% had been on sick leave due to their asthma during the previous three months.

Lung function parameters measured at the inclusion visit are presented in Table 1. The reasons of not measuring PEF in less than half of the patients (43%) reported by physicians were mainly poor clinical condition of patient or difficulties to measure it. Lung function test was also realized in 17% of patients at the inclusion visit as outlined in Table 1.

Almost all patients (95%) were currently treated with anti-asthmatics, mainly a fixed or free combination of long-acting beta2-agonist and corticosteroids (68%), short-acting β 2-agonists (40%), anti-leukotriens (18%), inhaled corticosteroids (14.5%), or long-acting β 2-agonists (2.5%).

Compared to the register population, patients included in the study population were significantly more often women (52% versus 49%; $P = 0.01$), professionally active (62% versus 59%; $P = 0.013$) and living in urban area (61% versus 58%; $P = 0.014$). Regarding asthmatic characteristics, history of asthma was

longer [18.2 (S.D.: 12.9) versus 17.2 (S.D.: 13.7) years; $P \leq 0.001$] and percentage of predicted FEV₁ was lower [87.8 (S.D.: 55.6) versus 91.3 (S.D.: 71.1) %; $P = 0.013$] in the study population compared to the register population. No significant difference between the two populations was observed according to age, BMI, PEF and current anti-asthmatic treatment.

3.2. Factors associated with poorly controlled asthma (univariate analysis)

Asthma was poorly controlled (ACT score <20) in 62% of patients. The baseline characteristics of patients with poorly controlled asthma were significantly different compared to those with controlled asthma according to age, gender, obesity, habitual activity, smoking habits, lung function and reasons of consultation as outlined in Table 1. The proportion of patients with percentage of predicted PEF value below 85% was significantly higher in poorly controlled patients than in well-controlled (73% versus 47%; $P \leq 0.001$). Likewise, the proportion of patients with a predicted FEV₁ below 80% was significantly higher in poorly controlled than in well-controlled patients (52% versus 30%; $P \leq 0.001$).

Regarding hospitalization, emergency or absenteeism due to exacerbation of asthma during the previous three months poorly controlled patients were more likely to be hospitalized (3% versus 1%; $P \leq 0.001$) and have emergency visit (18% versus

Table 1
Characteristics of the study population by level of asthma.

Characteristics	Study population (<i>n</i> = 2165)	Level of asthma control		<i>P</i>
		ACT score < 20 ^a (<i>n</i> = 1343)	ACT score ≥ 20 ^b (<i>n</i> = 822)	
Female gender, <i>n</i> (%)	1128 (52.3%)	737 (55.2%)	391 (47.6%)	0.001
Age, years	46.1 ± 16.5	46.9 ± 16.7	44.7 ± 16.2	0.003
BMI, <i>n</i> (%)				0.010
Underweight (BMI < 18.5 kg/m ²)	64 (3.0%)	45 (3.4%)	19 (2.3%)	
Normal weight (BMI [18.5–25] kg/m ²)	1059 (49.6%)	627 (47.4%)	432 (53.1%)	
Overweight (BMI [25–30] kg/m ²)	737 (34.5%)	452 (34.2%)	285 (35.1%)	
Obesity (BMI ≥ 30 kg/m ²)	276 (12.9%)	199 (15.0%)	77 (9.5%)	
Habitual activity, <i>n</i> (%)				≤ 0.001
Actively employed	1340 (62.1%)	781 (58.4%)	559 (68.1%)	
Retired	448 (20.8%)	301 (22.5%)	147 (17.9%)	
Unemployed	45 (2.1%)	33 (2.5%)	12 (1.5%)	
No activity	210 (9.7%)	158 (11.8%)	52 (6.3%)	
Others	115 (5.3%)	64 (4.6%)	51 (6.2%)	
Urban localization, <i>n</i> (%)	1323 (61.3%)	837 (62.6%)	486 (59.3%)	0.133
Smoking habits, <i>n</i> (%)				≤ 0.001
Current smoker	410 (19.0%)	305 (22.8%)	105 (12.8%)	
Former smoker	537 (24.9%)	341 (25.5%)	196 (23.9%)	
Non-smoker	1208 (56.1%)	690 (51.7%)	518 (63.3%)	
History of asthma, <i>n</i> (%)				0.174
≤ 10 years	719 (34.1%)	466 (35.6%)	253 (31.7%)	
11–20 years	617 (29.3%)	370 (28.3%)	247 (31.0%)	
> 20 years	770 (36.6%)	472 (36.1%)	298 (37.3%)	
Co-morbidities, <i>n</i> (%) ^c				
Rhinitis	1197 (55.3%)	722 (53.8%)	475 (57.8%)	0.068
Atopic dermatitis	314 (14.5%)	209 (15.6%)	105 (12.8%)	0.078
Allergic conjunctivitis	555 (25.6%)	352 (26.2%)	203 (24.7%)	0.447
Food allergy	158 (7.3%)	92 (6.9%)	66 (8.0%)	0.308
Others ^d	274 (13.3%)	169 (13.1%)	105 (13.5%)	0.841
Lung function parameters ^e				
Measurement of PEF, <i>n</i> (%)	1228 (56.9%)	754 (56.4%)	474 (57.9%)	0.502
PEF, % predicted	76.7 ± 22.8	71.1 ± 22.6	85.8 ± 20.1	≤ 0.001
Pulmonary function testing, <i>n</i> (%)	366 (17.0%)	220 (16.5%)	146 (17.9%)	0.442
FEV ₁ , % predicted	87.8 ± 55.6	82.1 ± 42.6	96.5 ± 70.3	≤ 0.001
FVC, % predicted	92.6 ± 28.1	89.5 ± 29.5	97.3 ± 25.3	0.001
Within 3 months prior to visit				
Patients with an emergency visit, <i>n</i> (%)	278 (13.0%)	243 ^f (18.3%)	35 (4.3%)	≤ 0.001
Hospitalized patients, <i>n</i> (%)	48 (2.2%)	42 (3.1%)	6 (0.7%)	≤ 0.001
Patients receiving oral corticoids, <i>n</i> (%)	53 (2.5%)	42 (3.1%)	11 (1.3%)	0.009
Reasons of the current visit, <i>n</i> (%)				
A follow-up visit	1572 (72.6%)	827 (61.6%)	745 (90.6%)	≤ 0.001
Exacerbation of asthma	468 (21.6%)	434 (32.3%)	34 (4.1%)	≤ 0.001
Others	138 (6.4%)	92 (6.9%)	46 (5.6%)	0.277

n: number of cases; ACT: Asthma Control Test; BMI: body mass index; PEF: peak expiratory flow; FEV₁: forced expiratory volume in one second; FVC: forced vital capacity. Results are presented as mean ± S.D. or *n* (%) when appropriate.

^a Poorly controlled asthma.

^b Well-controlled asthma.

^c Several answers could be chosen.

^d Other allergies, respiratory diseases, cardiovascular diseases, digestive diseases, and other disorders.

^e Measured at the inclusion visit.

^f Including 30 patients hospitalized within 3 months prior to visit (unknown reason of hospitalization: related or not to the emergency visit).

4%; $P \leq 0.001$) as shown in Table 1, or be on sick leave (16% versus 2%; $P \leq 0.001$) than well-controlled patients.

Whatever the level of asthma control, almost all patients were currently treated with anti-asthmatics at the inclusion visit (poorly controlled: 94%; well-controlled: 95%). However, the use of fixed

or free combinations of long-acting β_2 -agonist and corticosteroids was significantly lower in poorly controlled patients than in well-controlled (63% versus 74%; $P \leq 0.001$). The use of short-acting beta2-agonists was significantly higher in poorly controlled patients than in well-controlled (49% versus 25%; $P \leq 0.001$).

Regarding other anti-asthmatic treatments, poorly controlled patients were more often treated with theophyllin (4% versus 1%; $P = 0.001$), oral corticoids (3% versus 1%; $P = 0.009$) and anti-cholinergic bronchodilator drugs (short- or long-acting) (5% versus 2%; $P = 0.014$) than well-controlled patients. There was no statistically significant difference with respect to the use of inhaled corticoids not associated with long-acting β_2 -agonists (15% versus 13%; $P = 0.115$), short-acting β_2 -agonists not associated with inhaled corticoids (3% versus 2%; $P = 0.570$), and anti-leukotriens (19% versus 16%; $P = 0.120$).

3.3. Factors associated with poorly controlled asthma (multivariate analysis)

3.3.1. Logistic model ($ACT < 20$; $ACT > 20$)

Logistic regression analysis identified several independent factors associated with poorly controlled asthma as shown in Table 2. The risk of having poorly controlled asthma was significantly four-fold higher in patients who consulted on emergency for exacerbation of asthma during the past three

Table 2
Factors associated with poorly controlled asthma identified in the final multivariate logistic regression model ($n = 2165$).

Independent variables	OR [95% CI]	P
<i>Emergency visit due to exacerbation of asthma within 3 months</i>		
No	1.00	
Yes	4.307 [2.945; 6.298]	<0.0001
<i>Obesity</i>		
No	1.00	
Yes	1.657 [1.226; 2.239]	0.0010
<i>Atopic dermatitis</i>		
No	1.00	
Yes	1.397 [1.059; 1.842]	0.0178
<i>Female gender</i>		
No	1.00	
Yes	1.357 [1.109; 1.661]	0.0030
<i>Habitual activity</i>		
Actively employed	1.00	
Retired	1.712 [1.333; 2.200]	<0.0001
Unemployed	1.864 [0.863; 4.029]	0.1131
No activity	1.936 [1.342; 2.793]	0.0004
Other	0.845 [0.551; 1.297]	0.4407
<i>Smoking habits</i>		
Non-smoker	1.00	
Former smoker	1.375 [1.084; 1.744]	0.0086
Current smoker	2.136 [1.624; 2.809]	<0.0001
<i>Short-acting β_2-adrenergic agonist</i>		
No	1.00	
Yes	2.757 [2.245; 3.387]	<0.0001
<i>Theophyllin</i>		
No	1.00	
Yes	2.579 [1.228; 5.415]	0.0123
<i>No use of combination of LABA and corticosteroid (fixed or free)</i>		
No	1.00	
Yes	1.519 [1.228; 1.878]	0.0001

OR: odds ratio; CI: confidence interval; LABA: long-acting β_2 -adrenergic agonist.

months, nearly three-fold higher in patients treated by short-acting β_2 -agonists or theophyllin, nearly two-fold higher in current smokers, and 1.5-fold higher in patients not treated with a combination of corticosteroids and long-acting β_2 -agonists (free or fixed) as outlined in Table 2. The other factors associated with poorly controlled asthma found in this analysis were also: to be a woman, professionally inactive (retired, unemployed or without any professional activity), obese, and to present an atopic dermatitis (Table 2).

3.3.2. Linear model (ACT in continuous variable)

The median score of ACT was 18 [5–25] and the mean score of ACT was 17.2 (S.D.: 4.9). The mean ACT scores obtained according to characteristics of included patients are presented in Table 3.

In the final multivariate linear analysis, the following parameters were associated to a decrease of ACT, i.e. associated with poorly controlled asthma: to have consulted on emergency

Table 3
Score obtained in the Asthma Control Test (ACT) according to characteristics of the study population ($n = 2165$).

Continuous variables	ACT score	<i>P</i>
<i>Age</i>		0.005
18–44 years (<i>n</i> = 1061)	17.4 ± 5.0	
45–59 years (<i>n</i> = 605)	17.1 ± 5.0	
≥60 years (<i>n</i> = 499)	16.6 ± 5.0	
<i>Gender</i>		≤0.001
Male (<i>n</i> = 1029)	17.5 ± 4.9	
Female (<i>n</i> = 1128)	16.7 ± 5.0	
<i>Obesity</i>		≤0.001
BMI <30 kg/m ² (<i>n</i> = 1860)	17.3 ± 5.0	
BMI ≥30 kg/m ² (<i>n</i> = 276)	15.8 ± 4.9	
<i>Overweight</i>		0.006
BMI <25 kg/m ² (<i>n</i> = 1123)	17.4 ± 5.0	
BMI ≥25 kg/m ² (<i>n</i> = 1013)	16.8 ± 5.0	
<i>Habitual activity</i>		≤0.001
Actively employed (<i>n</i> = 1340)	17.6 ± 5.0	
Retired (<i>n</i> = 448)	16.6 ± 5.0	
Unemployed (<i>n</i> = 45)	15.6 ± 5.2	
No activity (<i>n</i> = 210)	15.3 ± 5.0	
Other (<i>n</i> = 115)	17.8 ± 4.6	
<i>Smoking habits</i>		≤0.001
Current smoker (<i>n</i> = 410)	15.7 ± 5.0	
Former smoker (<i>n</i> = 537)	17.1 ± 4.8	
Non-smoker (<i>n</i> = 1208)	17.6 ± 5.0	
<i>Rhinitis</i>		0.089
No (<i>n</i> = 968)	16.9 ± 5.1	
Yes (<i>n</i> = 1197)	17.3 ± 5.0	
<i>Atopic dermatitis</i>		0.046
No (<i>n</i> = 1851)	17.2 ± 5.0	
Yes (<i>n</i> = 314)	16.6 ± 4.9	
<i>Allergic conjunctivitis</i>		0.039
No (<i>n</i> = 1610)	17.2 ± 5.0	
Yes (<i>n</i> = 555)	16.7 ± 5.0	
<i>Hospitalization within 3 months</i>		≤0.001
No (<i>n</i> = 2116)	17.2 ± 5.0	
Yes (<i>n</i> = 48)	13.5 ± 5.3	

Table 3 (Continued)

Continuous variables	ACT score	P
<i>Emergency within 3 months</i>		≤0.001
No (n = 1868)	17.7 ± 4.8	
Yes (n = 278)	13.4 ± 4.9	
<i>Combination of LABA and corticosteroids</i>		≤0.001
No (n = 702)	16.2 ± 5.1	
Yes (n = 1463)	17.6 ± 4.9	
<i>Inhaled corticoids (without LABA)</i>		0.030
No (n = 1852)	17.2 ± 5.0	
Yes (n = 313)	16.5 ± 5.1	
<i>Short-acting β₂-adrenergic agonist</i>		≤0.001
No (n = 1299)	18.1 ± 4.9	
Yes (n = 866)	15.6 ± 4.9	
<i>Theophyllin</i>		≤0.001
No (n = 2106)	17.2 ± 5.0	
Yes (n = 59)	14.0 ± 5.0	
<i>Oral corticoids</i>		≤0.001
No (n = 2112)	17.2 ± 5.0	
Yes (n = 53)	14.2 ± 5.8	
<i>Anti-cholinergic bronchodilators</i>		≤0.001
No (n = 2084)	17.2 ± 5.0	
Yes (n = 81)	15.3 ± 4.4	

n: number of cases; ACT: Asthma Control Test; BMI: body mass index; LABA: long-acting β₂-adrenergic agonist.

because of exacerbation of asthma in the past three months, to be obese, to be older than 60 years, to present atopic dermatitis and to be treated with short-acting β₂-agonist, theophyllin or anti-cholinergic bronchodilators as outlined in Table 4.

Table 4
Multivariate linear regression analysis to evaluate variables that affect the control of asthma (n = 2165).

Independent variables	Estimated parameters ^a	Pr > t ^b	95% CI	
Constant ^c	20.41764	<0.0001	19.95068	20.88460
Emergency in the past 3 months	−3.64987	<0.0001	−4.23758	−3.06216
Short-acting β ₂ -adrenergic agonist	−2.14763	<0.0001	−2.55541	−1.73985
Theophyllin	−1.95354	0.0014	−3.15177	−0.75531
Current smoker	−1.65349	<0.0001	−2.18329	−1.12370
Obesity	−1.33413	<0.0001	−1.91572	−0.75253
Anti-cholinergic bronchodilator	−1.30292	0.0148	−2.35071	−0.25513
No use of a combination of LABA and corticosteroids	−1.11993	<0.0001	−1.54599	−0.69387
Age: ≥60 years	−1.09821	<0.0001	−1.61951	−0.57690
Female gender	−0.75454	0.0002	−1.15776	−0.35132
Atopic dermatitis	−0.72410	0.0106	−1.27908	−0.16913
Former smoker	−0.53844	0.0312	−1.02807	−0.04881
Age: 45–59 years	−0.40574	0.0890	−0.87338	0.06190

CI: confidence interval; LABA: long-acting β₂-adrenergic agonist.

^a Estimated parameters of the independent variables in the linear regression model.

^b Significance of estimated parameters.

^c Intercept of the model.

4. Discussion

The observational ATHMOS study provided useful information on the French asthmatic population and showed a high rate of poorly controlled asthma (62%) in patients who attended an outpatient asthma consultation during 2006–2007. The ATHMOS population had relatively similar characteristics to those of the large cohort (n = 16,580) in the French ER'Asthma survey conducted in 2003 regarding gender (52% versus 46% of women), obesity (13% versus 11% of obese), smoking habits (18.5% versus 19% of smokers), professional activity (62% versus 50% of actively employed) and co-morbidities (55% versus 43% of patients with allergic rhinitis) despite different inclusion criteria [4]. An even higher percentage of 72% of unacceptable asthma control was assessed by general practitioners in the ER'Asthma survey [4]. Additionally, our results were consistent with those obtained in the latest French survey (ESPS) that assessed asthma in French overall population in 2006 [2].

As medical care differs throughout the world, the rate of uncontrolled asthma varies among different countries. Thus a great variability in the prevalence of uncontrolled asthma emerged across Europe among inhaled corticosteroids users (from 20% in Iceland to 67% in Italy) [13]. Almost two-third of asthmatic patients included in a study evaluating the degree of asthma control in Spain in 2006 were poorly controlled [14]. More recently, Nguyen et al. found 46% of patients with not well-controlled asthma in five New England States according to the National Asthma Education and Prevention Program (NAEPP) during 2006–2007 [15]. We found a similar high rate of asthmatic patients with inadequate control of asthma (ACT score <20) in real life despite the fact that 95% of patients were treated with anti-asthmatics. Our findings were consistent with those observed in the INSPIRE study which examined the attitudes and actions of 3415 physician-recruited adults aged ≥16 years with asthma in eleven countries who were prescribed regular maintenance therapy [16].

We identified several independent factors associated with the risk of poorly controlled asthma. Emergency visit due to exacerbation of asthma in the past 3 months was the main factor associated with poorly controlled asthma in the ATHMOS study. Patients with poorly controlled asthma were more likely to be hospitalized, to consult in emergency or to be more frequently on sick leave. Among patients (n = 243, 18% of study cohort) with poorly controlled asthma having an emergency visit due to exacerbation of asthma during the previous three months, only 12% of them (30 patients) were hospitalized. Overall, we found extremely few hospitalized patients (2%, 48 patients) within 3-month period. These results confirm the trend observed in France that the asthma hospitalization rate has declined in recent years while patients remain poorly controlled. Poorly controlled asthma represents a high socio-economic burden [17]. Globally, the economic costs associated with asthma were estimated at 1.5 billion Euros in France in 2001 [17].

Several asthmatics' individual characteristics, namely demographic and clinical characteristics, were also found to be associated with poorly controlled asthma. Compared to

patients with well-controlled asthma, patients with poorly controlled asthma were significantly more likely to be older, women, overweight, smokers, inactive and with a lower lung function in the ATHMOS study. At our knowledge, the finding that being a woman was significantly associated with poorly controlled asthma was not previously observed in real life [2,14]. In the 2006 French ESPS survey, women were more numerous to show a poorer control of symptoms of asthma and have greater frequency of emergency and hospital admissions due to asthma than men (59% versus 41%) [2]. However, even if women were more likely to have uncontrolled asthma than men in this study, gender was not identified as a factor with a significant influence on the likelihood of being inadequately controlled rather than controlled [2]. Additionally, co-morbid conditions may alter response to asthma treatment and negatively impact asthma control [9]. The latest GINA updated (2011) mentioned that asthma was more frequently observed in obese subjects and more difficult to control [8]. In the ATHMOS study, we identified obesity as a co-morbid factor associated with poorly controlled asthma as previously reported [2,18]. A logistic regression analysis demonstrated a positive association between BMI and uncontrolled asthma (OR: 1.5; 95% CI [1.02; 2.2]) in a cross-sectional study conducted in the outpatient central reference clinic of the Program for Control of asthma in the state of Bahia [18]. Furthermore, it has been shown that asthma predisposes to overweight [19] and obesity negatively impacts respiratory function [20]. Recently, it has been reviewed the current understanding of the potential mechanistic links between obesity and asthma, emphasizing the potential influence of metabolic abnormalities on asthmatic processes, therapeutic implications, and expected challenges [21]. However, further investigations into the metabolic aspects of asthma will be necessary to define an obese-asthma phenotype that may influence asthma severity and contribute to the level of asthma control [21]. Another co-morbid factor shown in our study to be related to poorly controlled asthma was atopic dermatitis. Atopic dermatitis is considered as the usual initial manifestation of atopy to later progression to allergic rhinitis, asthma and food allergy [22]. New understandings on the genetics and pathophysiology of atopic dermatitis attribute an important role of structural abnormalities in the epidermis as well as immune dysregulation not only for this skin disease but also for the development of asthma [23]. Additionally, we did not confirm in the ATHMOS study that symptoms of rhinitis were associated with uncontrolled asthma as it was previously shown by Barros et al. (OR: 3.68; 95% CI [1.5; 9.01]) [18]. Regarding smoking status, we demonstrated a reduction of the risk of uncontrolled asthma in non-smokers. In the French ESPS survey, asthmatics current smokers had a significant propensity to have uncontrolled asthma compared to non-smokers [2]. In a Canadian study [24], patients with well-controlled asthma tended to be more frequently non-smokers (48%) or ex-smokers (49%) than current smokers (39%) but difference was not statistically significant. However, tobacco smoke is a well-known irritant for many respiratory diseases, and is harmful to asthmatics as both active and passive smoking worsen asthma [25].

Beyond the asthmatics' individual characteristics, we showed that the use of short-acting β_2 -agonists or theophyllin were associated with poorly controlled asthma. At the opposite, we confirmed that the use of combinations (free or fixed) of corticosteroids and long-acting β_2 -agonists was associated with optimal control of asthma as previously shown in the ER'Asthma survey [4]. The aim to achieve well-controlled asthma is important because patients with poorly controlled asthma are often more sensitive to multiple factors that are ubiquitous in the environment. Additionally, maintaining asthma control leads to reduce risk of exacerbations, prevent most attacks, avoid troublesome symptoms, and keep patients physically active. Compliance is a crucial determinant of the treatment outcome of asthma. Treatment adherence was not assessed in the ATHMOS study. For asthma medication, rate of non-compliance is estimated around 50% [8]. There are many reasons influencing treatment adherence: the patient–physician relationship, the patient's understanding of the disease and its treatment, patient's beliefs and perception of the disease and its treatment, and, importantly, the patient's willingness to actively participate in his/her treatment which has been shown to have a central position in the complex inter-relationship between all these factors [26]. Additionally, poor control of asthma despite therapeutic management may also be due, as previously mentioned [2,14], to resistance to treatment, difficulty for patients to recognize exacerbations and adjust medication, or underestimation of the disease severity by physicians with the consequence of underprescribing and inappropriate prescription of medication. As patients may overestimate levels of asthma control or the extent of improvement achieved with treatment, it is important for practitioners to identify patients with poorly controlled asthma in routine clinical practice [3,4]. Knowledge of factors associated with poorly controlled asthma should help physicians to identify patients with a high-risk of poor asthma control, and improve asthma management by implementing preventive measures with the greatest impact on asthma control. Furthermore, assessment tools, such ACT, should be useful for patients to assess for themselves their level of asthma control, as many patients have poorly or suboptimal controlled asthma and are probably often not aware that better control can be achieved.

The present study has some potential limitations. First, a large number of physicians participated to the ATHMOS study, including 76% of GPs, which is representative of asthma management in France. Even if no selection bias was led for participating physicians who were drawn at random, men were overrepresented in GPs in comparison to the national geographic distribution as it has been commonly reported in epidemiological studies [27]. The study was based on a relatively representative sample of French chest physicians and allergists. Second, our patient sample was probably biased toward the more severe asthma conditions. In the ATHMOS study, 95% of patients were already on GINA step 3 treatment. The number of patients treated with oral corticosteroids was quite low (3% of poorly controlled asthma patients) compared to the 28.5% of French asthmatic patients receiving oral corticosteroids evaluated in a French survey in 2006 [17]. Indeed,

history of asthma was longer and more severe in included patients than in those reported in register. Unfortunately, we were not able to compare their ACT scores as ACT scores were only reported by included patients in accordance with the protocol. A misinterpreting of the main study objective (“describe the level of asthma control using ACT in real life”) may have led the participant physicians to include patients with poorly controlled asthma. Another explanation should be that patients with a mild asthma (GINA step 1 and 2), especially those with intermittent asthma, are less assigned to integrated care pathways than patients with moderate or severe asthma. We can suppose that patients without any condition related to asthma or estimating to present well-controlled asthma did not want to participate in the study. Third, it was not possible to establish the temporal sequence between factors and asthma control, and consequently identify predictive factors of asthma control. The further analysis of follow-up data will probably permit to identify predictive factors of asthma control. Finally, this study provides an overview of asthma management in France in 2006–2007. Our findings cannot be extrapolated to asthma management in 2014.

5. Conclusions

More than half of asthmatic patients still had poorly controlled asthma in France during 2006–2007 despite guidelines for asthma control and available and effective current treatments. The ATHMOS study provides useful information on the characteristics of French asthmatic population and level of asthma control in real life during this period. Factors associated with poorly controlled asthma were emergency visit for exacerbation of asthma during the past three months, use of short-acting beta2-agonists or theophyllin, being professionally inactive (retired, unemployed or without any professional activity), being obese, presenting an atopic dermatitis, and being a woman.

These results should help physicians to identify patients with a high-risk of poorly controlled asthma and improve asthma management, determining the preventive measures with the greatest impact on asthma control.

Disclosure of interest

No conflict of interest was associated with this work. All authors contributed to conception and design of the study, analysis and interpretation of data, and participated in the preparation of the manuscript and approved its final form.

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