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To cite this article: Nicolas Roche MD, PhD, Céline Pribil MD, Philippe Devillier MD, PhD, Eric Van Ganse MD, PhD, Stéphane Schück MD, Johanna Doussaint PhD, Jennifer Martin MSc, Gaëlle Nachbaur MSc & Isabelle Boucot MD (2015): Limited treatment adaptation despite poor asthma control in asthma patients treated with inhaled corticosteroids, *Journal of Asthma*, DOI: [10.3109/02770903.2015.1065421](https://doi.org/10.3109/02770903.2015.1065421)

To link to this article: <http://dx.doi.org/10.3109/02770903.2015.1065421>



Published online: 29 Oct 2015.



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ORIGINAL ARTICLE

Limited treatment adaptation despite poor asthma control in asthma patients treated with inhaled corticosteroids

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Abstract

Objective: Current asthma guidelines recommend use of inhaled corticosteroids (ICS) in patients with persistent disease. This study was designed to investigate (1) the proportion of patients prescribed ICS-containing maintenance treatment who achieve asthma control, (2) determinants of control and (3) how physicians adapt treatment to the level of control. **Methods:** General practitioners (GPs) and chest physicians (CPs) in France recruited patients consulting for asthma and prescribed an ICS. Over a 2-year follow-up period, asthma symptoms in the previous 3 months and treatments prescribed were documented at each visit. Variables independently associated with asthma control were determined by multiple logistic regression. **Results:** Data were available for 924 patients recruited by GPs and 455 recruited by CPs. Asthma control was acceptable in only 24% of patients at inclusion, and in 33.6% at the last follow-up visit. Five factors were independently associated with asthma control: age (or time since diagnosis), gender, smoking status, allergic aetiology of asthma and treatment. Most patients (56.3%) were prescribed the same ICS dose regimen at the end of follow-up as at inclusion. The intensity of controller therapy had been increased in only 12.2% of patients unacceptably controlled at inclusion. **Conclusions:** Asthma was unacceptably controlled in most patients receiving ICS-containing maintenance treatment and remained so during follow-up. Despite this, treatment adaptations by GPs and CPs were very infrequent. This unsatisfactory situation may be improved by adopting a more dynamic approach to tailoring controller therapy to the needs of the patient.

Keywords

Asthma, asthma control, treatment adaptation, inhaled corticosteroids

History

Received 5 November 2014

Revised 22 May 2015

Accepted 20 June 2015

Published online 8 October 2015

Introduction

Therapeutic management of asthma involves controller therapy to prevent symptoms, exacerbations and lung function deterioration, combined with short-acting bronchodilators as needed to relieve symptoms. Treatment decisions are now based firstly on the level of asthma control assessed over a duration of a few weeks and secondly current treatment [1]. In clinical trials, it has been shown that the use of maintenance treatment, associated with appropriate monitoring, can allow the majority of patients to achieve guideline-defined asthma control [2]. Nonetheless, in daily practice, asthma control is only achieved in a minority of patients [3–7]. Several factors may contribute to the poor level of asthma control actually achieved, including inadequate evaluation of underlying disease severity, inappropriate treatment with respect to the

severity of the disease, smoking or exposure to other pollutants or to aeroallergens, obesity, comorbidities, poor inhaler technique and poor patient compliance [8–12]. Few data are available on the way physicians adapt treatment to poor control.

In the context of an initiative by the French health authorities to obtain information on the use and effectiveness of asthma treatments in everyday practice in France, we have performed a pharmacoepidemiological study of patients with asthma treated with ICS-containing maintenance therapy under conditions of everyday clinical practice. The objectives of the study were to describe the severity and control of asthma and the appropriateness of treatment in this specific population, to analyse potential associations between these three variables, to determine the factors associated with unacceptable asthma control, and to compare findings on the one hand between patients followed by primary care physicians and those followed by specialists and, on the other hand, between treatment categories. The study was also designed to follow the evolution of asthma control and treatment adaptations over time in the context of everyday care.

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Patients and methods

This was an observational pharmacoepidemiological study conducted in France. To cover the whole range of asthma care in the country, the study had two distinct settings, one in primary care and the other in secondary care. It should be noted that, in France, although patients are encouraged to visit specialists only when referred by their general practitioner (GP), they are also allowed to go directly to specialists. Accordingly, two independent physician panels were recruited, one of the GPs and one made up of chest physicians (CPs). Due to differences in the organisation of care between GPs and CPs, the two panels used partly different procedures for patient recruitment and data collection. However, collected data were analysed in the same way for both. The study comprised a cross-sectional phase and a longitudinal phase with 2 years of follow-up. Patients were recruited and followed from May 2004 to March 2007 for the GP panel and between September 2005 and April 2009 for the CP panel.

Participating physicians

For the GP panel, the study was performed by physicians belonging to the Thalès network. This is a computerised network of 1200 GPs who collect exhaustive anonymous data on patient consultations and prescriptions. GPs participating in the Thalès network are representative of the French GP population according to geographical area, age and gender. Activity and prescription habits of the panel have been shown to be comparable with national data [13]. The database currently includes records for >1.6 million patients, routinely collected since 2002. For the study, 881 GPs were selected at random from the 1200 panel members and invited to participate in the study. Of these, 418 agreed to take part. For the CPs, 153 of the hospital- and community-based CPs identified from a national database (CEGEDIM database) agreed to take part in the study.

Patients

Eligibility criteria were identical in both panels. Patients who had consulted at least twice in the previous year, who were aged at least 15 years and who had received a prescription for an ICS in the previous 6 months were eligible. Patients with a diagnosis of COPD, chronic bronchitis, occupational pulmonary disease or emphysema were excluded. Given the marked difference in the mean number of patients with asthma followed by GPs and CPs and the target patient numbers for each cohort, the recruitment strategy differed between the two cohorts.

For the GP cohort, participating physicians were expected to recruit all patients identified in the Thalès database as having consulted for asthma or having been prescribed an asthma therapy (class R03 in the World Health Organization Anatomical Therapeutic Chemical classification) in the 3 years preceding the study and who fulfilled the eligibility criteria. When one of these patients consulted their GP for whatever reason, the Thalès database automatically triggered the display of the study questionnaire on the GP's computer screen. The CPs were expected to recruit all

patients consulting for asthma and who fulfilled the eligibility criteria.

Data collection

At the inclusion visit, demographic data as well as treatment history were collected from the patient records. Data on current symptoms, disease history, tobacco use, atopic status and current treatments were documented in the study questionnaire. In addition, the physician measured peak expiratory flow rate (PEF), as well as forced expiratory volume in one second (FEV1) in the CP panel only. At each consultation during the 2-year follow-up, current symptoms, lung function and treatment were documented.

Assessment of asthma control

Asthma control was determined at each visit. The present analyses focus on the inclusion and last follow-up visits in order to assess evolution of asthma control over the 2-year follow-up. Asthma control was defined using the guidelines published by the French National Health Authorities (ANAES) in 2004 [14], themselves derived from earlier Canadian asthma guidelines [15] and close to the subsequent GINA guidelines [1,16]; these definitions are compared in Table 1. Since it was not possible to document the "best possible compromise" that contributes to the definition of optimal control in the ANAES guidelines, we have only considered two levels of asthma control (acceptable or unacceptable).

Asthma medications prescribed at inclusion and at the follow-up visit preceding the last one were classified as described in Table 1. Treatment modifications were classified by change in treatment intensity into "step-up" (e.g. addition of another controller therapy or increase in ICS dose), neutral (e.g. switch from one ICS to another at equivalent dose) or "step-down" (e.g. reduction in ICS dose) as described in Table 1.

Statistical analysis

Data are described using means and standard deviations for quantitative variables and percentages for categorical variables. Asthma control comparisons between the GP and CP patient cohorts and between treatment groups were performed using the χ^2 test or Fisher's exact test for categorical variables and the Wilcoxon test or Student's *t*-test for continuous variables. Missing data were not replaced. All analyses were performed using SAS[®] software (Cary, NC) Version 9.1. Recruitment was stopped when a sufficient number of patients had been enrolled to describe the key outcome variables with a precision of <5%.

Factors associated with asthma control at the last follow-up visit in the study were identified by multivariate regression analysis in both panels combined. The type of treating physician was entered into the multivariate analysis to determine whether this was independently associated with asthma control. In a first step, baseline demographic, clinical and treatment variables were transformed into categorical variables (if this was not already the case) and evaluated for association with the level of asthma control

Table 1. Definitions of asthma control and treatment.

Definition of asthma control	ANAES 2004	GINA 2014
Daytime symptoms	<4 days/week	≤2 times/week
Night-time symptoms	<1 night/week	None
Physical activity	Normal	No limitations
Use of short-acting β ₂ -agonists	<4 doses/week	Twice or less a week
Exacerbations	Mild or infrequent	Twice or less a week
Absence from work or school	None	
FEV1 or PEF	>85% of personal best ^a	
Optimal control ^b /Controlled ^c	All parameters normal ^d	All of the above fulfilled
Acceptable control ^b /Partially controlled ^c	All of the above fulfilled ≥1	1 or 2 of the above in any week
Unacceptable control ^b /Uncontrolled ^c	criterion not met	3 or 4 of the above in any week
Classification of controller therapy		
No controller therapy	Untreated or only prescribed rescue medication (RM)	
ICS alone	Inhaled corticosteroids (ICS) as the only controller therapy prescribed	
ICS + LABA	ICS + LABA (long-acting β-agonists) prescribed as controller therapy	
ICS + OCT ^e	ICS and any another class of controller therapy (OCT) other than a LABA	
ICS + OCT ^e + LABA	ICS + LABA and another controller therapy (OCT)	
OCT ^e only	An OCT as the only controller therapy ^f	
Classification of changes in controller therapy		
No change	Identical asthma therapy prescription at inclusion and at penultimate follow-up visit	
Step-up	Increase of ICS dose (same or different ICS) from low to intermediate or high dose or from intermediate to high dose ^g	
	Addition of another OCT or a LABA	
Step-down	Discontinuation of ICS	
	Reduction of ICS dose (same or different ICS) from high to intermediate or low dose or from intermediate to low dose ^g	
	Discontinuation of another OCT or a LABA	
Neutral	Any other change to asthma controller therapy	
Classification of corticosteroid dose		
Low	200–500 µg beclomethasone equivalents	
Intermediate	>500–1000 µg beclomethasone equivalents	
High	>1000–2000 µg beclomethasone equivalents	

Criteria for asthma control are compared between those proposed by the French health authorities (ANAES 2004) [14] and the Global Initiative for Asthma (GINA 2015) [1].

^aOr predicted if personal best not available.
^bANAES terminology.
^cGINA terminology.
^dOr the best possible compromise achieved between level of control, treatment acceptability and adverse events.
^eThe “other controller therapy” (OCT) group includes theophylline, montelukast and omalizumab.
^fWith or without LABA.
^gAs defined in the GINA guidelines [17].

using univariate analysis. Those variables showing an association at a probability level of <0.25 were then entered into a descending stepwise multivariate regression analysis to identify variables independently associated with asthma control. The criterion to be retained at each iteration of the stepwise model was association with control at a probability threshold of 0.05. The retained variables were entered into a final model in order to generate odds ratios with their 95% confidence intervals (95% CI). The robustness of the model was assessed with the Hosmer–Lemeshow test and its predictive power by calculation of the area under the receiver operating characteristics (ROC) curve.

Ethics

The study was performed in accordance with the Declaration of Helsinki, Good Epidemiological Practice and relevant national guidelines. All patients provided informed consent before inclusion. The survey protocol was approved by the National Advisory Committee on Medical Research Information and the Commission Nationale de L’informatique et des Libertés, the French national data protection agency.

Results

Participants

Study flow charts are provided in Figure 1. For the GP panel, 319 of the 418 network GPs who agreed to participate in the study (76.3%) included at least one patient. Of the 6048 patients in the Thalès database who had consulted a participating GP for asthma in the previous 3 years, 924 patients with adequate follow-up data could be analysed (82.8% of included patients). The mean follow-up duration was 19 ± 5 months. Compared to other eligible but non-participating patients in the database, patients included in the study were somewhat older (mean age: 53 years versus 50 years; *p* < 0.0001) and were less frequently considered to have severe asthma by their physician (9.2% versus 16.3%; *p* < 0.0001). For the CP panel, 67 (43.8%) of the 153 CPs who agreed to participate in the study, included at least one patient. Overall, 577 patients were included by the CPs, of whom 455 were analysable and constituted the study population. These patients were followed for a mean duration of 20 ± 6 months.

The demographic and clinical characteristics of patients included in the two panels are presented in Table 2.

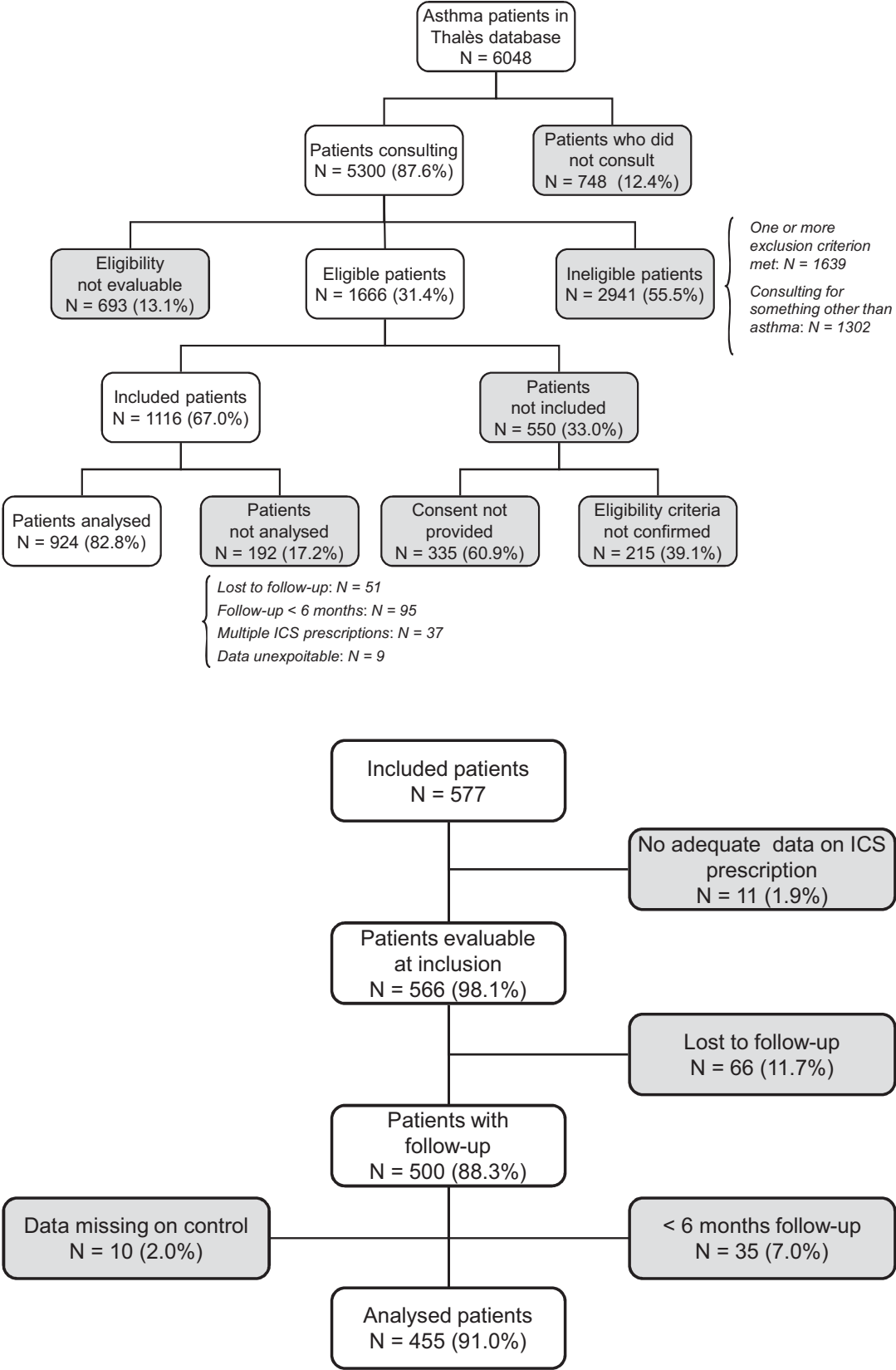


Figure 1. Patient flow diagram. Top: GP panel; bottom: CP panel. Percentages are calculated with respect to the preceding line on the flow diagrams.

The patients in the GP panel were older than those in the CP cohort, had more recent onset of disease and were more likely to be current smokers. Patients in the CP panel consulted their CP less frequently, had atopic asthma more often, had more frequent asthma symptoms and their asthma was more frequently rated as severe by their physician. In addition, the proportion of patients who were hospitalised, reported emergency visits or who took days off work for their asthma was higher in the CP panel.

Table 2. Patient characteristics at baseline.

	GP panel (N = 924)	CP panel (N = 455)	Total (N = 1379)	p*
Gender				
Men	393 (42.5%)	173 (38.0%)	566 (41.0%)	0.12
Women	531 (57.5%)	282 (62.0%)	813 (59.0%)	
Age				
Mean ± SD	53.6 ± 18.8	48.6 ± 17.6	52.0 ± 18.5	<0.0001
Age at disease onset				
Mean ± SD	35.4 ± 20.7	29.5 ± 18.9	33.5 ± 20.3	<0.0001
Before age of 15	198 (21.5%)	123 (28.0%)	321 (23.6%)	
Disease duration				
Mean ± SD	18.2 ± 14.0	19.0 ± 14.2	18.5 ± 14.1	0.32
Consultations per year (N)				
Mean ± SD	4.6 ± 2.4	2.5 ± 0.9	3.9 ± 2.3	<0.0001
Smoking				
Current smoker	154 (16.7 %)	37 (8.1%)	191 (13.9%)	<0.0001
Atopic asthma	479 (51.8%)	312 (69.3%)	791 (57.6%)	
Severity grade assessed by the physician				
Intermittent	386 (41.8%)	56 (12.8%)	442 (32.5%)	<0.0001
Mild persistent	305 (33.0%)	132 (30.3%)	437 (32.1%)	
Moderate persistent	200 (21.6%)	165 (37.8%)	365 (26.8%)	
Severe persistent	33 (3.6%)	83 (19.0%)	116 (8.5%)	
Frequency of daytime symptoms				
At least once a week	637 (68.9%)	259 (57.2%)	896 (65.1%)	<0.0001
2–6 days a week	208 (22.5%)	118 (26.0%)	326 (23.7%)	
Once a day	61 (6.6%)	50 (11%)	111 (8.1%)	
Several times a day	18 (1.9%)	26 (5.7%)	44 (3.2%)	
Frequency of nocturnal symptoms				
Less than twice a month	758 (82.0%)	342 (75.5%)	1100 (79.9%)	0.02
2–4 nights a month	87 (9.4%)	60 (13.2%)	147 (10.7%)	
More than once a week	79 (8.5%)	51 (11.3%)	130 (9.4%)	
Impact on activities of daily living				
None	433 (46.9%)	167 (36.8%)	600 (43.5%)	<0.0001
Occasional	417 (45.1%)	214 (47.1%)	631 (45.8%)	
Prominent	74 (8.0%)	73 (16.1%)	147 (10.7%)	
Asthma-related events during previous 3 months				
Hospitalisation	9 (1.0%)	21 (4.6%)	30 (2.2%)	<0.0001
Emergency department stay	14 (1.5%)	14 (3.1%)	28 (2.0%)	0.08
Absenteeism	5 (0.5%)	32 (7.2%)	37 (2.7%)	<0.0001
PEF or FEV1 above predicted value (%)				
≥80%	417 (47.3%)	240 (54.1%)	657 (49.6%)	0.01
[60–80%]	272 (30.9%)	135 (30.4%)	407 (30.7%)	
≤60%	192 (21.8%)	69 (15.5%)	261 (19.7%)	

Data were missing for certain variables in a small number of patients (<20 in either panel, except for PEF/FEV1 which was missing in 43 patients in the GP panel and 11 in the CP panel). Percentages are calculated excluding patients for whom data was missing.

*Comparison between GP and CP panels (χ^2 test for categorical variables and Student's *t*-test for continuous variables).

Treatments

At inclusion, the ICS most frequently prescribed were fluticasone propionate (46.7%), followed by budesonide (35.5%) and beclometasone (17.8%), with no significant difference in prescription patterns between the GP and CP panels. The majority of patients (63.8%) were prescribed ICS in the form of a fixed combination with a LABA (fluticasone propionate + salmeterol or budesonide + formoterol) and the majority were receiving a medium dose of ICS (44.0%). Since the fixed association of beclometasone and formoterol was only licensed in France in 2007, no patients were thus using this treatment at inclusion and only two patients in the CP group were switched to this treatment during the follow-up period. CPs more frequently prescribed ICS + LABA combinations than did GPs (88.6% versus 80.4%; $p = 0.001$) and more frequently prescribed ICS at high doses (42.2% versus 35.5%; $p = 0.009$). At the last follow-up visit, 56.9% of patients in the GP panel and 60.4% of those in the CP panel were receiving the same ICS at the same dose as at inclusion,

13.7% and 35.2%, respectively ($p < 0.0001$), had changed the dose or switched to another ICS, and 29.3% and 4.4%, respectively ($p < 0.0001$), were no longer being prescribed an ICS. The treatments that the patients were being prescribed when they consulted for the last follow-up visit are listed in Table 3. The majority were receiving an ICS + LABA combination (56.5%). Other controller treatments included principally montelukast (the only leucotriene receptor antagonist marketed in France, $N = 286$), slow-release theophylline ($N = 74$) and omalizumab ($N = 12$).

Asthma control

At inclusion, 332 patients were considered acceptably controlled, corresponding to 224 patients in the GP panel (24.2% [95% CI: 21.6–27.1%]) and 108 in the CP panel (24.0% [20.3–28.2%]). At the last follow-up visit, this number had risen to 463 patients, 316 (34.2% [31.2–37.3%]) in the GP panel and 147 (32.3% [28.2–36.7%]) in the CP panel. However, only 173 patients were acceptably controlled both

Table 3. Inhaled corticosteroid prescription and asthma control at the last follow-up visit.

	GP panel (N = 924) Prescribed	CP panel (N = 455) Prescribed	Total (N = 1379) Prescribed
No controller therapy	62 (6.7%)	6 (1.3%)	68 (4.9%)
ICS alone	137 (14.8%)	42 (9.2%)	179 (13.0%)
ICS + LABA	520 (56.3%)	259 (56.9%)	779 (56.5%)
ICS + OCT	22 (2.4%)	9 (2.0%)	31 (2.2%)
ICS + OCT + LABA	160 (17.3%)	135 (29.7%)	295 (21.4%)
OCT only	23 (2.5%)	4 (0.9%)	27 (2.0%)

ICS, inhaled corticosteroids; LABA, long-acting β -agonists; OCT, other controller therapy.

at inclusion and at follow-up, 109 (11.8% [9.9–14.0%]) in the GP panel and 64 (14.1% [11.2–17.6%]) in the CP panel). Overall, 288 patients (GP: $n = 207$, 22.4% [19.8–25.2%]; CP: $n = 81$, 17.8% [14.6–21.6%]) who were unacceptably controlled at inclusion achieved acceptable control at the last follow-up visit, and 159 patients (GP: $n = 115$, 12.4% [10.5–14.7%]; CP: $n = 44$, 9.7% [7.3–12.7%]) who were acceptably controlled at inclusion were no longer controlled at the last follow-up visit.

Figure 2 shows the evolution of asthma control as a function of the treatment strategy between baseline and last follow-up. The rate of treatment step-up was similar in patients who were unacceptably controlled at inclusion and in those who were acceptably controlled. In the GP panel, but not the CP panel, patients whose treatment intensity had been stepped up were more frequently acceptably controlled at the last follow-up visit than those whose treatment intensity had been stepped down, or left at the same level.

Variables associated with asthma control

Demographic and clinical characteristics for patients achieving or not achieving acceptable asthma control at the last follow-up visit in the GP and CP panels (univariate analysis) are presented in Table 4. Factors associated with asthma control in one of the panels or both combined were gender, age, duration of disease, atopic asthma, smoking status, asthma severity and treatment prescribed at the last follow-up visit.

The variables identified in the univariate analyses were entered into the logistic regression analysis with the exception of asthma severity as assessed by the physician. Asthma severity was excluded due to the strength of its association with asthma control ($p < 0.0001$), the criteria used to define asthma control being the same as those used to define asthma severity, although the time-frame of assessment is different. Similarly, for the principal analysis, treatment was not entered into the model since it was considered to be an extrinsic determinant of asthma control. However, a sensitivity analysis was performed in which treatment was included in the logistic regression. Since age at last follow-up visit, time since diagnosis and age at diagnosis were inter-related, only the variable showing the strongest association with asthma control in the univariate analysis (time since diagnosis) was included in the multivariate analysis.

In the multivariate analysis of the two panels combined, four variables were associated with acceptable asthma

control, namely male gender, atopic asthma, not smoking and a short duration of illness (Table 5). The fit to the data was good (Hosmer–Lemeshow test: $p = 0.87$) but the predictive power limited (area under the ROC curve: 0.574). A sensitivity analysis was performed in which treatment prior to the last follow-up visit was also entered into the multivariate analysis, which indicated that patients not prescribed any controller therapy were less likely to achieve acceptable control than patients prescribed ICS and LABA (OR: 0.41 [95% CI: 0.22–0.78]).

Discussion

The principal finding of this observational study was that asthma control in patients treated with ICS was poor and remained so during follow-up, with only one quarter of patients at inclusion and one third at the last follow-up visit being acceptably controlled. Most importantly, although asthma control was not stable over time, treatment was seldom modified. Of the patients who were acceptably controlled at inclusion, only half remained so at the last follow-up visit. In both panels, only 11% of patients were acceptably controlled at both inclusion and last follow-up visit. Independent determinants of control were time since diagnosis, smoking status, gender, atopic status and treatment step.

A similar low level of asthma control has been reported in several recent studies elsewhere in Europe and in North America, using various definitions of asthma control [3,4,6,7]. Our study focused on a specific population of patients prescribed ICS alone or combined with other controller therapy. These treatments are primarily used in patients with persistent asthma, who are by definition more difficult to control than those with intermittent disease. Our data can be compared with those of the INSPIRE study [6], an international study conducted in 2004–2005, in which telephone interviews were conducted with 3415 adults with asthma prescribed regular maintenance therapy with ICS or ICS plus LABA to collect data on asthma symptoms and treatment. In this study, 74% of interviewees required rescue medication with short-acting β_2 -agonists daily, 51% required medical intervention due to an exacerbation and only 28% were classified as well-controlled with the Asthma Control Questionnaire (ACQ). These findings in patients prescribed controller therapy are very consistent with ours.

We did not observe any significant difference in the level of control between patients who were followed by CPs and those followed by GPs. This finding is at first sight surprising, since the two cohorts differed in terms of frequency of symptoms and lung function (PEF or FEV1), as well as in a number of characteristics that are associated with asthma control such as smoking status and atopy. One explanation could be that, although the frequency of each individual symptom criterion used to define poor control is higher in CP patients, the between-group differences are not of great magnitude. In addition, these symptom criteria probably covary and thus may not be independent determinants of control. Additionally, although patients in the CP group were more symptomatic, their FEV1 or PEF was more often $>80\%$, suggesting that these two components of control (symptoms

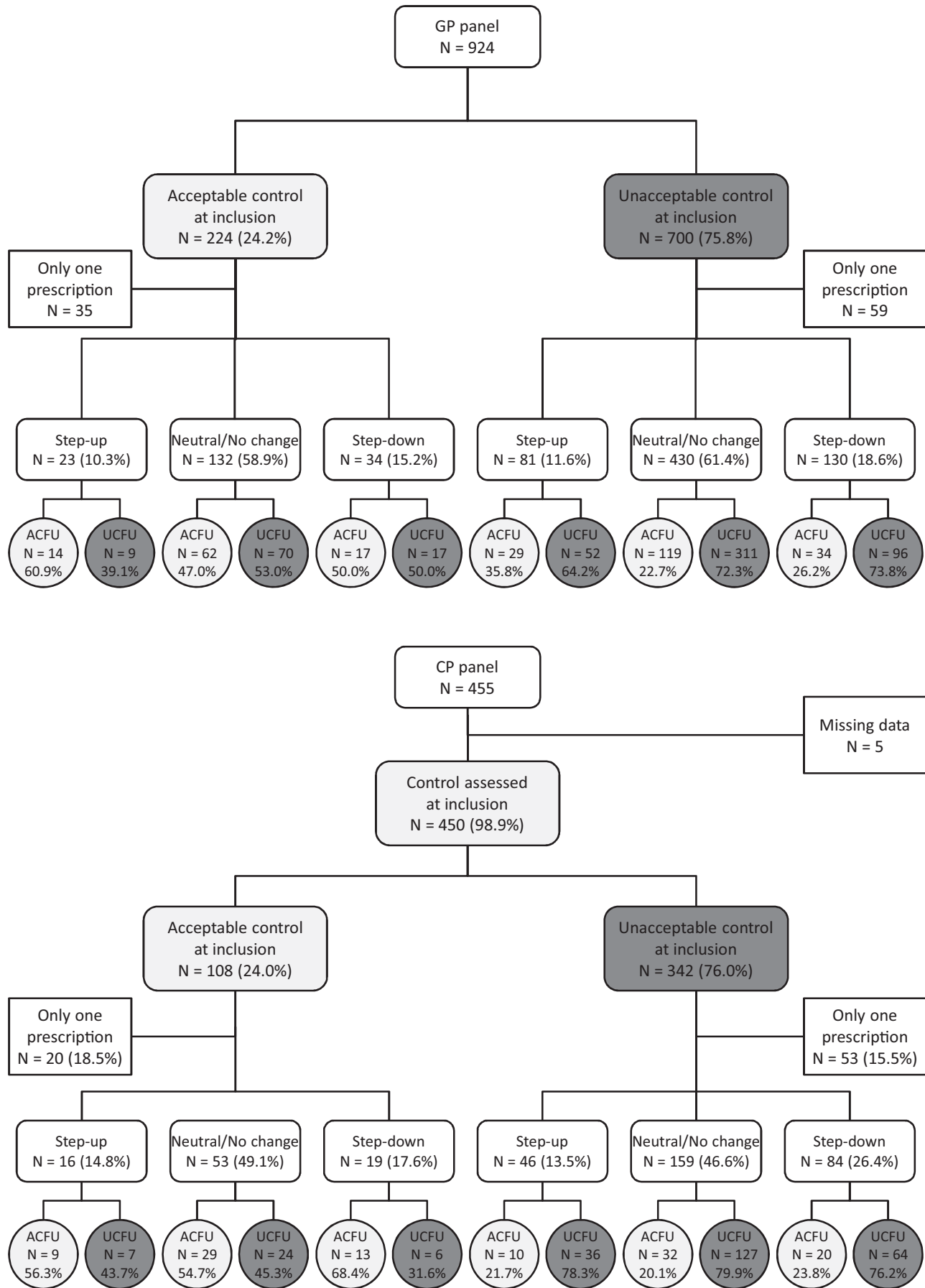


Figure 2. Treatment trajectories as a function of level of asthma control at inclusion. Treatment changes (step-up, step-down, neutral or no change) are defined in Table 2. ACFU, acceptable control at follow-up; UCFU, unacceptable control at follow-up. Top: GP panel; Bottom: CP panel. ¹It was not possible to determine asthma control at inclusion in these subjects, due to missing data on certain symptoms or on spirometry.

Table 4. Asthma control as a function of demographic and clinical variables at last follow-up.

Study variable	GP panel (N=924)			CP panel (N=455)		
	Acceptable (N=316)	Unacceptable (N=608)	p	Acceptable (N=147)	Unacceptable (N=308)	p
Gender						
Men	143 (45.3%)	250 (41.1%)	0.23	64 (43.5%)	109 (35.4%)	0.09
Women	173 (54.7%)	358 (58.9%)		83 (56.5%)	199 (64.6%)	
Age						
16–39 years	61 (19.3%)	130 (21.4%)	0.07	51 (34.7%)	70 (22.7%)	0.03
40–64 years	144 (45.6%)	230 (37.8%)		66 (44.9%)	164 (53.2%)	
65 years or older	111 (35.1%)	248 (40.8%)		30 (20.4%)	74 (24.0%)	
Age at diagnosis						
Before age of 15	59 (18.7%)	139 (22.9%)	0.04	42 (30.0%)	81 (27.1%)	0.89
15–29 years	67 (21.2%)	108 (17.8%)		33 (23.6%)	74 (24.7%)	
30–49 years	114 (36.1%)	178 (29.3%)		38 (27.1%)	89 (29.8%)	
50 years or older	76 (24.1%)	182 (30.0%)		27 (19.3%)	55 (18.4%)	
Disease duration						
Less than 5 years	28 (8.9%)	48 (7.9%)	0.51	16 (11.4%)	22 (7.4%)	0.06
5–10 years	54 (17.1%)	89 (14.7%)		29 (20.7%)	43 (14.4%)	
10 years or more	234 (74.1%)	470 (77.4%)		95 (67.9%)	234 (78.3%)	
Number of consultations						
Less than two	20 (6.3%)	28 (4.6%)	0.17	37 (25.2%)	83 (26.9%)	0.50
Two to four	144 (45.6%)	251 (41.3%)		104 (70.7%)	205 (66.6%)	
Four or more	152 (48.1%)	329 (54.1%)		6 (4.1%)	20 (6.5%)	
Current smoker at inclusion	39 (12.3%)	115 (18.9%)	0.01	11 (7.5%)	26 (8.4%)	0.74
Atopic asthma	181 (57.3%)	298 (49.0%)	0.02	106 (74.1%)	206 (67.1%)	0.13
Severity at last follow-up						
Intermittent	270 (85.4%)	427 (70.2%)	NA	86 (58.5%)	25 (8.2%)	<0.0001
Mild persistent	30 (9.5%)	66 (10.9%)		41 (27.9%)	92 (30.1%)	
Moderate persistent	16 (5.1%)	92 (15.1%)		13 (8.8%)	121 (39.5%)	
Severe persistent	0 (0%)	23 (3.8%)		7 (4.8%)	68 (22.2%)	

NA, not available, since there were no patients in some control × severity subgroups.

Table 5. Multivariate logistic regression analysis of variables associated with acceptable asthma control in the GP and CP panels combined.

Study variable	Odds ratio [95% CI]	p
Gender		
Women	1	0.03
Men	1.29 [1.02–1.62]	
Time since diagnosis		
More than 10 years	1	0.04
5–10 years	1.37 [1.01–1.86]	
Less than 5 years	1.46 [0.97–2.17]	
Atopic status		
Non-atopic	1	0.006
Atopic	1.39 [1.10–1.75]	
Smoking status		
Current smoker	1	0.03
Non-smoker or ex-smoker	1.46 [1.03–2.07]	

Data were analysed for the 1359 patients for whom data on all variables entered into the model were available. Treatment class was not entered into this model.

and lung function) could influence control in opposite directions. Regarding risk factors that influence control, atopy and smoking status were associated with asthma control in the multivariate logistic regression. On the one hand, atopic asthma (associated with more frequent acceptable control) was reported in fewer patients in the GP panel (52%) than in the CP panel (69%) and there were more current smokers in the GP panel (17% versus 8%). These differences would be expected to lead to a lower rate of acceptable control in the GP panel. On the other hand, patients with moderate to severe

asthma were more frequently represented in the CP panel, which would be expected to lead to better control in the GP panel. It is thus possible that differences in exposure to risk factors and differences in underlying asthma severity may have counterbalanced each other and their contributions to asthma control may have cancelled each other out.

Treatment represents a major modifiable determinant of asthma control. Current treatment guidelines [1] specify that asthma control should be reassessed regularly and treatment adjusted as necessary, i.e. increased when control is not acceptable and decreased to the minimal effective strategy when control is obtained and maintained. In the present study, there was little evidence that such a treatment-to-target strategy was being followed in everyday practice. In spite of the fact that most patients experienced unacceptable control of their asthma, the dose or kind of treatment was only modified between inclusion and the last follow-up in 13.7% of patients cared for by GPs and 34.6% of patients cared for by CPs. Moreover, 29.3% of patients in the GP panel were no longer being prescribed an ICS at the end of their participation in the study. In particular, treatment intensity was stepped up in only around ten percent of patients with unacceptable control, and this occurred no more frequently than in those with acceptable control. This lack of treatment adaptation may contribute to the persistently poor control observed in the two patient cohorts. Thus, there is clearly a need to evolve towards a more dynamic treatment strategy, particularly in primary care, whereby physicians regularly evaluate the control of their patients' asthma and adapt treatment as necessary.

This study has a number of limitations. The participating CPs and, to a lesser extent participating GPs, may not be representative of all physicians treating asthma in France. Since participation was voluntary and unremunerated, it is possible that participants were more motivated or interested by asthma and its treatment than non-participants and may have had different, perhaps more appropriate, prescribing habits than non-participants. This may limit the extent to which the findings may be generalised to all asthma care. Since this was an observational study, the duration and frequency of follow-up varied between patients and some of them (4.6% in the GP panel and 11.7% in the CP panel) did not return for a follow-up visit at all, and thus were excluded from the analysis. Finally, three known modifiable risk factors for unacceptable asthma control, namely obesity, poor medication adherence and poor inhalation device technique, were not evaluated in our study.

One methodological feature of our study deserves particular mention, relating to the definition of asthma control used as the primary outcome measure. This was based on the ANAES 2004 criteria, which are different from the GINA 2008 or 2014 classification, currently regarded as the gold standard. The rationale for this choice as the primary outcome measure was that, at the time the study started, this was how French physicians were recommended to assess asthma control in national practice guidelines. Despite the differences between the ANAES and GINA criteria, and in their respective thresholds for asthma control, we believe our results remain pertinent for two reasons. First, the ANAES criteria for control are less strict than the GINA criteria and thus the already high proportion of patients who are poorly controlled according to the ANAES criteria, is probably an underestimate with respect to the GINA criteria. For this reason, our principal message of a very high frequency of insufficient control remains relevant. Second, even if thresholds or scoring methods differ, all asthma control definitions provide satisfactory ways of discriminating between controlled and uncontrolled patients and for identifying risk factors associated with poor control.

Conclusions

Disease control was inadequate in the majority of patients receiving ICS for the treatment of their asthma, regardless of whether they were followed in primary or secondary care. The proportion of unacceptably-controlled patients whose treatment was modified was low. This unsatisfactory situation may be improved by adopting a more dynamic approach to adapting controller therapy to the needs of the patient.

Acknowledgements

The authors would like to express their thanks to Professor Françoise Neukirch, Epidemiology of Respiratory Diseases Unit, INSERM U700, Xavier Bichat School of Medicine, Paris, France and to the late Professor Philippe Godard, Respiratory Medicine Department, Hôpital Arnaud de Villeneuve, CHU Montpellier, France for their invaluable advice and insight into the design, implementation and interpretation of this study.

Declaration of interest

N.R., P.D. and E.V.G. were members of the study steering committee, for which they received honoraria from GlaxoSmithKline. N.R. has received grants, funding, honoraria, speaker fees or consultancy fees from Aerocrine, Almirall, Astra-Zeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Meda Pharma, MundiPharma, Novartis, Takeda-Nycomed, Pfizer, Roche and Teva. P.D. has received honoraria, speaker fees and consultancy fees from GlaxoSmithKline, Astra Zeneca and Chiesi, honoraria from Takeda-Nycomed and is an advisory board member for Chiesi and Takeda-Nycomed. E.V.G. has received consultancy fees from Astra-Zeneca and Boehringer Ingelheim, grants or funding from Boehringer Ingelheim and Pfizer and honoraria from Astra-Zeneca and Chiesi. I.B., G.N. and C.P. are employees of GlaxoSmithKline. S.S., J.M. and J.D. are employees of Kappa Santé, the contract research organisation mandated by GlaxoSmithKline for the implementation of the study. This study was funded by Laboratoire GlaxoSmithKline, manufacturer of fluticasone propionate and beclometasone, inhaled corticosteroids (ICS) used in the treatment of asthma, as well as several bronchodilators. The funding source, together with the steering committee, and in close coordination with the French health authorities designed the study. Operational management of the study and data analysis were subcontracted to Kappa Santé, an independent contract research organisation. The funding source, together with the steering committee and Kappa Santé, were responsible for the interpretation of the findings and preparation of the study report and the present article.

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