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Four seasons of Czech asthma study: asthma characteristics and management reality in the Czech Republic

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ABSTRACT

Objective: To describe the characteristics and management of asthma in clinical practice in the Czech Republic in the context of international guidelines and clinical realities.

Methods: Data were collected over four seasons from summer 2016 to spring 2017 and are mostly presented using descriptive statistics.

Results: We obtained valid data for 4557 adult patients with asthma, including detailed phenotyping (71% eosinophilic allergic, 10% eosinophilic non-allergic, 19% non-eosinophilic non-allergic asthma) from 58 allergologists and 56 pulmonologists. The average time to diagnosis was 3 years. In more than half of the subjects, bronchodilator testing (BDT) results were available at primary diagnosis. More than 10% of physicians did not test for mold allergy. Occupational asthma was diagnosed in 0.7% of subjects. According to the attending physician, 68% of patients had well-controlled and 10% had uncontrolled asthma. Ninety-four percent of patients were on preventive treatment, with 91% using an inhaled corticosteroids (ICS) at an average dose of 705 µg/day budesonide equivalent. Approximately 75% of patients were on an ICS/LABA, with 91% using fixed combinations. Among patients using ICS/formoterol, a maintenance and reliever therapy regime was prescribed in 67%.

Conclusions: The quality of asthma management in the Czech Republic is comparable to that of other developed countries and better in some respects (frequent BDT, phenotyping, and use of preventive treatment). Nevertheless, there is unnecessary delay in diagnosis and lack of research on possible environmental causes (workplace, molds). Pharmacotherapy shows good adherence to guidelines. Although 10% of patients show poor control, there is concurrently a trend for overtreatment.

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Introduction

Asthma represents a major global health problem and economic burden. Despite development of effective therapies with a potential to achieve full disease control in more than 95% of patients, most epidemiological studies from developed countries report a significant proportion of patients with inadequate control (1–5). This may be due to multiple reasons and related to geographical, cultural, social, political, economic, and health-care system characteristics of the countries such as differences in access to primary care and specialists, quality and priorities of care including drug availability, and existence and content of national guidelines (2,5–8). The above factors vary across nations, resulting in different asthma prevalence and characteristics and heterogeneous levels of

diagnostic and therapeutic management, closely linked to the level of control achieved.

A detailed analysis of common clinical practice in asthma care in the Czech Republic has not yet been performed. Therefore, the Czech Initiative for Asthma (CIPA), the local partner of the Global Initiative for Asthma (GINA), together with the Czech Society for Allergy and Clinical Immunology (CSAKI) and Czech Society of Pulmonology and Phthisiology (CPFS), initiated a multicentric, observational, cross-sectional study involving the clinical practice of pulmonologists and allergologists. The main aim of the study was to obtain representative data that could be used by professional medical societies in negotiations with national authorities and would provide background for future modifications of the national asthma

guidelines. The healthcare system and clinical practice in the Czech Republic can be described as follows: (a) patients have a free choice to seek treatment from a general practitioner or specialist, (b) most patients with asthma are treated by pulmonologists and allergologists (8,9), with unlimited access to lung function testing, measurement of fractional exhaled nitric oxide (FeNO), and skin prick testing or specific IgE investigation; (c) during the years 1999–2003, CIPA initiated a major educational activity targeting both general practitioners and pediatric general practitioners with a goal to disseminate GINA guidelines and emphasize the concept of long-term preventive treatment as a mainstay of asthma pharmacotherapy; (d) there are national guidelines that follow GINA guidelines, and recommend assessing eosinophilia and allergy in each patient (10,11); (e) for severe asthma, all treatment options (including biological therapy and bronchial thermoplasty) are available through the network of National Centers for Severe Asthma (NCSA; www.tezke-astma.cz) (12); and (f) the national health insurance system covers most of the asthma treatment costs.

In this article, we discuss the (i) characteristics of the adult asthma population in the Czech Republic, including their phenotype based on the presence of eosinophilia, allergy, and frequency of specific sensitization types and (ii) quality of the diagnostic process and therapeutic reality and their comparison with current national and international guidelines and findings in other developed countries.

Methods

Study design, population, and data collection (sampling)

This epidemiological, multicentric, non-interventional, observational, and cross-sectional study was conducted with patients ≥ 18 years of age treated for asthma in the outpatient specialist care sector (allergologists and pulmonologists) throughout the Czech Republic. The study was approved by the State Institute for Drug Control and the appropriate Ethics Review Board. Informed consent was not required for this study.

At the beginning of 2016, all office-based specialists (allergologists and pulmonologists) were invited via e-mail to participate in the study. A total of 5000 patients was the planned sample size. The number of questionnaires sent to individual participating physicians was calculated based on the density of the patient population in the physician's regions and the

regional distribution of respiratory specialists (pulmonologists and allergologists).

Data were collected in four rounds covering each season from summer (June) 2016 to spring (April) 2017. During each season, unselected sequential data collection from a given number of patients with asthma was performed for no more than 10 days, regardless of the reason for the visit. Each patient underwent clinical examination including spirometry (preferably pre-bronchodilator); additionally, some patients underwent FeNO testing. Questionnaires (see below) were filled with current clinical data and targeted medical history. Physicians completed a major part of the questionnaires, whereas nurses filled in the demographic and basic clinical data and issued the asthma control test (ACT) questionnaire to the patients. The patients completed the ACT in the waiting room before assessment by the physician. The physicians were blinded to the ACT scores during the appointment and at the time of patient data entry. The ACT scores were entered after completion of all other data.

The questionnaire used comprised three groups of questions addressing: (i) demographic and socioeconomic characteristics of patients and their comorbidities, (ii) disease history and recent clinical data describing detailed asthma characteristics and the quality of the diagnostic process, and (iii) recent clinical data related to therapy, adherence to therapy, and level of asthma control.

The demographic data also included the degree of education (higher level = full secondary school and university). Furthermore, we evaluated the effect of selected demographic variables (smoking status, pet ownership) on patient's asthma status at present and at the time of disease onset. Comorbidities assessed included obesity, nonsteroidal anti-inflammatory drugs (NSAID) intolerance, and coincidence with chronic obstructive pulmonary disease (COPD) [Asthma COPD overlap syndrome, ACO(S)].

Asthma severity was determined by the physicians using the previous GINA severity classification scheme retained in the Czech national guidelines (minimal level of pharmacotherapy needed to obtain full control of asthma) (11,13). The Czech national guidelines define three clinically relevant asthma phenotypes: (i) eosinophilic allergic ("atopic") asthma, (ii) eosinophilic non-allergic asthma, and (iii) non-eosinophilic non-allergic asthma. The three-step diagnostic algorithm for these phenotypes is shown in Figure 1. In patients with allergies, a detailed sensitization profile was confirmed.

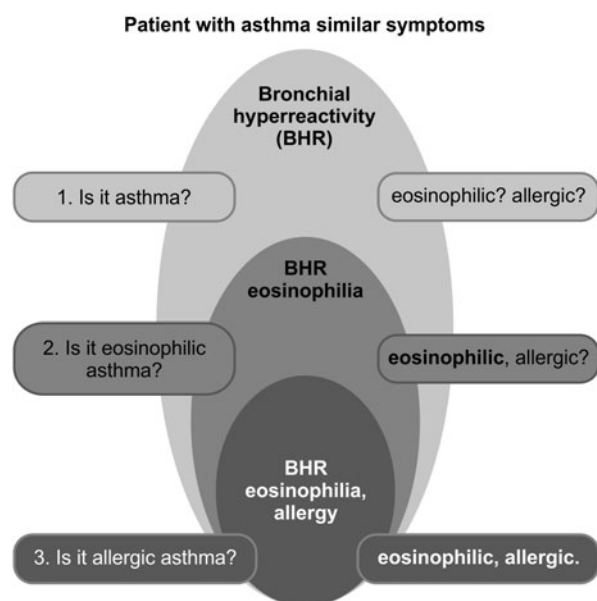


Figure 1. Three-step diagnostic algorithm adapted from [11].

The level and quality of the diagnostic process were assessed from the time of disease onset to the time of diagnosis (age at first asthma symptoms and at the time of diagnosis), use of bronchodilator testing in asthma diagnosis, allergological examination at the time of initial diagnosis and in last 5 years, and phenotyping according to the national guidelines (11).

Data on asthma therapy included, in addition to classical pharmacotherapy, details of allergen immunotherapy and adherence to treatment (physician review and ratio of prescription vs. actual use of preventive treatment in the past week). The level of asthma control was assessed both by patients using the ACT and physicians using the GINA guidelines, including long-term assessment of asthma control (ACT scores: 25, fully controlled; 20–24, well-controlled; 16–20, not well controlled; 5–15, very poorly controlled asthma; GINA: well, partly, and uncontrolled asthma) (10). For asthma control, data on exacerbation, asthma-related healthcare use, and productivity/school loss were also collected (acute/unscheduled treatments, hospitalization for asthma).

Digitalization and statistical analyses

The questionnaire data were digitized by Institute of Biostatistics and Analysis staff. Continuous data are described as means, standard deviations, and medians and 5–95th percentiles. Categorical data are presented using absolute and relative frequencies based on the number of completed data. Statistical tests included the Pearson's chi-squared test, McNemar's test of marginal homogeneity of symmetry, and Cohen's

kappa as an indicator of agreement. All analyses were performed using SAS 9.4 for Windows (Copyright © 2014, SAS Institute Inc., Cary, NC).

Results

We invited 512 allergologists and 546 pulmonologists (representing the vast majority of all certified specialists in the country) to participate in the study. A total of 114 respiratory specialists, 58 allergologists and 56 pneumologists, registered (three physicians were declared having both certifications, and assigned to one of the groups based on their main activity). Of the 5027 obtained records/questionnaires, 4557 were valid (a physician provided valid data of 10.2 patients in each season on average). The number of patients reported by each specialty was similar (pulmonologists, 2315; allergologists, 2242).

Patients and asthma characteristics

Patients' characteristics

Among adult patients with asthma in the Czech Republic, women, subjects with higher education, and overweight individuals were prevalent. Obesity was the most common comorbidity, and more frequent than ACO(S). At the time of diagnosis, a significant proportion of patients with asthma owned pets and 17% of patients were smokers. After asthma was diagnosed, both active smoking and pet ownership were decreased. Detailed data are shown in Table 1.

Sex: According to the data by the Czech Statistical Office, there is only a slight predominance of women in the general population of the Czech Republic (51%) (14). In this study, however, the proportion of women was higher, representing nearly two-thirds of the asthma population in the country.

Age: The average age of the patients with asthma in this study was slightly higher (48.1 years) than that of the adults in the Czech Republic (46.9 years) (15).

Education: In the Czech Republic, 41% of the population attains a higher level of education (16). In this study, adults with a higher level of education were predominant (59%), with most patients having completed secondary education.

Pets: At the time of first symptom onset, 41% of patients had at least one pet. However, this percentage decreased to 36% among those diagnosed with asthma. Furthermore, dogs were more common pets than were cats. While the ownership of dogs did not change notably after diagnosis, that of cats decreased significantly from 17 to 12%.

Table 1. Patients' characteristics.

Parameter	Characteristics	Value
Sex (<i>N</i> = 4518)		
Woman	<i>N</i> (%)	2835 (62.7%)
Man	<i>N</i> (%)	1683 (37.3%)
Age	<i>N</i>	4,557
	Mean (SD)	48.1 (16.74)
	Median (P5; P95)	47.6 (21; 75)
Education (<i>N</i> = 4389)		
Basic	<i>N</i> (%)	451 (10.3%)
Partially secondary school	<i>N</i> (%)	1378 (31.4%)
Full secondary school	<i>N</i> (%)	1832 (41.7%)
University	<i>N</i> (%)	728 (16.6%)
Pets at time of diagnosis (<i>N</i> = 4557)	<i>N</i> (%)	1795 (39.4%)
Cat (<i>N</i> = 1795)	<i>N</i> (%)	763 (16.7%)
Dog (<i>N</i> = 1795)	<i>N</i> (%)	1160 (25.5%)
Rodent (<i>N</i> = 1795)	<i>N</i> (%)	190 (4.2%)
Bird (<i>N</i> = 1795)	<i>N</i> (%)	203 (4.5%)
Other (<i>N</i> = 1795)	<i>N</i> (%)	179 (3.9%)
Pets now/currently (<i>N</i> = 4557)	<i>N</i> (%)	1574 (34.5%)
Cat (<i>N</i> = 1574)	<i>N</i> (%)	569 (12.5%)
Dog (<i>N</i> = 1574)	<i>N</i> (%)	1084 (23.8%)
Rodent (<i>N</i> = 1574)	<i>N</i> (%)	138 (3.0%)
Bird (<i>N</i> = 1574)	<i>N</i> (%)	141 (3.1%)
Other (<i>N</i> = 1574)	<i>N</i> (%)	148 (3.2%)
BMI	<i>N</i>	4474
	Mean (SD)	27.5 (5.71)
	Median (P5; P95)	26.6 (20; 38)
BMI—category (<i>N</i> = 4474)		
Underweight (<18.5)	<i>N</i> (%)	60 (1.3%)
Normal weight (5–25)	<i>N</i> (%)	1628 (36.4%)
Overweight (25–30)	<i>N</i> (%)	1516 (33.9%)
Obesity (>30)	<i>N</i> (%)	1270 (28.4%)
Smoking now/currently (<i>N</i> = 4510)		
Yes	<i>N</i> (%)	476 (10.6%)
No	<i>N</i> (%)	3566 (79.1%)
Ex-smoker	<i>N</i> (%)	468 (10.4%)
Number of cigarettes per day (<i>N</i> = 4510)		
<10	<i>N</i> (%)	352 (78.0%)
11–20	<i>N</i> (%)	94 (20.8%)
>20	<i>N</i> (%)	5 (1.1%)
Smoking at time of diagnosis (<i>N</i> = 4557)		
Yes	<i>N</i> (%)	767 (16.8%)
No	<i>N</i> (%)	3488 (76.5%)
Ex-smoker	<i>N</i> (%)	276 (6.1%)
Unlisted	<i>N</i> (%)	26 (0.6%)
Number of cigarettes/day (at time of diagnosis) (<i>N</i> = 767)		
10 and less	<i>N</i> (%)	381 (49.7%)
11–20	<i>N</i> (%)	293 (38.2%)
More than 20	<i>N</i> (%)	37 (4.8%)
Comorbidities and concomitant allergic diseases		
Obesity (<i>N</i> = 4442)		1385 (31.2%)
Seasonal rhinitis (<i>N</i> = 4499)		2577 (57.3%)
Persistent rhinitis/rhinosinusitis without polyps (<i>N</i> = 4481)		1464 (32.7%)
Rhinosinusitis with polyps (<i>N</i> = 4371)		296 (6.8%)
Intolerance of NSAID (<i>N</i> = 4350)		240 (5.5%)
Gastroesophageal reflux disease (<i>N</i> = 4295)		855 (19.9%)
Thyreopathy (<i>N</i> = 4344)		586 (13.5%)
COPD (<i>N</i> = 4463)		405 (9.1%)
Other comorbidities (<i>N</i> = 4557)		848 (18.6%)

N, number of subjects.

Smoking: At the time of first symptom onset, 17% of patients were active smokers. Currently, only 11% of patients smoked an average of 8.7 cigarettes per day, and > 75% of these patients were smoking less than 10 cigarettes per day. Only 1.1% of the sample were heavy smokers smoking more than 20 cigarettes per day.

BMI: More than half of the patients were overweight (BMI > 25) with more than 25% of patients (28.4%) being obese.

Comorbidities: Comorbidities including concomitant allergic diseases are listed in Table 1. Among the observed comorbidities (in addition to seasonal and/or persistent rhinitis), obesity was the most common (31.2%). Concomitant thyropathies and gastroesophageal reflux disease were more common than comorbid COPD (ACO/S/). Nasal polyposis and NSAID intolerance were observed in 6.8% and 5.5% of patients, respectively. Both comorbidities significantly increased

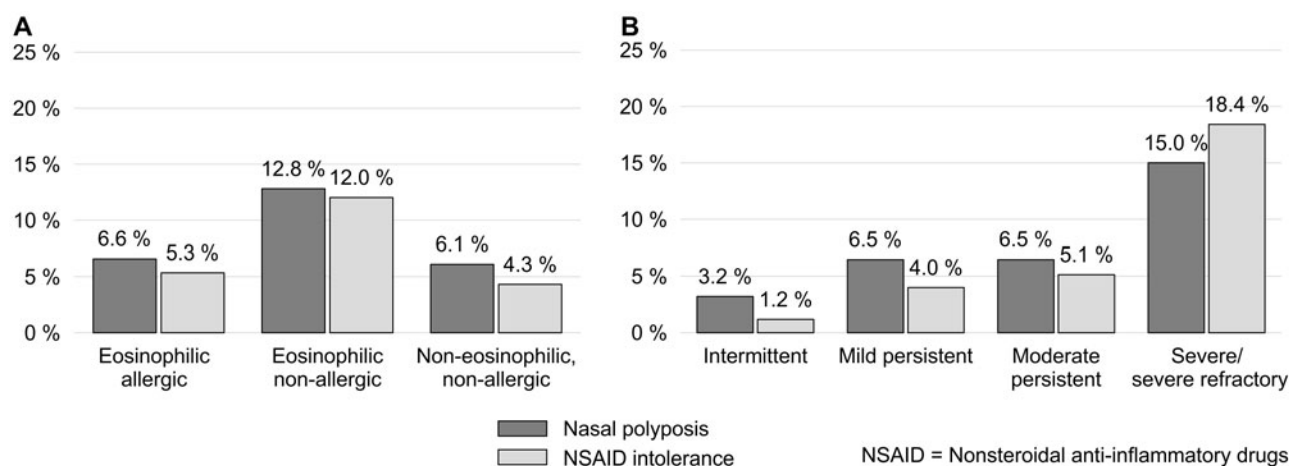


Figure 2. Nasal polyposis and NSAID intolerance in asthma phenotypes (A) and severity groups (B).

with the severity of asthma and were most often present in patients with the eosinophilic, non-allergic phenotype (Figure 2). Among the comorbidities not listed in the questionnaire, arterial hypertension, diabetes, and ischemic heart disease were reported by 8%, 1.9%, and 1.3% of the patients, respectively.

Asthma characteristics

In addition to asthma severity, we monitored three basic phenotypes, as well as frequency of individual types of sensitization, total IgE, and incidence of asthma as an occupational disease.

Severity: Most patients had mild to moderate asthma (Figure 3), and disease severity was not related to sex ($p = 0.69$).

Phenotyping: The Czech national guidelines define three clinically relevant phenotypes of asthma (see Methods). The phenotypes were distributed differently among men and women (Figure 3, $p < 0.001$ for both, chi-square test). Among the three phenotypes, the eosinophilic allergic phenotype was the most common in both sexes (approximately 72%), with a greater predominance in men. Compared to the prevalence in men, the eosinophilic non-allergic and non-eosinophilic non-allergic phenotypes were more prevalent in women. The highest recorded FeNO value among all patients was 432 ppb, and the eosinophilic, non-allergic phenotype had the highest mean FeNO value at 37.4 ppb (see Figure 4).

Allergy status: The most common allergens were pollens (present in 51% of patients) with the most dominant ones being grass pollens. Mite and cat allergens were the second and third most common (Figure 5).

Total IgE concentration: The mean IgE was 316.8 (633.3) IU/mL and the median was 152 (13; 1100) IU/mL. The highest IgE (11 000 IU/mL) value was observed in patients with the allergic phenotype,

whereas the lowest IgE values were observed in patients with the non-eosinophilic, non-allergic phenotype (Figure 4).

Asthma as an occupational disease: Occupational asthma was observed in only 0.7% of the patients.

Asthma management

Quality of diagnostic process

Pulmonary function testing: Spirometry is a routine test in the respiratory specialists' clinics in the Czech Republic. In this study, 99% of patients underwent spirometry.

Bronchodilator test (BDT): Bronchodilator test results for primary diagnosis of asthma were available for 58% of patients. In the remaining 42% of patients, the BDT results were unknown or unavailable or the BDT was not performed. The test results confirmed asthma in 84% of the tested patients.

FeNO: FeNO had been measured previously in 54% of patients and during the study visit in 52% of patients.

Allergy testing: Allergy testing had been performed anytime in the past in 89% of patients, and within the last 5 years in 70% of patients. A considerable number of physicians (19 out of 114) did not test for mold allergy.

Phenotyping: Phenotype classification based on the national guidelines was performed in 86.2% of patients (Figure 3).

Time from first onset of breathing problems to the diagnosis: The time from first onset of respiratory complaints to establishing the diagnosis of asthma was, in most cases, between 1 to 3 years (mean (SD) 2.7 (5.9), median (P5; P95) 1 (0; 13)).

Patients on long-term systemic corticosteroid therapy evaluated in the NCSA: A total of 4.9% of

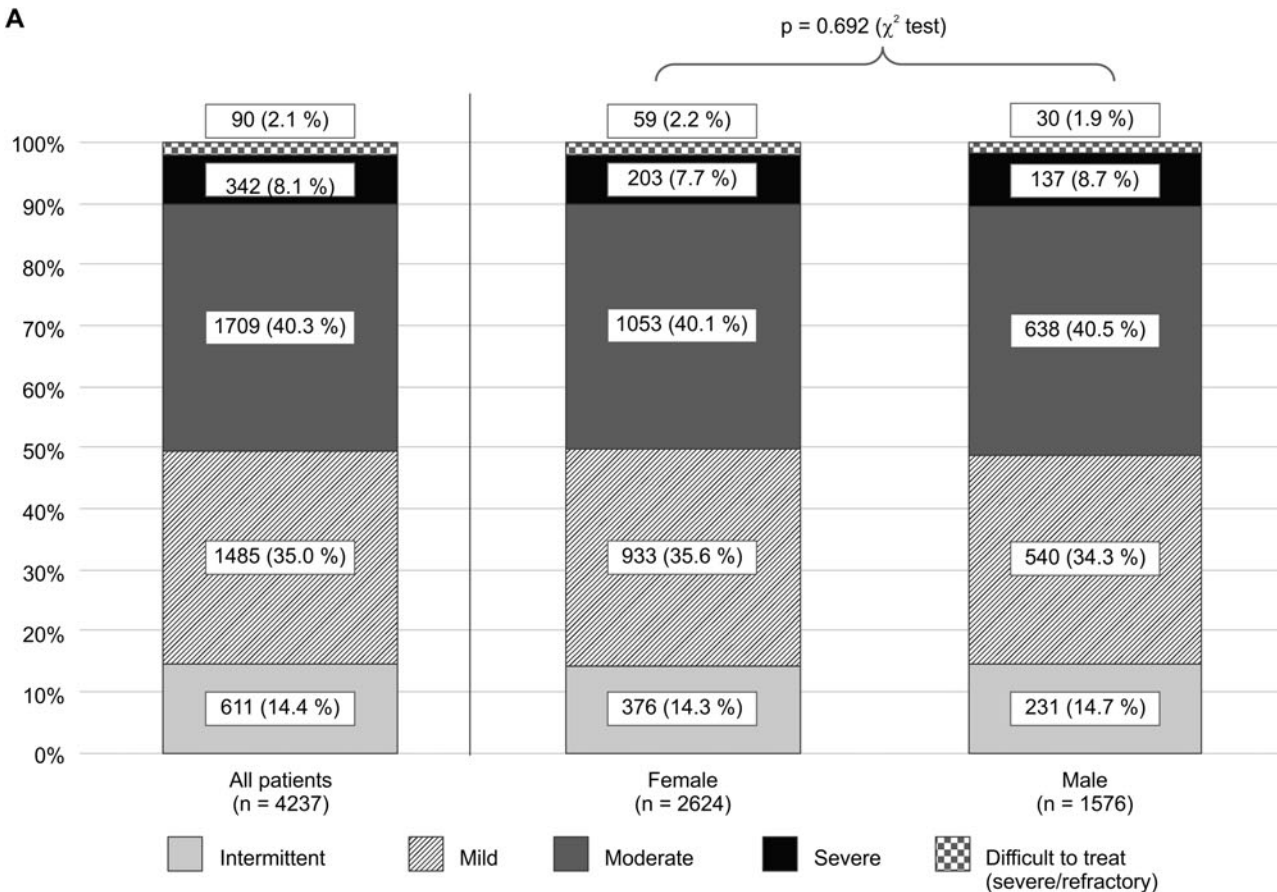
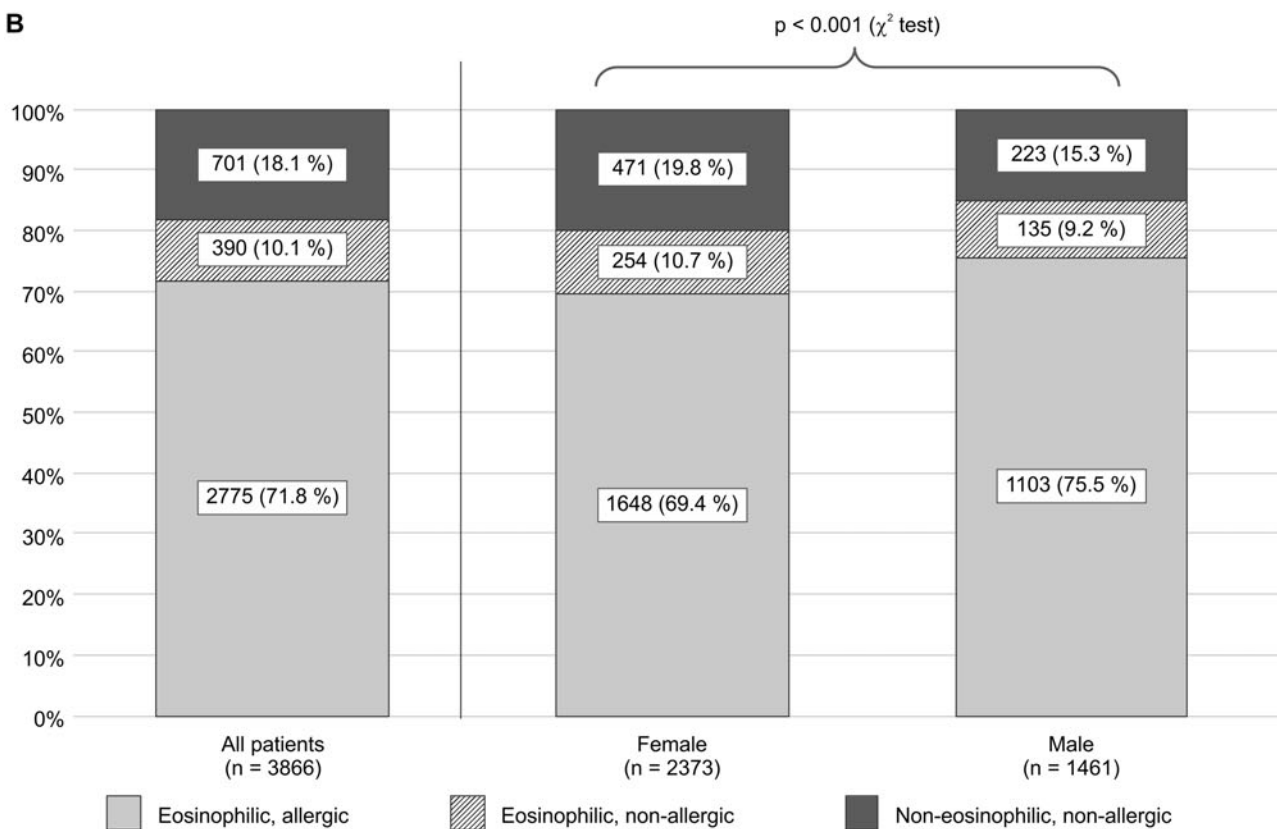
A**B**

Figure 3. Distributions of asthma severity (A) and phenotype (B).

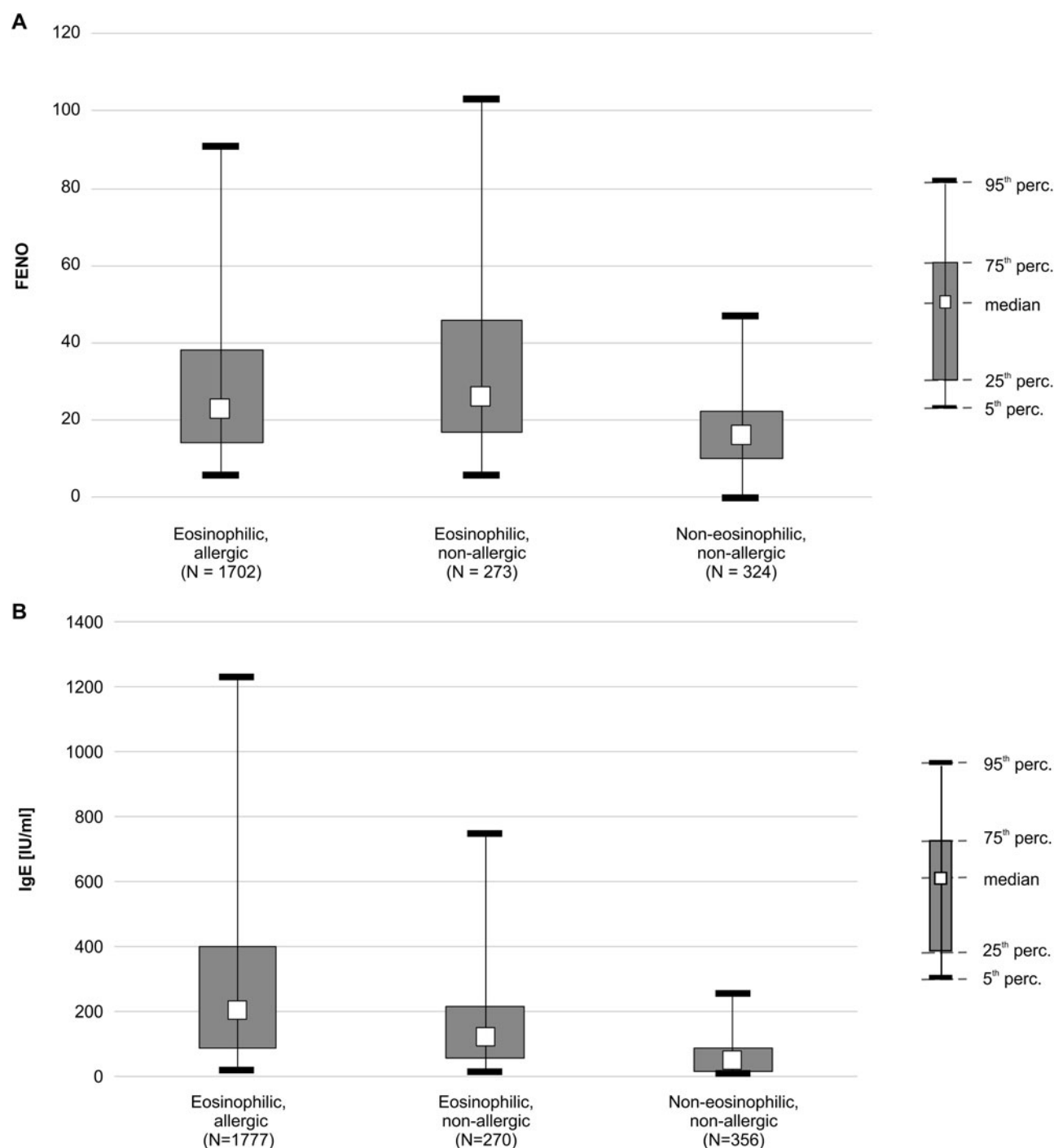


Figure 4. FENO (A) and total IgE (B) and asthma phenotypes.

patients with asthma were treated for more than 6 months during the last year by daily systemic corticosteroid therapy (Table 2). A total of 3.8% of patients were referred to the Severe Asthma Center.

Treatment reality and level of control

A detailed overview of asthma treatment is provided in Table 2, and data concerned/related to adherence and control are provided in Figure 6.

Reliever medications: Reliever medications largely comprised rapid-acting beta-2 agonists (RABA, 83%) and a combination of SABA/short-acting muscarinic antagonist (SAMA, 12%). A total 5.4% of the patients used a reliever medication as monotherapy. In 0.4% of patients, oral xanthines were reported as the only reliever medication.

Controller medications: A total 94% of the patients used regular preventive treatment, and 89%

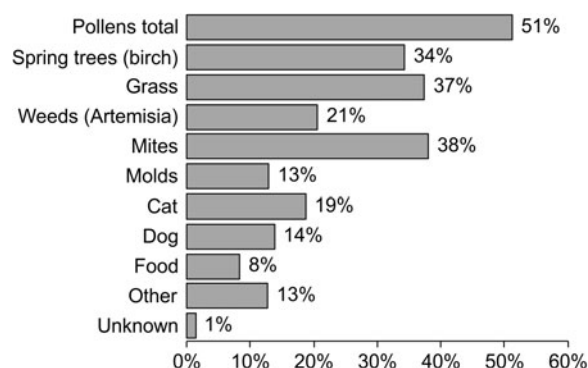


Figure 5. Frequency distribution of sensitization types.

of the patients used ICS. Approximately 75% of the patients were on an ICS/LABA combination, with 91% receiving a fixed combination of ICS + LABA. Among the patients on ICS/formoterol combination, the (S)MART regime was prevalent in approximately two-thirds of the cases. Preventive inhalation drugs were administered as dry powder inhalers in most patients (64%). The mean ICS dose (converted to the budesonide equivalent) was high (mean 705.2 (476.83) µg/day, median 548.6 (200; 1714) µg/day), and the highest reported daily ICS dose was 3400 µg.

Other preventive medications (leukotriene antagonists, tiotropium, cromoglycate, and oral xanthines/theophyllines) were administered (with the exception of antileukotrienes) mainly as ad-on therapy, not as monotherapy, and used in less than 20% of patients. We could not determine if theophylline was used as a reliever (bronchodilator) medication or corticosteroid-sparing drug. A very small proportion of patients (2.4%) at the time of enrollment in the study were on three preventive drugs, and only 0.1% of patients received a combination of four preventive drugs (excluding oral corticosteroids). In 4.9% of patients, systemic corticosteroids were used for more than 6 months per year.

Allergen immunotherapy: Approximately 12.9% of patients were on allergen immunotherapy. Among allergen vaccines, pollen allergens were dominant, and among perennial allergens, house dust mites were dominant (Table 2). The average duration of immunotherapy was 3 years with subcutaneous immunotherapy being prevalent. There was no difference in the frequency of allergen immunotherapy by asthma severity with the exception of severe therapy resistant asthma in which this treatment is contraindicated.

Asthma control: Asthma control was assessed both by patients (using the self-reported ACT) and by their physicians (by clinical assessment according to the GINA guidelines). Overall, 79% of the patients

Table 2. Therapy.

Parameter	Value
Type of therapy (N = 4557)	
Reliever use only	245 (5.4%)
Preventive + reliever use	3953 (86.7%)
Preventive treatment only	334 (7.3%)
Not filled	25 (0.5%)
Reliever use (N = 4198)	
Beta2-agonist	3468 (82.6%)
Anticholinergics	220 (5.2%)
Beta2-agonist and anticholinergics	493 (11.7%)
Theophyllines	398 (9.5%)
Preventive treatment (N = 4287)	
Systemic corticosteroids (N = 4204)	205 (4.9%)
Inhaler corticosteroids (ICS)—% of patients on preventive treatment	4032 (94.1%)
Inhaler corticosteroids (ICS)—% of all patients (N = 4557)	4032 (88.5%)
ICS—average daily dose converted to BUD equivalent (N = 4032)	
Mean (SD)	705.2 (476.83)
Median (P5; P95)	548.6 (200; 1714)
References of corticosteroid molecules (N = 4032)	
BDP	764 (18.9%)
BUD	1517 (37.6%)
FP	1138 (28.2%)
CIC	306 (7.6%)
MF	77 (1.9%)
FF	215 (5.3%)
ICS—type of inhaler (N = 3727)	
Dry powder	2383 (63.9%)
MDI	1337 (35.9%)
Both types	7 (0.2%)
Regularly used spacer (N = 1110)	148 (13.3%)
ICS—type of treatment (N = 3654)	
Monotherapy	912 (25.0%)
Combination with LABA	2742 (75.0%)
Formoterol (N = 2742)	1718 (62.7%)
Salmeterol (N = 2742)	725 (26.4%)
Vilanterol (N = 2742)	139 (5.1%)
Dosage regimen (N = 2128)	
Separate inhalers	192 (9.0%)
Fixed combination	1936 (91.0%)
SMART strategy* (N = 1093)	730 (66.8%)
Other preventive treatment	
Antileukotriene (N = 4218)	787 (18.7%)
Tiotropium (N = 4171)	237 (5.7%)
Cromones (N = 4159)	50 (1.2%)
Allergen immunotherapy (N = 4213)	543 (12.9%)
Type of administration	
Injection (N = 543)	284 (52.3%)
Peroral gtt. (N = 543)	94 (17.3%)
Sublingual tbl. (N = 543)	70 (12.9%)
Type of allergen	
Mites (N = 543)	133 (24.5%)
Pollens (N = 543)	286 (52.7%)
Molds (N = 543)	2 (0.4%)
Dog (N = 543)	4 (0.7%)
Unfilled (N = 543)	105 (19.3%)
Duration of treatment [years] (N = 410)	
Mean (SD)	2.8 (1.86)
Median (P5; P95)	3.0 (0; 5)

Data are reported as mean (SD) and median (P5, P95); N, number of subjects.

reported completely or well-controlled asthma, whereas the treating physicians reported that 54% of the patients had well-controlled asthma (Figure 6).

Asthma exacerbation, related healthcare, and productivity/school loss: During the last 12 months,

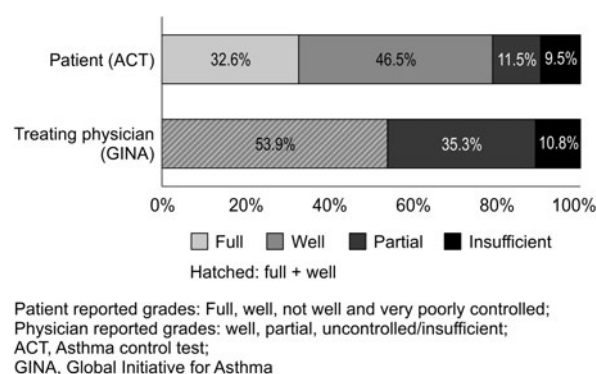


Figure 6. Asthma control assessment.

14.5% of patients had asthma exacerbations requiring systemic corticosteroids for more than 2 days, whereas 15.4% of patients received other acute treatment. Finally, 4.5% of patients experienced asthma exacerbations requiring hospital admission within the past 12 months.

A total 9.2% of the reported clinic visits were unplanned due to the worsening of asthma. The remaining visits were scheduled follow-up visits.

Discussion

This is the first robust, country-wide, observational study investigating the characteristics and management level of asthma in adult patients from the Czech Republic since its inception in 1993. Our findings are based on the data collected from a representative patient sample treated by specialists in allergy/clinical immunology and pulmonology. Our data (mainly related to the level of asthma management) may not be representative of the entire asthma population in the Czech Republic. However, we are confident that our results illustrate the current disease status in at least two-thirds of patients with asthma in the Czech Republic who are regularly seen by a specialist, regardless of the severity of their illness (9). The health-care reality in the Czech Republic is significantly different from that in many comparable and even geographically neighboring countries, including Germany where most patients with asthma are treated by a general practitioner (8).

In our patient sample, asthma was more prevalent among women and adults with a higher education compared to the general population. The higher prevalence of asthma in women compared to men is well-known (17,18); however, it was even more pronounced in our study. This observation could partly be influenced by our study design, in which data were collected from unselected consecutive visits. Women adhere better to clinic assessment schedules, so their

asthma prevalence may have been over-represented. We also found that asthma severity was similar between men and women, including among the most severe patients (Figure 3). These results are comparable with those of studies performed in other countries (19). Likewise, for both sexes, the atopic phenotype was more prevalent than were the other phenotypes. This was again in line with the data from our neighboring country (20). However, unlike in other countries, detailed phenotyping of patients with asthma has been performed in the Czech Republic since 2015 (11). Our results show that both non-allergic phenotypes are exhibited more frequently by women than by men (Figure 3(B)).

Obesity, assessed by the physicians, was the most commonly reported comorbidity and well correlated with BMI (Table 1). The proportion of obese individuals in the Czech asthma population is greater than twice that reported by a study in France. This discrepancy might be due to the time gap in the data collection between the two countries; the French study was performed in 2006 (7).

The incidence of NSAID intolerance and nasal polyposis was significantly associated not only with the severity of asthma but also with eosinophilic, non-allergic phenotype, i.e. “late adult onset non-atopic (highly) eosinophilic/severe asthma” in the related literature (21–24).

In contrast to those of German authors (25), our results relating the type of pet ownership to the prevalence of sensitization indirectly support a higher sensitization potential of cat than of dog allergens. Even though the proportion of patients with asthma with dogs was prevalent, sensitization to cats was significantly higher (Figure 5). Consistent with the clinically relevant sensitizing potential of cats and dogs, diagnosis of asthma led to a decrease in the presence of these pets in households, with a greater reduction in the presence of cats (see Table 1).

Diagnosis of asthma also led to cessation of smoking in more than one third of patients (a decrease from 17 to 11%). The percentage of patients with asthma who smoke in the Czech Republic is surprisingly lower than that reported worldwide, including in European countries (approximately 25%) (2,4,26,27). A similarly low proportion of patients with asthma who smoke was reported by studies from Spain (28).

Overall, we found a good level of the diagnostic process, not only in diagnosing asthma but also in phenotyping the disease (Figure 1).

In the Czech Republic, lung function testing is a routine part of most clinical visits among patients

with respiratory problems. In contrast, it is uncommon even in some developed countries (1,29). In more than half of the patients (58%), the attending physician had bronchodilator test results from the initial diagnosis available, with positive test results in 84% of the patients.

In most of our patients (86%), the diagnostic process did not just determine the severity of asthma, but also assessed the clinical relevance of eosinophilia and allergy as the cornerstones of phenotypical classification, which is emphasized in our national guidelines. This is associated with the good availability of allergy testing (*in vitro* total and specific IgE and skin prick tests) and FeNO examinations.

Most patients requiring long-term systemic corticosteroid therapy were referred to one of the centers for problematic severe asthma (12,30). In these specialized clinics of the NCSA, more detailed airway-specific and direct tests, including tests for sputum eosinophils, bronchial biopsy, and bronchoalveolar lavage, are performed to confirm residual eosinophilia. Hence, if physicians refer patients with "corticodependent" asthma to one of these specialized centers, it is considered as a "sign of good care."

Observations of diagnostic quality may have been subject to bias. The average time from the onset of respiratory symptoms to asthma diagnosis was short (median duration, 1 year), but in some cases the period was prolonged (see mean and SD in the Results). This certainly requires attention, considering that untreated patients with recurrent obstructive respiratory problems have limited quality of life, reduced productivity, and are at risk for irreversible airway remodeling and severe exacerbations (10, 31). Clearly, quality assessment of the diagnostic process based only on the time to diagnosis is not accurate and may be biased by many factors including delay by the patient in seeking medical care for symptoms, incorrect or delayed diagnosis by primary care practitioners, or poor availability of specialized care in some regions. Additionally, the gaps in the diagnostic process found by this study included inconsistency in testing for mold allergies and insufficient research for the possible cause of asthma. Indeed, both factors can severely affect patients. Some patients with dominating or isolated mold allergies may be mistaken for non-allergic patients with asthma and may have difficulty in receiving anti-IgE or other phenotypically targeted treatment (antimycotics) for their unrecognized severe allergic asthma (32,33). Previous studies have reported higher than 12% prevalence of occupational causes of adult asthma (34–37). In addition to

unavailability of occupational disease financial compensation, persistence of exposure to an unidentified causative agent may lead to disease progression (38,39).

The data on current asthma therapies obtained from this study show evidence of good awareness and adherence to international and national guidelines and, interestingly, reveal both overtreatment and undertreatment for asthma. Regular preventive treatment is administered to 94% of the patients with persistent disease, in contrast to the low level of preventive treatment in most European countries, particularly in Germany (1,5,40). Furthermore, more than 90% of patients on preventive treatment use ICS (mean 705 µg/day), and of these patients, 75% (about 70% of all patients with asthma) are using ICS + LABA combination therapy despite the fact that half of the asthmatic population only has intermittent or mild asthma.

In 64% of the patients, inhaled preventive medications are administered by dry powder inhalers. This is in line with the data from the Scandinavian countries and in contrast to those from the United Kingdom. These differences can mostly be explained by the country traditions and market-drug availability (41,42). In patients using ICS + LABA, high preference of fixed combinations exists. In the fixed combination of ICS/formoterol, the (S)MART mode of administration was prevalent (67%).

The popularity of the (S)MART mode was obvious. Unfortunately, we were unable to determine whether the (S)MART mode had been used rationally, i.e. without a co-prescription of SABA. Therefore, we initiated a further complementary study based on the findings by Chapman et al. (43), who demonstrated that this treatment strategy is commonly misapplied. Although most physicians (72%) in Chapman's study (similar to our study), prescribed SMART/MART, the majority (91%) co-prescribed a short-acting bronchodilator at least some of the time. Allergen immunotherapy has been traditionally recommended in the Czech Republic to patients with allergic asthma, provided that the disease is under full control and at the time of enrollment in the study, was administered to 12.9% of the patients with asthma enrolled in this study. The average duration of immunotherapy was 3 years, with prevalent injected vaccines.

We did not incorporate data on biological treatment into this study. This information is easily accessible from the network of the NCSA (12,30).

Compared to the Asthma Insight and Management and Asthma Insight and Reality and other studies, our data on patient reported level of control are noticeably

better (1,3,4,20,44). We attribute the overall better level of control to the fact that our study sample represents patients treated by respiratory specialists. Our findings also showed differences in patient versus physician reported level of satisfactory asthma control (79 versus 54%, Figure 6). Discordance concerning the level of asthma control between patients and doctors is a frequent phenomenon and may be due to several factors (1,3,45). Patients preferably assess current symptom control, while doctor assessments are more comprehensive and consider a longer duration. Moreover, in our study, the criteria of assessment by patients and doctors were not entirely identical.

Conclusions

The level of asthma management in the Czech Republic is comparable to that in other developed countries and progressively involves pragmatic phenotypic classification based on the presence of eosinophilia and allergy as prerequisites for the rational use of targeted treatment, especially in severe asthma. Therapies used for treatment reveal adherence to both international and national guidelines. Nevertheless, there is unnecessary delay in diagnosis, lack in detection of possible environmental causes of asthma (workplace, molds), and a tendency toward disease overtreatment.

Disclosure statement

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

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References

- Nathan RA, Thompson PJ, Price D, Fabbri LM, Salvi S, González-Díaz S, Maspero JF, et al. Taking aim at asthma around the world: global results of the Asthma Insight and Management Survey in the Asia-Pacific Region, Latin America, Europe, Canada, and the United States. *J Allergy Clin Immunol Pract* 2015; 3:734–742. doi:10.1016/j.jaip.2015.04.013.
- Chen H, Johnson CA, Haselkorn T, Lee JH, Israel E. Subspecialty differences in asthma characteristics and management. *Mayo Clin Proc* 2008;83:786–793. doi: 10.4065/83.7.786.
- Price D, Fletcher M, Thys van der Molen. Asthma control and management in 8,000 European patients: the REcognise Asthma and LInk to Symptoms and Experience (REALISE) survey. *NPJ Prim Care Respir Med* 2014;24:14009.
- Rabe KF, Adachi M, Lai CKW, Soriano JB, Vermeire PA, Weiss KB, Weiss ST, et al. Worldwide severity and control of asthma in children and adults: the global asthma insights and reality surveys. *J Allergy Clin Immunol* 2004;114:40–47. doi:10.1016/j.jaci.2004.04.042.
- Vermeire PA, Rabe KF, Soriano JB, Maier WC. Asthma control and differences in management practices across seven European countries. *Respir Med* 2002;96:142–149.
- Agache I, Ryan D, Rodriguez MR, Yusuf O, Angier E, Jutel M. Allergy management in primary care across European countries – actual status. *Allergy* 2013;68: 836–843. doi:10.1111/all.12150.
- Laforest L, Van Ganse E, Devouassoux G, Chretien S, Osman L, Bauguil G, et al. Management of asthma in patients supervised by primary care physicians or by specialists. *Eur Respir J* 2006;27:42–50. doi:10.1183/09031936.06.00035805.
- Roberts N, Papageorgiou P, Partridge MR. Delivery of asthma and allergy care in Europe. *J Asthma* 2009;46: 767–772.
- IHIS CR. Retrieved July 5, 2018, from <http://www.uzis.cz/en/about-us/ihis-cr/documents-ihis-cr>
- GINA. Global strategy for asthma management and prevention. 2015. [cited 2016 29 Jan]; Available from: http://www.ginasthma.org/local/uploads/files/GINA_Report_2015_Aug11.pdf
- Terl M, Sedlák V, Cap P, Dvořáková R, Kašák V, Kočí T, et al. Asthma management: a new phenotype-based approach using presence of eosinophilia and allergy. *Allergy* 2017;72:1279–1287.
- Sedlák V, Chlumský J, Terl M, Novotná B, Kral B. Doporučený postup diagnostiky a léčby obtížné léčitelného bronchiálního astmatu. <http://www.pneumologie.cz/guidelines/>
- GINA. 2012. Global strategy for asthma management and prevention. 2012. Available from: <http://ginasthma.org/>
- CSO 2017/I. Women and Men in Data. Prague. 2017. Publication code: 300004-17 [online]. Available from: <https://www.czso.cz/csu/czso/zeny-a-muzi-v-datech-2017> [last accessed 19 April 2018].
- CSO 2017/II. Age distribution of the population – 2017 [online]. Available from: <https://www.czso.cz/csu/czso/age-distribution-of-the-population-2017> [last accessed 19 April 2018].
- CSO 2016. Labour Market in the Czech Republic - Time Series - 1993 – 2016[online]. Retrieved from <https://www.czso.cz/csu/czso/101r-k-vek-a-vzdelani-populace-y4czet1j88> [last accessed 19 April 2018].
- Haldar P, Pavord ID, Shaw DE, Berry MA, Thomas M, Brightling CE, Wardlaw AJ, et al. Cluster analysis and clinical asthma phenotypes. *Am J Respir Crit Care Med* 2008;178:218–224. doi:10.1164/rccm.200711-1754OC.
- Almqvist C, Worm M, Leynaert B. Impact of gender on asthma in childhood and adolescence: a GA2LEN

- review. *Allergy* 2008;63:47–57. doi:[10.1111/j.1398-9995.2007.01524.x](https://doi.org/10.1111/j.1398-9995.2007.01524.x).
19. Ganse Van E, Antonicelli L, Zhang Q, Laforest L, Yin DD, Nocea G, et al. Asthma-related resource use and cost by GINA classification of severity in three European countries. *Respir Med* 2006;100:140–147. doi:[10.1016/j.rmed.2005.03.041](https://doi.org/10.1016/j.rmed.2005.03.041).
20. Kardos P, Wittchen H-U, Mühlhig S, Ritz T, Buhl R, Rabe K, Klotsche J, et al. Controlled and uncontrolled allergic asthma in routine respiratory specialist care - a clinical-epidemiological study in Germany. *Curr Med Res Opin* 2011;27:1835–1847. doi:[10.1185/03007995.2011.606805](https://doi.org/10.1185/03007995.2011.606805).
21. Wenzel SE, Phenotypes and endotypes: Emerging concepts on asthma heterogeneity. In: Akdis CA, Agache I, eds. *The global atlas of asthma: The pathogenesis of asthma*. Zurich: European Academy of Allergy and Clinical Immunology; 2013. p. 34–35.
22. Bel EH. Clinical phenotypes of asthma. *Curr Opin Pulm Med* 2004;10:44–50.
23. Chung KF, Wenzel SE, Brozek JL, Bush A, Castro M, Sterk PJ, Adcock IM, et al. International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma. *Eur Respir J* 2014;43:343–373. doi:[10.1183/09031936.00202013](https://doi.org/10.1183/09031936.00202013).
24. Hashimoto S, Bel EH. Current treatment of severe asthma. *Clin Exp Allergy* 2012;42:693–705. doi:[10.1111/j.1365-2222.2011.03936.x](https://doi.org/10.1111/j.1365-2222.2011.03936.x).
25. Schmitz R, Ellert U, Kalcklosch M, Dahm S, Thamm M. Patterns of sensitization to inhalant and food allergens - findings from the German Health Interview and Examination Survey for Children and Adolescents. *Int Arch Allergy Immunol* 2013;162:263–270. doi:[10.1159/000353344](https://doi.org/10.1159/000353344).
26. Laforest L, Van Ganse E, Devouassoux G, Chretien S, Bauguil G, Pacheco Y, Chamba G, et al. Quality of asthma care: results from a community pharmacy based survey. *Allergy* 2005;60:1505–1510. doi:[10.1111/j.1398-9995.2005.00923.x](https://doi.org/10.1111/j.1398-9995.2005.00923.x).
27. von Bülow A, Backer V, Bodtger U, Söes-Petersen NU, Assing KD, Skjold T, Porsbjerg C, et al. The level of diagnostic assessment in severe asthma: a nationwide real-life study. *Respir Med* 2017;124:21–29. doi:[10.1016/j.rmed.2017.01.010](https://doi.org/10.1016/j.rmed.2017.01.010).
28. Urrutia I, Plaza V, Pascual S, Cisneros C, Entrenas LM, Luengo MT, Caballero F, et al. Asthma control and concordance of opinions between patients and pulmonologists. *J Asthma* 2013;50:877–883. doi:[10.3109/02770903.2013.819886](https://doi.org/10.3109/02770903.2013.819886).
29. Gershon AS, Victor JC, Guan J, Aaron SD, To T. Pulmonary function testing in the diagnosis of asthma: a population study. *Chest* 2012;141:1190–1196. doi:[10.1378/chest.11-0831](https://doi.org/10.1378/chest.11-0831).
30. Ruzickova Kirchnerova O, Valena T, Novosad J, Terl M. Real-world effectiveness and safety of omalizumab in patients with uncontrolled severe allergic asthma from the Czech Republic. *Adv Dermatol Allergol* 2018;36(1):34–43. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6409880/>
31. Pohunek P, Warner JO, Turzíkóvá J, Kudrmann J, Roche WR. Markers of eosinophilic inflammation and tissue re-modelling in children before clinically diagnosed bronchial asthma. *Pediatr Allergy Immunol* 2005;16:43–51. doi:[10.1111/j.1399-3038.2005.00239.x](https://doi.org/10.1111/j.1399-3038.2005.00239.x).
32. Agarwal R. Severe asthma with fungal sensitization. *Curr Allergy Asthma Rep* 2011;11:403–413. doi:[10.1007/s11882-011-0217-4](https://doi.org/10.1007/s11882-011-0217-4).
33. Akuthota P, Weller PF. 2017. Clinical manifestation and diagnosis of allergic bronchopulmonary aspergillosis. <http://www.uptodate.com/>
34. Karjalainen A, Kurppa K, Martikainen R, Klaukka T, Karjalainen J. Work is related to a substantial portion of adult-onset asthma incidence in the Finnish population. *Am J Respir Crit Care Med* 2001;164:565–568. doi:[10.1164/ajrccm.164.4.2012146](https://doi.org/10.1164/ajrccm.164.4.2012146).
35. Knoeller GE, Mazurek JM, Moorman JE. Characteristics associated with health care professional diagnosis of work-related asthma among individuals who describe their asthma as being caused or made worse by workplace exposures. *J Occup Environ Med* 2012;54:485–490. doi:[10.1097/JOM.0b013e3182479f93](https://doi.org/10.1097/JOM.0b013e3182479f93).
36. Kogevinas M, Zock J-P, Jarvis D, Kromhout H, Lillienberg L, Plana E, Radon K, et al. Exposure to substances in the workplace and new-onset asthma: an international prospective population-based study (ECRHS-II). *Lancet* 2007;370:336–341. doi:[10.1016/S0140-6736\(07\)61164-7](https://doi.org/10.1016/S0140-6736(07)61164-7).
37. Mazurek JM, Syamlal G. Prevalence of asthma, asthma attacks, and emergency department visits for asthma among working adults - National Health Interview Survey, 2011–2016. *MMWR Morb Mortal Wkly Rep* 2018;67:377–386. doi:[10.15585/mmwr.mm6713a1](https://doi.org/10.15585/mmwr.mm6713a1).
38. Heederik D, Henneberger PK, Redlich CA. ERS Task Force on the Management of Work-related Asthma, Primary prevention: exposure reduction, skin exposure and respiratory protection. *Eur Respir Rev* 2012;21:112–124. doi:[10.1183/09059180.00005111](https://doi.org/10.1183/09059180.00005111).
39. Tarlo SM. Management and prevention of occupational asthma. *Minerva Med* 2017;108:229–238. doi:[10.23736/S0026-4806.16.04972-7](https://doi.org/10.23736/S0026-4806.16.04972-7).
40. Steppuhn H, Langen U, Mueters S, Dahm S, Knopf H, Keil T, Scheidt-Nave C, et al. Asthma management practices in adults-findings from the German Health Update (GEDA) 2010 and the German National Health Interview and Examination Survey (DEGS1) 2008–2011. *J Asthma* 2016;53:50–61. doi:[10.3109/02770903.2015.1059853](https://doi.org/10.3109/02770903.2015.1059853).
41. Lechuga-Ballesteros D, Noga B, Vehring R, Cummings RH, Dwivedi SK. Novel cosuspension metered-dose inhalers for the combination therapy of chronic obstructive pulmonary disease and asthma. *Future Med Chem* 2011;3:1703–1718. doi:[10.4155/fmc.11.133](https://doi.org/10.4155/fmc.11.133).
42. Lavorini F, Corrigan CJ, Barnes PJ, Dekhuijzen PRN, Levy ML, Pedersen S, Roche N, et al. Retail sales of inhalation devices in European countries: so much for a global policy. *Respir Med* 2011;105:1099–1103. doi:[10.1016/j.rmed.2011.03.012](https://doi.org/10.1016/j.rmed.2011.03.012).
43. Chapman KR, Hinds D, Piazza P, Raherison C, Gibbs M, Greulich T, et al. Physician perspectives on the burden and management of asthma in six countries The Global Asthma Physician Survey (GAPS.). *BMC Pulm Med* 2017;17:1–11. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6409880/>

- [gov/pmc/articles/PMC5701503/pdf/12890_2017_Article_492.pdf](https://pubmed.ncbi.nlm.nih.gov/pmc/articles/PMC5701503/pdf/12890_2017_Article_492.pdf)
44. Zahran HS, Bailey CM, Qin X, Johnson C. Long-term control medication use and asthma control status among children and adults with asthma. *J Asthma* 2017;54:1065–1072. doi:[10.1080/02770903.2017.1290105](https://doi.org/10.1080/02770903.2017.1290105).
45. Sastre J, Fabbri LM, Price D, Wahn HU, Bousquet J, Fish JE, Murphy K, et al. Insights, attitudes, and perceptions about asthma and its treatment: a multinational survey of patients from Europe and Canada. *World Allergy Organ J* 2016;9:13. doi:[10.1186/s40413-016-0105-4](https://doi.org/10.1186/s40413-016-0105-4).