

The Burden Associated with Ocular Symptoms in Allergic Rhinitis

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Key Words

Allergic rhinitis · Epidemiology · Ocular symptoms · Medical management

Abstract

Background: Ocular symptoms remain widely neglected while they concern the majority of subjects with allergic rhinitis (AR) and impair their daily activities. We describe the characteristics of ocular symptoms in subjects suffering from AR in the French INSTANT study and their impact on daily activities. **Methods:** This cross-sectional observational survey was carried out in November 2006 using face-to-face interviews. **Results:** 31.7% of the population-based sample (n = 4,019) suffered from AR and 52.0% of AR subjects (n = 663) described ocular symptoms. Men had significantly less ocular symptoms than women (odds ratio 0.71, 95% CI 0.57–0.89). 57.5% of subjects suffered from ocular symptoms for >5 years, 30.2% for >6 months in the past 12 months, and 92.2% during the pollen season. The troublesome ocular symptoms were itching eyes (51.1%), watery eyes (38.6%), red eyes (6.6%) and swollen eyelids (3.6%). The trigger factors were pollens (51.3%), household dust and mites (34.8%), pets (12.2%) and air pollution (3.8%). Ocular symptoms had a negative impact on daily activities (blurred sight 47.8%, reduction in daily activities 38.8%, reduction in efficacy at work

25.8%, sleep disturbances 16.3%, and sick leave 12.9%). They were diagnosed in 38.9% of subjects and followed up in 34.8%. Treatment for ocular symptoms was prescribed to 35.4% of subjects and to 61.9% of subjects with a regular follow-up care. **Conclusions:** This survey confirms the impact of ocular symptoms on AR patients' lives and suggests that they are still neglected and undertreated.

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Introduction

Allergic rhinitis (AR) is a prevalent and bothersome inflammatory condition affecting the upper airways, nose and eyes [1–4]. Ocular symptoms are common in AR patients and are known to be underappreciated [1, 4]. In fact, the association of nasal and ocular symptoms has been scarcely explored, with most studies reporting on either the proportion of AR patients suffering from ocular symptoms or the associated burden [5]. Conjunctivitis occurred in 52% and in 64–66% of AR patients in two French pharmacoepidemiologic surveys, respectively, in the ERASM survey and the DREAM survey [6, 7]. More recently, 75% of AR patients in the French CESAR survey and 83% in a Spanish survey reported suffering from nasal and ocular symptoms [8, 9]. Ocular symptoms com-

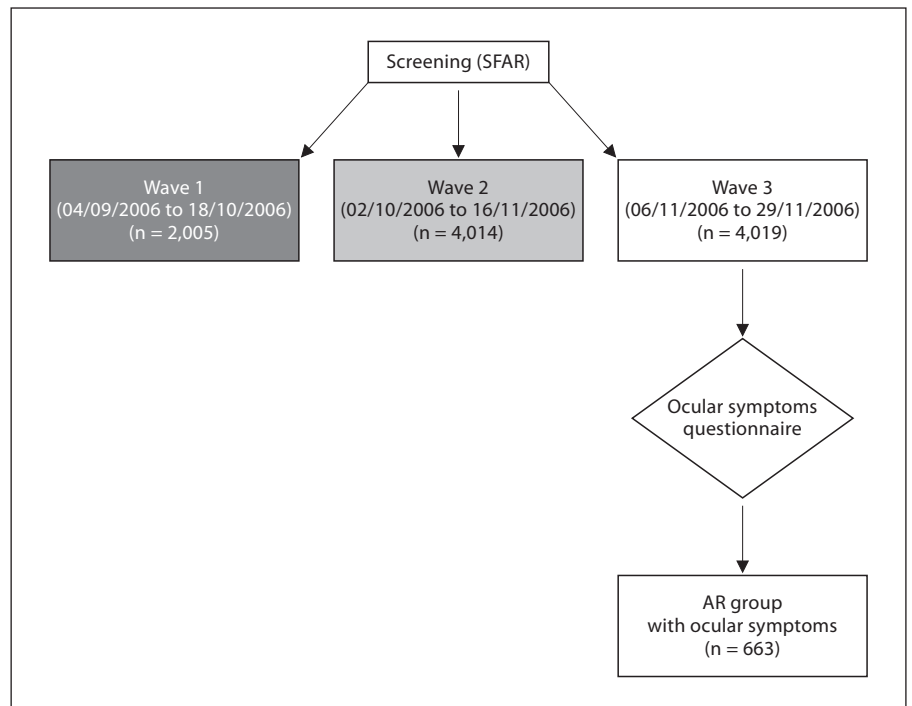


Fig. 1. Design of the INSTANT study.

monly characterized by recurrent bilateral conjunctival inflammation with pronounced itching (pruritus), tearing (epiphora) and redness (erythema) are salient, may constitute disabling features and may be as severe as nasal symptoms, as reported by some studies [1, 5, 10, 11]. Additionally, ocular symptoms are recognized as exerting negative effects on quality of life (QoL) and are responsible for patient discomfort, indicating a larger impact than previously suggested [5, 12–14]. The presence of ocular symptoms has been shown to be correlated with sleep impairment, limitations in daily activities and emotional distress [12–14]. Their severity seems to have a greater impact on QoL than the duration of such symptoms [7]. No investigation has given a holistic approach of ocular symptoms in the case of AR encompassing their description and consequences. In this context, the aim of the INSTANT study was to describe the characteristics of ocular symptoms in the French AR population and their impact on daily activities.

Methods

Study Design

INSTANT is a cross-sectional observational survey implemented in Metropolitan France (excluding Corsica). A population-based sample of individuals >18 years old was established

following the Quota Method according to age, gender, socio-professional status and geographic areas. The survey concerned AR and was conducted in three successive waves (fig. 1), described in detail elsewhere [15].

In this article, we focused on subjects included during the last (third) wave of the INSTANT survey carried out in November 2006 who presented with AR and ocular symptoms. The objectives of the study were to describe the characteristics and impact on daily activities of AR-associated ocular symptoms in the AR population of the French INSTANT study.

Data Collection

Data were collected using a Computer-Assisted Personal Interviewing system and the software CONVERSO® (developed by Conversoft®, France). Subjects were interviewed face to face during 20 min. Data collection was done by ISL® (Institut de sondage, Issy les Moulineaux, France), a company performing the face-to-face interview at home.

During the interview, the screening SFAR (score for allergic rhinitis) questionnaire, a simple and validated questionnaire, was filled out by subjects to identify AR subjects (with a SFAR ≥ 7) and non-AR subjects (with a SFAR < 7) [16]. For all subjects who reported ocular symptoms (answering with ‘yes’ to item 2 of the SFAR questionnaire: ‘During the last 12 months, were your nasal symptoms accompanied with watery or itching eyes?’), a second questionnaire (online supplementary figure 1, available at www.karger.com/doi/10.1159/000334286) was used to describe ocular symptoms in terms of number of patients, history, symptomatology, diagnosis, medical management and impact on daily activities (‘In the past 12 months, have you been bothered by your ocular problems in your daily activities? When you have ocular prob-

lems, is your sight blurred? If you wear lenses, do you think that the wear of lenses aggravates your symptoms? Do you have sleep disturbance? Are you less effective at work?').

Statistical Analysis

Statistical analyses of the collected data were performed using SAS software, version 8 (SAS Institute, Cary, N.C., USA).

All data on subjects with an available SFAR were included in the analysis. No a posteriori treatment data have been conducted.

Quantitative variables were described by the usual measures (mean, standard deviation, median, minimum and maximum) and qualitative variables by number of cases and percentages. Comparative analyses were performed according to SFAR, ocular symptoms or treatment with a 5% significance level for test, using χ^2 tests for qualitative variables and analysis of variance for Gaussian quantitative variables in combination with the Kruskal-Wallis non-parametric test for semi-quantitative or non-Gaussian quantitative variables.

Results

Study Population

A total of 4,019 subjects were interviewed in the third wave of the INSTANT survey: 2,743 subjects (68.3%) did not have AR (SFAR <7) and 1,276 subjects (31.7%) had AR (SFAR $\geq$ 7).

Among all subjects, 763 patients (19%, 763/4,019) reported ocular symptoms accompanied by nasal symptoms (answering 'yes' to item 2 of the SFAR questionnaire): 663 were AR subjects (52.0% of AR subjects, 663/1,276) and 100 subjects had no AR (3.7% of non-AR subjects, 100/2,743).

The mean age of AR subjects was 43.8 ± 17.3 years, with no significant difference in the presence of ocular symptoms or not (with vs. without ocular symptoms: 44.2 ± 17.4 vs. 43.4 ± 17.2 years; $p = 0.346$). Men had significantly less ocular symptoms than women (odds ratio 0.71, 95% CI 0.57–0.89).

The following results will focus only on AR subjects with ocular symptoms ($n = 663$).

Characteristics of Ocular Symptoms in the AR Population

Among the 663 subjects, 57.5% ($n = 381$) suffered from ocular symptoms for >5 years. Moreover, 35.4% of subjects ($n = 235$) were treated for ocular symptoms. Treated subjects had a longer history of ocular symptoms than untreated subjects, as shown in table 1. During the past 12 months, 30.2% ($n = 200$) suffered from ocular symptoms for >6 months and 92.2% ($n = 611$) during the pollen season, with no difference in treated and untreated subjects (table 1).

Table 1. History of ocular symptoms in AR patients ($n = 663$) according to treatment

	AR subjects not treated for ocular symptoms ($n = 428$), %	AR subjects treated for ocular symptoms ($n = 235$), %	p
History of ocular symptoms			<0.01
<1 year	11.0 ($n = 47$)	8.1 ($n = 19$)	
1–2 years	14.3 ($n = 61$)	6.8 ($n = 16$)	
2–5 years	18.9 ($n = 81$)	24.7 ($n = 58$)	
>5 years	55.8 ($n = 239$)	60.4 ($n = 142$)	
During the last year, ocular symptoms occurred			0.133
For at least 6 months	32.2 ($n = 138$)	26.4 ($n = 62$)	
During the pollen season	91.8 ($n = 393$)	92.8 ($n = 218$)	0.763

Table 2. Clinical characteristics of the most bothersome ocular symptoms according to treatment for ocular symptoms

	AR subjects not treated for ocular symptoms ($n = 428$), %	AR subjects treated for ocular symptoms ($n = 235$), %	p
The most bothersome ocular symptoms			<0.01
Itching eyes ($n = 339$)	47.7 ($n = 204$)	57.5 ($n = 135$)	
Watery eyes ($n = 256$)	43.2 ($n = 185$)	30.2 ($n = 71$)	
Red eyes ($n = 44$)	6.5 ($n = 28$)	6.8 ($n = 16$)	
Swollen eyelids ($n = 24$)	2.6 ($n = 11$)	5.5 ($n = 13$)	

Compared to nasal symptoms, ocular symptoms were more troublesome for 51.7% of subjects. Treated subjects were significantly more numerous to consider ocular symptoms more bothersome than nasal symptoms compared to untreated subjects (65.1 vs. 44.4%; $p < 0.01$). The troublesome ocular symptoms were: itching eyes (51.1%, $n = 339$), watery eyes (38.6%, $n = 256$), red eyes (6.6%, $n = 44$) and swollen eyelids (3.6%, $n = 24$), with a significant difference ($p < 0.01$) between treated and untreated subjects, as shown in table 2.

Trigger factors of ocular symptoms mostly reported were pollens (51.3%, $n = 340$), household dust and mites (34.8%, $n = 231$), pets (12.2%, $n = 81$) and air pollution (3.8%, $n = 25$). Pollens and pets were significantly more frequently reported in treated subjects than in untreated subjects (pollens: 63.0 vs. 44.9%, $p < 0.01$; pets: 16.2 vs. 10.1%, $p < 0.05$). Subjects who did not know which factor was responsible for their ocular symptoms were less numerous among treated than among untreated subjects (7.7 vs. 14.7%; $p < 0.01$).

Table 3. Impact of ocular symptoms on daily activities according to treatment

	AR subjects not treated for ocular symptoms (n = 428), %	AR subjects treated for ocular symptoms (n = 235), %	p
For the previous 12 months, in daily activities			<0.01
Terribly bothered	11.2 (n = 48)	17.9 (n = 42)	
Quite bothered	23.4 (n = 100)	28.5 (n = 67)	
Slightly bothered	35.3 (n = 151)	36.6 (n = 86)	
Not at all bothered	30.1 (n = 129)	17.0 (n = 40)	
During period with ocular symptoms			
Blurred sight	43.5 (n = 186)	55.7 (n = 131)	<0.01
Aggravation of symptoms with the wear of lenses	4.4 (n = 19)	9.4 (n = 22)	<0.05
Sleep disturbance	12.9 (n = 55)	22.6 (n = 53)	<0.01
Lack of efficacy at work	21.0 (n = 90)	34.5 (n = 81)	<0.01
Away from work	7.8 (n = 7)	18.5 (n = 15)	<0.05

The impact of ocular symptoms on daily activities was 'very important' or 'moderate' in 38.8% of subjects (n = 257). The sight was blurred in 47.8% of subjects (n = 317). A total of 16.3% of subjects (n = 108) had sleep disturbances. Regarding professional activities, efficacy was reduced in 25.8% of subjects (n = 171), and 12.9% of subjects (n = 22) were on sick leave because of their ocular symptoms for 1 (9.1%, n = 2), 2 (31.8%, n = 7) or ≥ 3 days (59.1%, n = 13). Significant differences in the impact of ocular symptoms on daily activities were observed between treated and untreated subjects, as shown in table 3.

Diagnosis and Follow-Up of Ocular Symptoms in the AR Population

Ocular symptoms were diagnosed by a doctor in 38.9% of subjects (n = 258) as seasonal allergic conjunctivitis (SAC, n = 98), allergic conjunctivitis (n = 61), not known (n = 29), ophthalmologic problems (n = 25), allergies (n = 16), others (n = 15), perennial allergic conjunctivitis (n = 14), AR (n = 4), atopic allergic keratoconjunctivitis (n = 4), acute allergic conjunctivitis (n = 4), vernal keratoconjunctivitis (n = 3) and sinusitis (n = 2). Moreover, 34.8% of subjects (n = 231) were followed up for their ocular symptoms more often by an ophthalmologist (n = 142), a general practitioner (n = 95) or an allergist (n = 26).

Medical Management of Ocular Symptoms in the AR Population

Treatment for ocular symptoms was prescribed in 35.4% of subjects (n = 235). Among 231 patients with a regular follow-up care, 61.9% (n = 143) received a prescription for ocular symptoms. No significant difference was observed between subjects with or without a regular

follow-up care according to the most prescribed treatments (H_1 non-cholinergic antihistamine 36%, antidegranulating eye drops 18%, H_1 cholinergic antihistamine 10%, and antihistaminic eye drops 8%).

A total of 143 subjects with a regular follow-up had given their opinion about their current treatment for ocular symptoms, listed in figure 2. The majority of them were satisfied (very satisfied 37.8%, satisfied 40.5%, moderately satisfied 15.4%, dissatisfied 4.2%, and very dissatisfied 2.1%).

Discussion

This large-scale epidemiological survey describes recent insights into AR-associated ocular symptoms. The French INSTANT study was conducted in a population-based sample following strict methods and using validated tools such as the SFAR to identify AR subjects.

In our study, 19% of individuals reported AR-associated ocular symptoms. This rate was consistent with the 16–20% reported in the literature for the prevalence of SAC in the general population [10]. The proportion of ocular symptoms (52%) that we found in AR patients was less than the 74% of AR subjects observed by Bousquet et al. [7]. The reason for this difference could be in part attributable to differences in recruitment. In fact, the DREAMS study was carried out in specialist practices in patients consulting for AR, in majority with a persistent form. Didier et al. [17] observed a rate of 66% of AR subjects who reported itching or tearing eyes during 230 telephone interviews. In a French survey enrolling 12,000 AR patients between 2003 and 2004, a lower frequency of

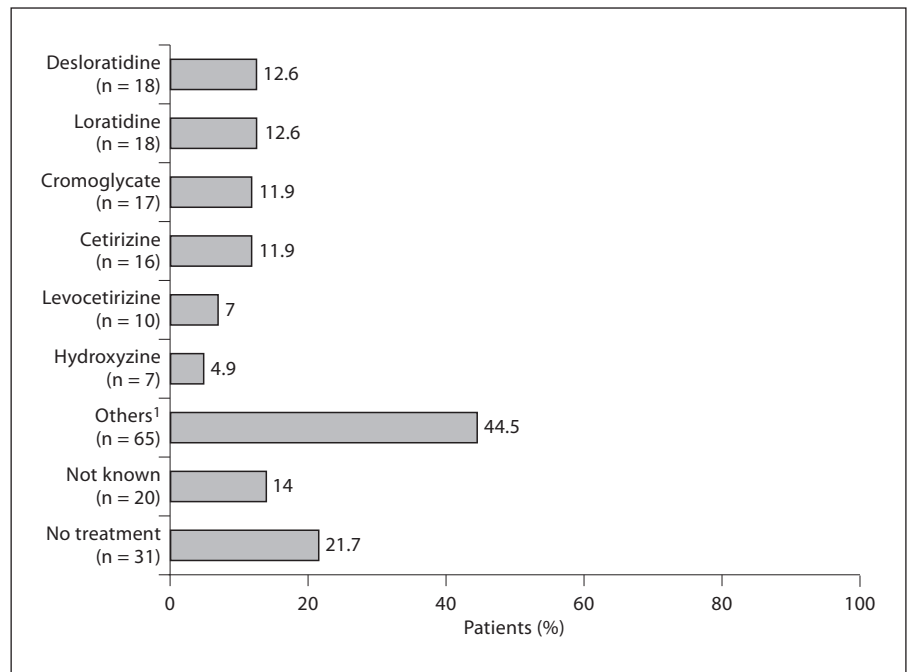


Fig. 2. Type of treatment for ocular symptoms in AR subjects (n = 143). ¹ Less than 4% of patients for each treatment. Patients could choose several treatments.

conjunctivitis was established by Demoly et al. [18], with a significant difference between AR patients seen by general practitioners and those seen by ear, nose and throat specialists (25.9 vs. 16.0%; $p < 0.0001$). As the burden of ocular symptoms was very high in AR patients during the pollen season (92% of subjects), we can conclude that the majority of people suffered from SAC. Such results are consistent with the 95% rate of AR-associated SAC patients [19]. However, the design of our study does not allow evaluating an under-diagnosis of ocular symptoms. In our study, only 38.9% of subjects had their ocular symptoms diagnosed by a doctor, including SAC (38%) and allergic conjunctivitis (24%), suggesting an underdiagnosis and underestimation of ocular symptoms in the AR population. It has been mentioned that only 10% of individuals with allergic eye symptoms seek out medical attention [12]. In the CESAR survey, ocular troubles were the reason for the return of 30% of patients included for consultation [8]. Additionally, pollen sensitization was reported in our study as the most frequent trigger factor of ocular symptoms (51%) before mite dust (35%) and pets (12%). Furthermore, ocular problems were reported by 51.7% of patients to be more bothersome than nasal problems. Recently, Mullol [9] found that 15.9% of AR patients reported either itchy-red eyes or watery eyes as the most troublesome symptom, whereas 55.7% of patients reported nasal symptoms to be the most troublesome. The most

troublesome ocular signs reported in our study were itching (51.1%) and tearing eyes (38.6%), percentages consistent with previous data. Thus, in the ERNANI French survey implemented between April and July 2005, Demoly et al. [20] showed that watery eyes affect about 46% of AR subjects. Moreover, itching and watery eyes were reported as bothersome symptoms by 53 and 51% of AR patients in a review published in 2007 [21], respectively.

The presence of ocular symptoms in addition to nasal symptoms impairs the QoL of AR subjects in meaningful ways, causing ocular discomfort, sleeping disorders, activity impairment and decreased vision, influencing work productivity and mental health [14]. QoL scores were significantly reduced in SAC subjects enrolled in two studies implemented in England and in Spain [12, 13]. The results presented here confirm that the negative impact of ocular symptoms extended to work productivity and the financial domain, with 25.8 and 12.9% of subjects who were less efficacious and on sick leave, respectively. Among 201 Spanish patients with SAC, slightly fewer than half of the respondents experienced reduced productivity and 20% reported taking time away from work [13]. Additionally, costs allocated to allergic conjunctivitis including absenteeism and reduced productivity were estimated at EUR 198/year and shown to be higher than those associated with AR [12, 13]. A USA study on 2,065 AR patients to whom a questionnaire on

work productivity was mailed revealed that their ability to engage in productive work was influenced by sleep quality, health-related QoL, specific symptoms (such as watery eyes and sneezes) and prescribed antihistamine use [22]. Our results reinforce these previous findings by clearly illustrating the negative impact of ocular symptoms on a patient's life, including 38.8% of subjects who were terribly and quite bothered in their daily activities, 47.8% with blurred sight and 16.3% with sleeping disorders.

Traditionally, treatment options for managing ocular symptoms when symptom relief fails with non-pharmacological interventions generally encompass both topical ophthalmic formulations and oral or intranasal supplement therapies in patients experiencing both nasal and ocular symptoms, necessitating thereby the use of multiple treatments [8, 23]. Emerging evidence has suggested that inhaled nasal corticoids have a positive class effect on AR-associated ocular symptoms and could provide sufficient improvement for both ocular and nasal symptoms [8, 23–25]. The reason for their effectiveness is not known and some hypotheses have been made about the nasal-ocular reflex [14, 25]. However, some data show seemingly conflicting effects of inhaled nasal corticoids on ocular symptoms, and additional head-to-head studies are needed to fully elucidate the benefit of inhaled nasal corticoids in managing ocular symptoms in AR subjects [25–27].

In the current study, treatment for ocular symptoms was prescribed in 35.4% of subjects and in 62% of subjects with regular follow-up care. The most prescribed treatments were H₁ antihistamines and antidegranulating eye drops. The results presented here show that treated subjects were significantly more numerous than untreated subjects to be bothered in their daily activities, have blurred sight, suffer from sleep disturbance, lack efficacy at work and are on sick leave, illustrating a correlation

between the impact on daily activities and prescription of treatment. Despite having received treatment for ocular symptoms, they persisted as a significant bothersome factor, indicating that these patients were probably poorly treated. In fact, the management of ocular symptoms was not found optimal in 21.7% of subjects who were not really satisfied with their current treatment. Moreover, treated patients in this sample exhibited a longer history of ocular symptoms compared to untreated patients (>5 years: 60.4% treated vs. 55.8% not treated; $p < 0.01$). These findings confirm that ocular symptoms associated with nasal symptoms in AR subjects have a relevant and significant negative impact on patients' lives. In particular, they highlight unmet medical needs for ocular symptoms in AR subjects, while ocular symptoms are considered more bothersome than nasal symptoms by the majority of treated patients and thereby suggest that better diagnosis and treatment of ocular symptoms could be beneficial to patients.

In conclusion, this survey suggested that AR-associated ocular symptoms are still neglected and undertreated in France. Ocular symptoms were reported by 19% of individuals in the overall population studied and by 52% in the AR population. Ocular symptoms had a negative impact on daily activities of AR subjects and were reported as more bothersome than nasal symptoms in a majority of AR patients. These findings highlight the necessity for primary care physicians to systematically seek ocular symptoms in AR subjects, questioning subjects about their history of ocular symptoms as well as about their nasal symptomatology.

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Online supplementary Fig. 1

Questionnaire for ocular symptom assessment

How long have you had your ocular problems?

<1year / from 1 to 2 years / from 2 to 5 years / > 5 years

In which of the past 12 months did you have ocular problems? (*multi-choice*)

January / February / March / April / May / June / July / August / September / October / November / December

Which ocular symptom is the most bothersome for you? (*in a decreasing order of importance: first, second and third*)

Watery eyes / Itching eyes / Red eyes / Swollen eyelids

Which are the most bothersome symptoms for you?

Nasal symptoms / Ocular symptoms

What trigger factors provoke or increase your ocular problems?

Pollen / Acarids / Household dust / Pets / Others (please specify) / None

In the past 12 months, have you been bothered by your ocular problems in your daily activities?

Terribly bothered / Quite bothered / Slightly bothered / Not at all bothered

When you have ocular problems,

- **Is your sight blurred?** (YES/ NO)

- **If you wear lenses, do you think that the wear of lenses aggravates your symptoms?** (YES/ NO)

- **Do you have sleep disturbance?** (YES/ NO)

- **Are you less effective at work?** (YES/ NO)

If yes, were you on sick leave? If yes, how many days?

Has a doctor already diagnosed that you suffer from ocular symptoms? (YES/ NO)

If yes, which one?

- allergic conjunctivitis
- seasonal allergic conjunctivitis
- perennial allergic conjunctivitis
- vernal keratoconjunctivitis
- atopic keratoconjunctivitis
- acute allergic conjunctivitis
- others (please specify)

Do you have a follow-up care for your ocular symptoms with a practitioner? (YES/ NO)

If yes, with a GP / Ophthalmologist / Allergologist / Other (please specify)

Have you already been prescribed a treatment for your ocular symptoms? (YES/ NO)

If yes, which ones?

How satisfied are you with the efficacy of your current treatment for ocular symptoms?

Very dissatisfied / Dissatisfied / Moderately satisfied / Satisfied / Very satisfied