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Assessment of the underreporting of rhinitis in patients with asthma: A MASK-air® real-world study

Bernardo Sousa-Pinto[a,b], Gilles Louis[c], Rafael José Vieira[a,b], Ana Margarida Pereira[a,d,e], Bilun Gemicioglu[f,g], Maciej Kupczyk[h], Violeta Kvedariene[i,j], Renaud Louis[k,l], Oliver Pfaar[m], João A. Fonseca[a,b], Torsten Zuberbier[n,o] and Jean Bousquet[n,o]

[a]MEDCIDS-Department of Community Medicine, Information and Health Decision Sciences, Faculty of Medicine, University of Porto, Porto, Portugal; [b]CINTESIS@RISE - Centre for Health Technology and Services Research, Health Research Network, Faculty of Medicine, University of Porto, Porto, Portugal; [c]Department of Public Health, University of Liège, Liège, Belgium; [d]PaCeIT – Patient Centered Innovation and Technologies, Center for Health Technology and Services Research (CINTESIS), Faculty of Medicine, University of Porto, Porto, Portugal; [e]Allergy Unit, Instituto and Hospital CUF, Porto, Portugal; [f]Department of Pulmonary Diseases, Cerrahpaşa Faculty of Medicin, Istanbul University-Cerrahpaşa, Istanbul, Turkey; [g]Institute of Pulmonology and Tuberculosis, Istanbul University-Cerrahpaşa, Istanbul, Turkey; [h]Department of Pediatric Respiratory Diseases and Allergology, Medical University of Warsaw, Warsaw, Poland; [i]Institute of Clinical Medicine, Clinic of Chest Diseases and Allergology, Faculty of Medicine, Vilnius University, Vilnius, Lithuania; [j]Institute of Biomedical Sciences, Department of Pathology, Faculty of Medicine, Vilnius University, Vilnius, Lithuania; [k]Department of Pulmonary Medicine, CHU, Liège, Belgium; [l]GIGA I3 Research Group, University of Liège, Liège, Belgium; [m]Department of Otorhinolaryngology, Head and Neck Surgery, Section of Rhinology and Allergy, University Hospital Marburg, Philipps-Universität, Marburg, Germany; [n]Department of Allergology, Institute of Allergology, Charité-Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Germany; [o]Department of Immunology and Allergology, Fraunhofer Institute for Translational Medicine and Pharmacology ITMP, Immunology and Allergology, Berlin, Germany

ABSTRACT

Rhinitis is a common comorbidity in patients with asthma. However, the frequency of underreported rhinitis in asthma is not known. In this study, we aimed to assess the characteristics of patients with self-reported asthma and no self-reported rhinitis, as well as the extent of the underreporting of rhinitis. We performed a cross-sectional study of all MASK-air® users (2015–2022, 27 countries), comparing reported symptoms and medication use in patients with (i) self-reported asthma without rhinitis ("asthma alone"), (ii) self-reported rhinitis+asthma and (iii) self-reported rhinitis without asthma ("rhinitis alone"). In patients reporting asthma alone and providing MASK-air® data in at least three different months, a cluster analysis was performed to potentially identify groups of patients underreporting rhinitis and/or undertreated for rhinitis. We assessed 35,251 users (529,751 days): 671 (1.9%) reporting asthma alone 25,882 (73.4%) reporting rhinitis alone and 8698 (24.7%) reporting rhinitis+asthma. Overall, 27% of the patients reporting asthma alone were treated with rhinitis medications. Patients reporting asthma alone displayed a lower frequency of days under rhinitis medication and less severe nasal symptoms than those reporting rhinitis+asthma. Among patients reporting asthma alone, three clusters of patients were identified: (A; 22.2%) severe rhinitis symptoms and low frequency of rhinitis medication use, (B, 41.0%) moderate rhinitis symptoms and high frequency of rhinitis medication use (41.0%), and (C, 36.8%) mild or no rhinitis symptoms and almost no rhinitis medication use. This study suggests that, among patients with self-reported asthma, the underreporting or undertreatment of rhinitis may be common.

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Asthma; mHealth; rhinitis

Introduction

Patients with asthma have a high prevalence of comorbid rhinitis, although variable estimates of such prevalence have been reported (from 60% to more than 80%).[1,2] This may be partly explained by different rhinitis definitions,[2] as well as by the underdiagnosis[3] and/or underreporting of symptoms.[4] Many patients, even those with a moderate disease, do not know that they suffer from rhinitis and do not receive any treatment. Even patients who are treated for allergic rhinitis may not report that they have rhinitis. However,

CONTACT Jean Bousquet jean.bousquet@orange.fr

the extent of underreported rhinitis in asthma is not known, and it is not known whether patients with asthma and without rhinitis may be different from those with rhinitis.

In this study, we used real-life data from an mHealth app (MASK-air®,[5] a Best Practice of OECD – Organisation of Economic Cooperation and Development)[6] to assess the characteristics of patients with self-reported asthma and no self-reported rhinitis (comparing them with patients with self-reported rhinitis with and without self-reported asthma), as well as the extent of the underreporting of rhinitis.

Methods

We performed a cross-sectional study of all MASK-air® users (2015–2022, 27 countries) over 16 years of age. We assessed three groups of patients on asthma symptoms and medication use, namely patients with (i) self-reported asthma without self-reported rhinitis (ii) self-reported rhinitis+asthma and (iii) self-reported rhinitis without self-reported asthma.

MASK-air® includes a daily monitoring questionnaire in which patients report (i) their daily rhinitis and asthma symptoms by means of 0–100 validated visual analogue scales (VASs) and (ii) their daily medication use.[5]

We compared the three groups of participants ("asthma without rhinitis", "rhinitis+asthma" and "rhinitis without asthma", classified based on self-reported information) on their symptoms and medication use by computing effect size measures to show the clinical relevance of the differences. Effect sizes (Cohen's d values) of 0.2–0.5 are considered to represent small effect sizes, 0.5–0.8 medium effect sizes and > 0.8 large effect sizes.

Subsequently, we performed a cluster analysis on patients reporting asthma alone to characterise them better. Following a previously described approach,[7] we considered patients reporting data in at least three different months (however, this did not imply following-up patients longitudinally, with the day continuing to be our unit of analysis). We used k-means clustering to identify groups of patients according to the use of rhinitis medication (considering the number of days each patient reported the use of rhinitis medication) and nasal symptoms (considering the three highest values of VAS nose). Clusters were compared on reported symptoms and medication use.

We did not calculate the sample size since we used all patients of the database. When responding to the MASK-air® daily questionnaire, it is impossible to skip questions and data are saved to the dataset only after the final answer. This precludes any missing data. All analyses were performed using the software R (version 4.0.0).

Results

We assessed 35,251 users (529,751 days): 671 (1.9%) with "asthma alone", 25,882 (73.4%) with "rhinitis alone" and 8698 (24.7%) with "rhinitis+asthma" (Table 1; Table A1).

Although many patients who did not report rhinitis had rhinitis symptoms and/or were treated using rhinitis medications, patients with "asthma alone" reported a lower number of nasal symptoms (median: 1, IQR: 2) than those with "rhinitis alone" (median: 3, IQR: 4) or "asthma+rhinitis" (median: 3, IQR 2, effect size = 1.35). Patients with "asthma alone" also reported a lower frequency of days with rhinitis medication (27.0%) than the other two groups ("rhinitis alone": 46.5%; "rhinitis+asthma": 62.2%; effect sizes ranging from 0.32 to 0.72). Patients with "asthma alone" also displayed meaningfully lower median VAS nose and eye levels than the remainder.

There were 144 users with "asthma alone" reporting MASK-air® data in at least three different months. We identified three clusters (Table A2; Figure 1):

- Cluster A ($N = 32$; 22.2% users): Patients displaying more severe rhinitis symptoms (median maximal VAS nose = 100; 41.9% days with partly controlled or uncontrolled rhinitis[8] and a low frequency of rhinitis medication use (65.6% patients without any days of medication). Of note, this was also the cluster with the highest median maximal VAS asthma (96 compared to 51 for the remaining clusters).
- Cluster B ($N = 59$; 41.0% users): Patients displaying moderate rhinitis symptoms (median maximal VAS nose = 56; 15.6% days with partly controlled or uncontrolled rhinitis) and a high frequency of medication use (all patients reported at least two days of rhinitis medication use).

Table 1. Characteristics of users self-reporting asthma alone, rhinitis alone and rhinitis with asthma.

	A	R	R+A	Effect sizes		
				R vs A	R vs R+A	A vs R+A
N users (%)	671	25,882	8698	-	-	-
Reported days – N (average days per user)	13,214 (19.7)	331,212 (12.8)	185,325 (21.3)	-	-	-
Females – N (%)	406 (60.5)	14,240 (55.0)	5395 (62.0)	0.11	0.14	0.03
Age – mean (SD)	42.1 (16.9)	37.3 (14.5)	40.5 (14.5)	0.30	0.22	0.10
N nasal symptoms reported at baseline – median (IQR)	1 (2)	3 (4)	3 (2)	1.35	0	1.35
Rhinitis medication reporting – N (%)						
0 days	490 (73.0)	13,854 (53.5)	3286 (37.8)	0.41	0.32	0.72
1 day	54 (8.0)	3669 (14.2)	1301 (15.0)	0.20	0.02	0.22
2 days	24 (3.6)	1786 (6.9)	797 (9.2)	0.15	0.08	0.23
3 or more days	103 (15.4)	6573 (25.4)	3314 (38.1)	0.25	0.27	0.52
Total days reporting rhinitis medication – N (%) [a]	5178 (39.2)	143,944 (43.5)	95,442 (51.5)	0.09	0.16	0.25
Oral antihistamines monotherapy	929 (7.0)	61,741 (18.6)	32,817 (17.7)	0.36	0.02	0.33
Intranasal corticosteroids monotherapy	1765 (13.4)	31,021 (9.4)	24,715 (13.3)	0.13	0.12	0
Azelastine-fluticasone monotherapy	1076 (8.1)	15,589 (4.7)	9527 (5.1)	0.14	0.02	0.12
Oral antihistamines + intranasal steroids	532 (4.0)	19,591 (5.9)	16,983 (9.2)	0.09	0.13	0.21
Azelastine-fluticasone + other rhinitis medication	505 (3.8)	10,463 (3.2)	8659 (4.7)	0.03	0.08	0.04
VAS nose						
Maximum value – median (IQR)	34 (55)	58 (56)	59 (51)	0.59	0.03	0.65
Median value – median (IQR)	14 (38)	35 (54)	31 (47)	0.68	0.11	0.62
Days with poorly controlled rhinitis (VAS>35) – N (%)	1697 (12.8)	73,703 (22.3)	39,356 (21.2)	0.25	0.03	0.23
Days with medium controlled rhinitis (VAS 21-35) – N (%)	1102 (8.3)	45,835 (13.8)	28,079 (15.2)	0.18	0.04	0.22
Days with well controlled rhinitis (VAS<21) – N (%)	10,415 (78.8)	211,674 (63.9)	117,890 (63.6)	0.33	0.01	0.34
Maximum CSMS – median (IQR)	29.5 (32.2)	33.4 (31.7)	42.6 (32.3)	0.17	0.39	0.55
Maximum VAS global – median (IQR)	39 (53)	54 (52)	58 (46)	0.38	0.11	0.51
Maximum VAS eyes – median (IQR)	13 (44)	28 (55)	37 (57)	0.51	0.23	0.74
Maximum VAS asthma – median (IQR)	41 (58)	4 (16)	40 (56)	1.21	1.21	0.02
Maximum VAS work – median (IQR)	19 (43)	29 (45)	36 (44)	0.34	0.21	0.58
Total days reporting asthma medication – N (%) [a]	8801 (66.6)	13,412 (4.0)	91,764 (49.5)	1.51	1.16	0.35
SABA	1363 (10.3)	2118 (0.6)	10,971 (5.9)	0.50	0.34	0.16
LABA+ICS	5682 (43.0)	4250 (1.3)	55,957 (30.2)	1.20	0.94	0.27
ICS	3563 (27.0)	7346 (2.2)	34,390 (18.6)	0.80	0.59	0.20
OCS	35 (0.3)	17 (0.01)	113 (0.1)	0.09	0.04	0.05
LAMA	513 (3.9)	678 (0.2)	3602 (1.9)	0.31	0.19	0.12
Biologics	420 (3.2)	3 (<0.01)	499 (0.3)	0.35	0.10	0.25

A: Self-reported asthma with no self-reported rhinitis; R: Self-reported rhinitis with no self-reported asthma; R+A: Self-reported rhinitis + self-reported asthma.

CSMS: Combined symptom-medication score; ICS: Inhaled corticosteroid; IQR: Interquartile range; LABA: Long-acting beta-agonist; LAMA: Long-acting muscarinic antagonist; OCS: Oral corticosteroid; SABA: Short-acting beta-agonist; VAS: Visual Analogue Scale.

[a]There are medication schemes other than those listed below.

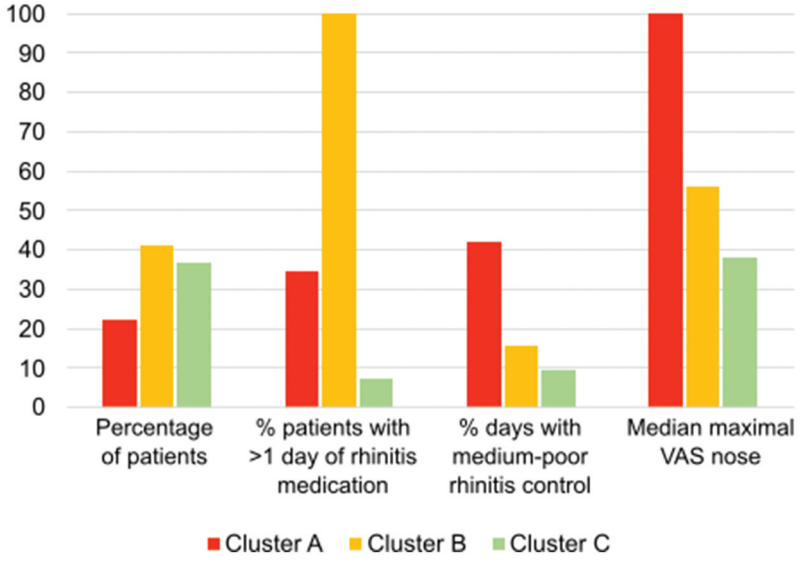

Figure 1. Rhinitis control in the three clusters of patients with self-reported asthma and no reported rhinitis.

- Cluster C ($N = 53$; 36.8% users): Patients displaying mild or no rhinitis symptoms (median maximal VAS nose = 38; 9.6% days with partly controlled or uncontrolled rhinitis) and almost no medication use (only 7.5% patients reported medication use). Twenty-three users (16.0% of all users reporting "asthma alone") did not report medication use and never reported a day of poor rhinitis control.

These clusters may be interpreted as corresponding to asthma with (A) uncontrolled and undertreated rhinitis, (B) treated but underreported rhinitis and (C) untreated mild or no rhinitis. Therefore, in almost two thirds of patients self-reporting asthma without self-reported rhinitis (clusters A and B), the underreporting of rhinitis is likely.

To account for seasonality, including only European patients who reported data for at least one month during the pollen season ($N = 78$), we identified similar results in the obtained clusters (Cluster A = 24.3% users, cluster B = 46.2% users, cluster = 29.5% users; Table A3).

Discussion

This study shows that many patients with self-reported asthma and without self-reported rhinitis have underreported and/or undertreated rhinitis. This high frequency of rhinitis in patients with asthma accords with previous studies.[9] In fact, in a smaller sample, we found that only one third of patients appear to have "asthma alone".

The major limitation of this paper is that many patients use MASK-air® for rhinitis. Thus, the number of patients reporting asthma alone may be low by comparison to the general population. However, this bias may have a lower impact, as this study does not aim to assess the prevalence of asthma alone. Another limitation is that we were unable to confirm these results in patients selected by physicians due to their low number (we were therefore unable to obtain any information on objective rhinitis assessments performed by physicians, such as results of atopy testing). However, in previous studies, we had found that patients with asthma selected by physicians have similar features to those in the full set of MASK-air® participants.[7]

This study has important clinical implications as it suggests that (i) only a minority of asthma patients do not have rhinitis and (ii) the prevalence of underreported rhinitis is high in patients with self-reported asthma alone (the question "do you have rhinitis?" is probably insufficient to diagnose rhinitis in these patients). In fact, our data suggest that only 16–37% of patients reporting asthma but no rhinitis may actually not have rhinitis. Additional strengths of this study include (i) the fact that the VASs used in MASK-air® have been validated,[10] (ii) the assessment of data available from 27 countries and (iii) the large number of included patients.

These results should be confirmed in other studies since observational studies are only hypothesis-generating. However, they do draw attention to the potential large extent of the underreporting and undertreatment of rhinitis.

Disclosure statement

JB reports personal fees from Cipla, Menarini, Mylan, Novartis, Purina, Sanofi-Aventis, Teva, Noucor, other from KYomed-Innov, other from Mask-air-SAS, outside the submitted work.

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ORCID

Ana Margarida Pereira http://orcid.org/0000-0002-5468-0932
Bilun Gemicioglu http://orcid.org/0000-0001-5953-4881
Jean Bousquet http://orcid.org/0000-0002-4061-4766

Author's contribution

BSP and GL did the analyses and paper writing.
RJV and AMP completed the analyses.
BG, MKUP, VK, RL and OP provided patients and help in the analysis of the paper.
JAF, TZ were major members of the think tank.
JB proposed the concept of the paper, participated in the analyses, and wrote the first draft of the paper.

Data sharing

Individual participant data underlying the results reported in this Article can be made available (after de-identification) between 12 and 36 months after Article publication. These data can be supplied to researchers who provide a methodologically sound proposal. Proposals should be directed to the corresponding author (jean.bousquet@orange.fr). We made every effort to follow the EU General Data Protection Regulation; therefore, we can transfer data only if there is a protocol and an agreement between the owner of the data and the person (or institution) requesting the data. To gain access, data requestors will need to sign a data access agreement.

Ethics committee

This is an observational study that does not need a specific ethics approval (analysis of anonymised data provided by participants who agree to have these data assessed in the terms of use of the app), considering that (i) an overall ethics approval for the use of MASK-air anonymised data for research purposes has been obtained (Köln-Bonn, Germany; 11 May 2017; N°17-069), (ii) all data were anonymised before the study, and (iii) users agree to the analysis of their data in the terms of use (translated into all languages and customised according to the legislation of each country).

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Appendix

Table A1. Distribution of observations per country.

Country	Data collection period	A – n (%)[a]	R – n (%)[a]	R+A – n (%)[a]	All observations – n (%)[b]
Argentina	2018–2022	55 (0.7)	6184 (82.2)	1285 (17.1)	7524 (1.4)
Australia	2016–2022	12 (0.4)	1715 (58.3)	1215 (41.3)	2942 (0.6)
Austria	2015–2022	92 (1.0)	6818 (76.4)	2020 (22.6)	8930 (1.7)
Belgium	2015–2022	3 (0.1)	1455 (58.1)	1047 (41.8)	2505 (0.5)
Brazil	2016–2022	306 (2.2)	9408 (69.0)	3925 (28.8)	13,639 (2.6)
Canada	2015–2022	12 (2.0)	459 (77.4)	122 (20.6)	593 (0.1)
Czech Republic	2017–2022	33 (0.4)	6217 (72.6)	2314 (27.0)	8564 (1.6)
Denmark	2015–2022	13 (0.8)	1213 (76.0)	371 (23.2)	1597 (0.3)
Finland	2015–2022	18 (0.3)	2666 (38.5)	4249 (61.3)	6933 (1.3)
France	2015–2022	473 (1.1)	31,584 (70.5)	12,767 (28.5)	44,824 (8.5)
Germany	2015–2022	832 (1.6)	33,230 (64.1)	17,753 (34.3)	51,815 (9.8)
Great Britain	2015–2022	51 (0.5)	6774 (71.9)	2594 (27.5)	9419 (1.8)
Greece	2015–2022	111 (0.9)	8463 (70.9)	3361 (28.2)	11,935 (2.3)
Hungary	2021–2022	65 (1.7)	3480 (91.0)	280 (7.3)	3825 (0.7)
Italy	2015–2022	1759 (3.0)	31,408 (54.3)	24,689 (42.7)	57,856 (10.9)
Japan	2019–2022	3 (0.04)	6304 (87.7)	881 (12.3)	7188 (1.4)
Lebanon	2021–2022	0	775 (98.4)	13 (1.7)	788 (0.2)
Lithuania	2015–2022	3560 (5.3)	37,378 (56.0)	25,766 (38.6)	66,704 (12.6)
Mexico	2015–2022	348 (0.4)	57,388 (68.0)	26,691 (31.6)	84,427 (15.9)
Netherlands	2015–2022	267 (2.1)	10,298 (79.2)	2433 (18.7)	12,998 (2.5)
Poland	2015–2022	2185 (6.7)	20,320 (62.5)	10,034 (30.8)	32,539 (6.1)
Portugal	2015–2022	1023 (3.1)	15,222 (46.6)	16,437 (50.3)	32,682 (6.2)
Slovenia	2020–2022	5 (0.2)	2415 (76.2)	748 (23.6)	3168 (0.6)
Spain	2015–2022	72 (0.2)	18,413 (55.8)	14,490 (43.9)	32,975 (6.2)
Sweden	2015–2022	155 (6.0)	984 (37.8)	1466 (56.3)	2605 (0.5)
Switzerland	2016–2022	148 (2.0)	4871 (66.8)	2272 (31.2)	7291 (1.4)
Turkey	2017–2022	1613 (12.0)	5770 (42.8)	6102 (45.3)	13,485 (2.6)

A: Self-reported asthma with no self-reported rhinitis; R: Self-reported rhinitis with no self-reported asthma; R+A: Self-reported rhinitis + self-reported asthma.

[a]Percentages having the total number of observations in each country as the denominator.

[b]Percentages having the total number of observations ($N = 529,751$) as the denominator.

Table A2. Clinical and demographic characteristics of patients reporting asthma alone in clusters A, B and C.

	Cluster A	Cluster B	Cluster C	Effect sizes		
				A vs B	A vs C	B vs C
N users (%)	32 (22.2)	59 (41.0)	53 (36.8)	-	-	-
Reported days – *N* (average days per user)	2349 (73.4)	6225 (105.5)	2975 (56.1)	-	-	-
Females – *N* (%)	19 (59.4)	35 (59.3)	29 (54.7)	0	0.09	0.09
Age – mean (SD)	29.4 (16.1)	45.7 (14.6)	47.2 (17.4)	1.06	1.06	0.09
N nasal symptoms reported at baseline – median (IQR)	2 (3)	2 (3)	0 (2)	0.17	0.78	0.62
Rhinitis medication reporting – *N* (%)						
0 days	21 (65.6)	0	49 (92.5)	1.89	0.70	2.59
1 day	3 (9.4)	0	4 (7.5)	0.62	0.55	0.07
2 days	0	6 (10.2)	0	0.65	0	0.65
3 or more days	8 (25.0)	53 (89.8)	0	1.44	1.05	2.49
Total days reporting rhinitis medication – *N* (%) [a]	329 (14.0)	4502 (72.3)	4 (0.1)	1.27	0.70	1.97
Oral antihistamines monotherapy	255 (10.9)	460 (7.4)	2 (0.1)	0.12	0.61	0.49
Intranasal corticosteroids monotherapy	10 (0.4)	1704 (27.4)	1 (0.03)	0.98	0.09	1.07
Azelastine-fluticasone monotherapy	9 (0.4)	1036 (16.6)	0	0.71	0.13	0.84
Oral antihistamines + intranasal steroids	1 (0.04)	505 (8.1)	0	0.54	0.04	0.57
Azelastine-fluticasone + other rhinitis medication	0	503 (8.1)	0	0.57	0	0.57
VAS nose						
Maximum value – median (IQR)	100 (14)	56 (42)	38 (40)	2.00	2.95	0.59
Three highest values – median (IQR)	97 (22)	35 (34)	22 (34)	3.22	4.37	0.51
Days with poorly controlled rhinitis (VAS>35) – *N* (%)	807 (34.4)	436 (7.0)	93 (3.1)	0.72	0.90	0.18
Days with medium controlled rhinitis (VAS 21-35) – *N* (%)	176 (7.5)	533 (8.6)	193 (6.5)	0.04	0.04	0.08
Days with well controlled rhinitis (VAS<21) – *N* (%)	1366 (58.2)	5256 (84.4)	2689 (90.4)	0.59	0.78	0.18
Maximum CSMS – median (IQR)	71.9 (35.1)	41.8 (31.6)	27.3 (22.2)	1.28	2.12	0.75
Maximum VAS global – median (IQR)	100 (22)	55 (48)	34 (38)	1.72	3.31	0.64
Maximum VAS eyes – median (IQR)	87 (44)	32 (51)	17 (29)	2.02	3.29	0.54
Maximum VAS asthma – median (IQR)	96 (22)	51 (50)	51 (46)	1.76	1.76	0
Maximum VAS work – median (IQR)	75 (39)	37 (38)	19 (40)	1.22	2.16	0.70
Total days reporting asthma medication – *N* (%) [a]	1025 (43.6)	5104 (82.0)	1764 (59.3)	0.82	0.32	0.51
SABA	252 (10.7)	538 (8.6)	399 (13.4)	0.07	0.08	0.15
LABA+ICS	728 (31.0)	2738 (44.0)	1612 (54.2)	0.27	0.47	0.20
ICS	243 (10.3)	2621 (42.1)	439 (14.8)	0.76	0.14	0.62
OCS	17 (0.7)	0	17 (0.6)	0.17	0.01	0.16
LAMA	143 (6.1)	214 (3.4)	119 (4.0)	0.13	0.10	0.03
Biologics	39 (1.7)	272 (4.4)	100 (3.4)	0.16	0.11	0.05

CSMS: Combined symptom-medication score; ICS: Inhaled corticosteroid; IQR: Interquartile range; LABA: Long-acting beta-agonist; LAMA: Long-acting muscarinic antagonist; OCS: Oral corticosteroid; SABA: Short-acting beta-agonist; VAS: Visual Analogue Scale.
[a]There are medication schemes other than those listed below.

Table A3. Characteristics of patients reporting asthma alone in clusters A, B and C (subanalysis of European patients who reported data in at least one month of the pollen season).

	Cluster A	Cluster B	Cluster C
N users (%)	19 (24.4)	36 (46.2)	23 (29.5)
Reported days – *N* (average days per user)	1659 (87.3)	5226 (145.2)	1858 (80.8)
Rhinitis medication reporting – *N* (%)			
0 days	11 (57.9)	0	20 (87.0)
1 day	2 (10.5)	0	3 (13.0)
2 days	0	1 (2.8)	0
3 or more days	6 (31.6)	35 (97.2)	0
VAS nose			
Maximum value – median (IQR)	100 (14)	57 (40)	36 (37)
Three highest values – median (IQR)	98 (20)	42 (39)	17 (30)
Days with poorly controlled rhinitis (VAS >35) – *N* (%)	375 (22.6)	178 (3.4)	47 (2.5)
Days with medium-controlled rhinitis (VAS 21-35) – *N* (%)	98 (5.9)	379 (7.3)	128 (6.9)
Days with well-controlled rhinitis (VAS <21) – *N* (%)	1186 (71.5)	4669 (89.3)	1683 (90.6)

IQR: Interquartile range; VAS: Visual Analogue Scale.