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Article type : Original article

Behavioural patterns in allergic rhinitis medication in Europe: A study using MASK-air® real-world data

Running title: Allergic rhinitis medication patterns across Europe

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Abstract

Background: Co-medication is common among patients with allergic rhinitis (AR), but its dimension and patterns are unknown. This is particularly relevant since AR is understood differently across European countries, as reflected by rhinitis-related search patterns in Google Trends. This study aims to assess AR co-medication and its regional patterns in Europe, using real-world data.

Methods: We analysed 2015-2020 MASK-air® European data. We compared days under no medication, monotherapy, and co-medication using the visual analogue scale (VAS) levels for overall allergic symptoms ("VAS Global Symptoms") and impact of AR on work. We assessed the monthly use of different medication schemes, performing separate analyses by region (defined geographically or by Google Trends patterns). We estimated the average number of different drugs reported *per* patient within one year.

Results: We analysed 222,024 days (13,122 users), including 63,887 days (28.8%) under monotherapy, and 38,315 (17.3%) under co-medication. The median "VAS Global Symptoms" was 7 for no medication days, 14 for monotherapy and 21 for co-medication ($p<0.001$). Medication use peaked during the spring, with similar patterns across different European regions (defined geographically or by Google Trends). Oral H_1-antihistamines were the most common medication in single and co-medication. Each patient reported using an annual average of 2.7 drugs, with 80% reporting two or more.

Conclusions: AR medication patterns are similar across European regions. One third of treatment days involved co-medication. These findings suggest that patients treat themselves according to their symptoms (irrespective of how they understand AR), and that co-medication use is driven by symptom severity.

Keywords: Allergic rhinitis; Co-medication; MASK-air; Visual analogue scales

Introduction

Allergic rhinitis (AR) is the most common disease in Europe[1], but it appears to be understood differently by individuals from different countries. An infodemiology study using Google Trends showed that different keywords defining AR (hay fever, allergy or pollen) are used differently between European countries. In fact, there are clusters of online search patterns on rhinitis-related terms, suggesting cultural differences.[2] Interestingly, whichever keyword is used, a clear seasonal pattern can be observed in online searches following pollen exposure.[2-4]

Cultural differences in AR assessment – along with differences in drug availability and cost – may be reflected in differences in medication use. A recent study showed major differences between countries in terms of rhino-conjunctivitis medication usage.[5] Despite the existence of AR treatment guidelines, their indications appear to be insufficiently followed by patients.[6] Patients increase their medications when needed in order to control their symptoms.[7,8] However, the seasonality and patterns of co-medication have not yet been investigated. Assessing real-world patterns of medication use is, therefore, essential for drafting recommendations that are evidence-based and that take patients' needs into account[9].

Mobile health apps can be a valuable source of real-world data. In AR, MASK-air® is an example of such an app. It comprises a daily monitoring questionnaire in which patients are requested to quantify the impact of their AR symptoms on that day, as well as to provide information on the medication used.[10,11] MASK-air® is available in 18 European countries, allowing for regional differences to be assessed. There are many unanswered questions that can be addressed using MASK-air® data, including the seasonal patterns of medication use in different European countries.

Therefore, in this study, we aimed to use real-world data from MASK-air® to assess AR medication patterns in Europe in order to assess whether such patterns were similar across European regions and were in accordance with AR guidelines. In particular, we assessed (i) the most commonly used medication classes and the frequency of co-medication use, (ii) seasonal patterns of medication use, and (iii) variation of medication use between European countries grouped either by geographical region or by clusters associated with cultural differences (i.e., clusters of online search patterns of rhinitis-related terms).

Methods

Study design

We performed a cross-sectional descriptive analysis of the different medication schemes reported to be used in the daily monitoring of MASK-air® in European regions. We described the frequency of use of each

medication group, and of co-medication. To assess whether medication use followed any seasonal pattern, we assessed the monthly use of the different medication groups. We estimated the number of different drugs at the patient level throughout a period of 12 months.

Setting and participants

MASK-air® has been available since 2015 and can be downloaded via the Apple App and Google Play Stores of 27 countries (www.mask-air.com).[10] According to methods previously described[12,13], we included the daily monitoring data from European MASK-air® users (18 different countries) from May 21, 2015 to December 6, 2020. The users were aged 16-90 years and had a self-reported diagnosis of allergic rhinitis. There were no exclusion criteria.

Countries in Europe were grouped using two different classifications, namely (i) three different European regions (Southern, Central-West and Northern-East) according to their seasonal exposure to allergens, and (ii) four groups based on a previous study using Google Trends by cultural clusters.[2]

Ethics

MASK-air® has a CE1 marking. It follows the GDPR regulations.[14] All data are anonymised (including data related to geolocation) using k-anonymity[15]. An independent Review Board approval was not required since the study is observational, and users agreed to the analysis of their data in the terms of use.

Data sources and variables

MASK-air®

The MASK-air® daily monitoring questionnaire comprises five mandatory questions assessing the impact of AR by means of visual analogue scales (VASs) ranging from 0 to 100 (Supplementary Table 1). In addition, users are asked to enter their daily medications using a regularly-updated scroll list that contains country-specific prescribed and OTC medications (the International Nonproprietary Names (INN) classification is used for drug nomenclature[16]). This enables medications to be clustered in groups (e.g., oral H1-antihistamines - OAH, intranasal corticosteroids - INCS). When responding to the MASK-air® daily monitoring questionnaire, it is not possible to skip any of the questions, and data is saved to the dataset only after the final answer. This therefore precludes any missing data.

Selection of medications

In order to more closely follow the patients' perspectives, monotherapy was defined as days when only one single drug formulation for AR was reported, even if with more than one active compound[7,8,13] (for example, nasal azelastine-fluticasone – AzeFlu – contains two drugs but, as it is a fixed combination, it was considered as monotherapy). Co-medication was defined as days with two or more drug formulations for AR. Asthma medications were not considered in co-medication. Allergic rhinitis medications were classified into seven groups (Supplementary Table 2).

Size of the study

In this study, data from all registered European users were included. No sample size calculation was performed.

Biases

There are potential information biases related to the self-reported nature of data collection. Potential selection biases might be introduced because app users are not representative of all patients with AR (e.g., there may be an overrepresentation of users suffering from moderate-to-severe AR[8], and of younger individuals who may be more familiar with apps). Finally, it is not known whether users fill in the MASK-air® daily monitoring questionnaire before or after treatment for a given day.

Analysis of the data

As previously published[7,8,13], we studied the full dataset of users meeting the eligibility criteria. We computed the frequency of three medication schemes: observations under no medication, monotherapy (including frequency of use of each medication group as defined above) and co-medication. For each medication group or combination, we computed the median VAS Global allergy symptoms (VAS assessing on a 0-100 scale how much allergic symptoms are bothering the patient on that day), as well as the median VAS Work (VAS assessing on a 0-100 scale the impact of allergic symptoms on work that day) and the respective confidence intervals.

To assess whether medication use followed any seasonal pattern, we analysed the monthly use of different medication groups and co-medication schemes.

To address across-Europe diversity, we performed separate analyses with data from Southern European countries (Greece, Italy, Portugal, and Spain), Central-Western European countries (Belgium, France, and Switzerland), and Northern-Eastern European countries (Austria, Czech Republic, Denmark, Finland, Germany, Lithuania, Netherlands, Poland, Slovenia, Sweden, and the United Kingdom). In addition, we performed separate analyses with European countries grouped as defined by clusters on search patterns

(assessed by Google Trends) for rhinitis and related terms (such clusters are displayed in Supplementary Table 3 and had been previously defined by Bousquet et al.[2]).

Subsequently, we compared the frequency of the different medication groups and co-medication schemes during and outside the pollen season (as defined by Bédard et al.).[8] Between-season differences were compared by computing Cohen's *h* [17]. We assumed that values between 0.2 and 0.5 correspond to small effect sizes (differences), values between 0.5 and 0.8 to moderate differences, and values over 0.8 to large differences.

Finally, we analysed medication schemes at the patient level, assessing the frequency of different medication groups within the period of one year. For this analysis, we included observations from patients who had registered medication use in at least four different months over the period of one year (namely over the first twelve months after starting the MASK-air® app). Observations of the remaining patients were excluded, being too scarce or too concentrated in a small amount of time, potentially biasing results.

Categorical variables were analysed using absolute and relative frequencies. Continuous variables were analysed using medians and interquartile ranges (IQR), with comparisons being performed using hierarchical regression models clustered by patient. *P*-values<0.05 were considered to indicate statistically significant associations. All analyses were performed using the software R (version 4.0.0.).

Results

We analysed 222,025 days, of which 102,202 (46.0%) involved the use of at least one medication. These days were provided by a total of 13,122 users aged 16 to 90 years. There were 113,401 (51.1%) observations from women, and the mean age of users was 39.3 ± 13.5 years (Supplementary Figure 1). Most days were from Northern East Europe (*n*=114,488; 51.6%), followed by Southern Europe (*n*=87,577; 39.4%) and Central West Europe (*n*=19,960; 9.0%) (Supplementary Table 4).

Medication use

On 119,823 days (54.0% of total days), no medication was used, compared to 63,887 days (28.8%) of monotherapy, and 38,315 days (17.3%) of co-medication.

Monotherapy days most commonly involved the use of OAH monotherapy (34,481 days; 54.0%), INCS monotherapy (13,050 days; 20.4%), or AzeFlu (8,928 days; 14.0%) (Table 1). Regarding co-medication,

the use of OAH and INCS on the same day (10,974 days; 28.6%) occurred more frequently than other combinations. Frequencies of the medication groups by region are available in Supplementary Table 5.

The median VAS Global allergy symptoms for co-medication days was 21 (IQR=36) *versus* 14 (IQR=23) for monotherapy days, and 7 (IQR=22) for non-medication days ($p<0.001$). A similar pattern was observed for VAS Work, with a median value of 15 (IQR=30) for co-medication days, compared to 10 (IQR=23) for monotherapy days, and 4 (IQR=16) for non-medication days ($p<0.001$).

Seasonality of medication

By analysing monthly data, we observed that the peak of medication use occurred during the spring. The percentage of days in which medication was reported reached its maximum in June (54.5%) and its minimum in January (34.9%) (Figure 1; Figure 2A; Supplementary Figure 2). The lowest percentage of days with co-medication was registered in January (11.6%), and the highest in April (21.7%) (Figure 2). Consistent results were observed when analysing data separately (i) from the different geographical regions, (ii) from different regions as defined by the online search patterns of rhinitis-related terms (Supplementary Figure 3), and (iii) from individual countries (Figure 3).

During the pollen season, the frequency of days without any medication was lower than outside the pollen season (47.0% *versus* 60.3%; Cohen's h=0.27) (Supplementary Table 6).

Medication use at patient level

A total of 975 patients were identified as having reported medications in at least four months over the period of one year (Table 2; Supplementary Table 7 for results presented by region). During that period, each patient reported 2.7 ± 1.5 (mean ± standard-deviation) different drugs. Two or more different drugs were reported by 779 (79.9%) patients. Approximately three-quarters of the patients (n=729; 74.5%) reported drugs from more than one group (mean ± standard-deviation: 2.1± 0.9). Most assessed patients (n=709; 72.5%) reported at least one day with co-medication.

Discussion

In this study, we observed that in Europe, for AR treatment, (i) OAH are the most commonly used medications in monotherapy, with their use peaking in spring, (ii) co-medication is common and follows a seasonal pattern that resembles that of OAH monotherapy, (iii) the reporting of the major medication groups follows similar patterns across the different European regions (despite cultural differences reflected in online search patterns for rhinitis-related terms), and (iv) the use of different medications (of the same or

of a different group) by the same patient throughout the year is common, suggesting self-medication and that patients overall do not follow indications by guidelines.

The first major finding of the study is the disconnection between the patients' variable perception of AR across countries and their similar therapeutic response to pollen exposure. Internet data are being increasingly integrated into health research and are becoming a useful tool for exploring human behaviour. The most popular tool for examining online behaviour is Google Trends[18,19]. A previous study assessing Google Trends terms related to allergy and rhinitis in European countries (2011-2016)[2] identified an annual and clear seasonality of queries in most countries during spring. However, the keywords "hay fever", "allergy", and "pollen" were found to demonstrate seasonality differently depending on the country, suggesting cultural differences.[2] In the present study, we found no major difference in medication seasonality in the different clusters of countries when considered in cultural clusters determined by Google Trends (or in geographical clusters).[2] One may hypothesize that the similar behaviour of MASK-air® users towards medication use across Europe during increased pollen exposure might be related to similarities in medication prescriptions. However, in a previous study, specifically designed to understand physicians' prescription patterns in different European countries, we observed that prescribed medications were significantly different between France (high INCS), Poland and Spain (medium INCS prescriptions), and Germany and Italy (low INCS prescriptions). That is, in countries with similar reported medication use behaviour during the pollen season (as observed in this study), different prescription patterns appear to be observed, suggesting that patients may not completely follow the physicians' prescriptions.

Secondly, as proposed earlier, but better assessed in this study,[7,8,20] patients attempt to control their disease by increasing medications, and by self-medicating with OTC medications. In this study, with a larger number of participants, the median level of VAS Global allergy symptoms increased from no treatment to one medication and multiple medications, with the highest value being associated with the use of over 4 medications on the same day. During the course of their disease, patients often use several medications of the same group. These two results reinforce the conclusion that patients do not follow the physicians' prescriptions and attempt to control their disease by increasing medications. [6,21,22]

Thirdly, most patients do not appear to follow the recommendations stated in guidelines. In fact, guidelines indicate that a combination of OAH and INCS does not increase the efficacy of INCS. Moreover, although OAH are important in patients with mild to moderate disease, and control a large group of allergic patients, they are not usually very effective in more severe cases. Thus, the largest increase in OAH during the pollen season with or without INCS suggests that patients do not follow guidelines. Overall, these findings imply that, across Europe, AR medication use is not guideline-driven, but rather symptom-driven (i.e., patients appear to use, increase or try different medications when feeling worse), although medication costs

and healthcare access – which we were not able to assess – may in some cases also influence medication patterns. This finding has important implications for clinical practice – clinicians should have this in mind when discussing the therapeutic management of AR with their patients, so as to increase the chances of a more effective therapeutic plan. Of note, the observed erratic medication pattern does not appear to increase control. This is difficult to truly assess with this methodology, but there is an urgent need to revise guidelines using real-world data to align the patients' needs and behaviour with recommendations, as was proposed recently by ARIA.[9] Moreover, value-added medicine is needed for a change in AR management stressing the importance of *pro re nata* treatment versus long-term treatment that is almost never used by AR patients.[23]

Our findings also point to unmet needs in research. For example, trials in a pollen exposure chamber can be performed to determine whether a subpopulation of more severely affected patients will benefit more from co-medication or up-dosing. Furthermore, real-life studies are needed to assess whether there is a trend of more patients presenting with more severe symptoms. This is related to the concept of "severe chronic upper airways diseases" (associated with different forms of upper airways diseases such as AR and non-allergic rhinitis)[24], in which patients have impaired quality-of-life, social functioning, sleep, and school/work performance, prompting the need for a precise diagnosis. A further assessment on the influence of asthma medication on rhinitis medication use should also be the focus of future studies. On a preliminary analysis, despite similarities in seasonal patterns, the use of AR medication (particularly in co-medication) appears to be more common in days when asthma medication is also used, with the latter also tending to significantly associate with lower VASs compared to no asthma medication days (Supplementary Table 8).

This study has limitations that are worth noting. Due to its cross-sectional design, we are not able to establish a temporal relationship between reported symptoms and medication use. That is, we do not know whether users provide information in their daily monitoring questionnaire on symptoms concerning only the period prior to medication use. Considering this limitation, and the need for specific methods addressing confounders and multiple observations reported by individual patients, assessing the effectiveness of specific medication groups was beyond the scope of this study. Nevertheless, future studies using such methods may be performed aiming at comparing differences in VAS across medication groups. Another limitation concerns the possibility of information biases, associated not only with the fact that AR in MASK-air® has been self-reported but also with the underreporting of medication use. While possibly resulting in an underestimation of co-medication days, this latter phenomenon is probably non-differential in terms of region or season. Underestimation of medication/co-medication use may also stem from the exclusion of cases for which there was no information on whether steroids were used for AR or asthma

(e.g., cases for which the only information available was the active compound of a steroid that can be used both in a nasal or inhaled formulation). Also, European MASK-air® users are not fully representative of European patients with AR, posing generalisability concerns. For example, geriatric patients may need some support and training to use mobile apps, which may affect the results of the study for this age group. Finally, there are limitations related to app adherence among MASK-air® users, with each user reporting an average of 17 days. To overcome such limitations, we performed a sensitivity analysis restricted to those users reporting at least 50 days of data in MASK-air® (980 users; 148,891 days; average of 152 days per user), observing similar seasonal patterns and frequency of medication group use compared to the main analysis (Supplementary Table 9).

This study also has important strengths. In fact, it used real-world data to assess the medication patterns of AR patients in different European countries. This aim has led us to consider among monotherapy days those when patients use a single AR drug formulation with more than one active compound – in the patient perspective, on those days, he/she is using a single drug. The daily monitoring questionnaire of MASK-air® provides a comprehensive list of available medications for each country (including commercial names), reducing the risk of information biases. In addition, the structure of the MASK-air® app precludes the existence of missing data within each daily monitoring questionnaire. Finally, the VASs used in MASK-air® have been compared to validated questionnaires and were found to have moderate-high validity, reliability and responsiveness[25].

In conclusion, medication patterns in patients with AR appear to be similar across European regions, with co-medication being common and presenting a seasonal pattern (particularly frequent during spring). All these findings suggest that AR patients treat themselves according to their symptoms, not following the guidelines' indications for AR treatment. However, they also suggest that patients apparently need co-medication according to the severity of their symptoms. This paper is essential for the future ARIA guidelines as they will be based on real-world data and evidence-based medicine, rather than only on evidence-based medicine. This study carried out in different European countries shows that guidelines are not used. Thus, this paper has a major clinical impact. Physicians should be aware that most of their patients do not follow their prescriptions and should adapt shared-decision making when discussing treatment options with them.

Conflict of interest :

IAnsotegui reports personal fees from Hikma, Roxall, Astra Zeneca, Menarini, UCB, Faes Farma, Sanofi, Mundipharma, Bial, Amgen, Stallergenes, Abbott, BayerJB reports personal fees from Chiesi, Cipla, Hikma, Menarini, Mundipharma, Mylan, Novartis, Sanofi-Aventis, Takeda, Teva, Uriach, other from KYomed-Innov, personal fees from PurinaVC reports personal fees from Allergopharma, GSK, grants from Thermofisher
AC reports grants and personal fees from GSK, personal fees from AstraZeneca, Sanofi, Boehriger Ingelheim, Eurofarma
TH reports personal fees from GSK, Mundipharma, Orion Pharma, and Sanofi
JCI reports personal fees from Laboratorios Casasco, Abbott Ecuador, Sanofi, Bago Bolivia, Eurofarma Argentina
MJ reports personal fees from ALK-Abello, Allergopharma, Stallergenes, Anergis, Allergy Therapeutics, Leti, HAL, GSK, Novartis, Teva, Takeda, Chiesi
PK reports personal fees from Adamed, AstraZeneca, Berlin Chemie Menarini, Boehringer Ingelheim, Lekam, Mylan, Novartis, GSK, Polpharma
VK reports other from Berlin CHemie Menarini, Norameda
DLL reports personal fees from Allakos, Amstrong, Astrazeneca, DBV Technologies, Grunenthal, GSK, Mylan/Viatris, Menarini, MSD, Novartis, Pfizer, Sanofi, Siegfried, UCB, Alakos, Gossamer, Carnot, grants from Sanofi, Astrazeneca, Novartis, Circassia, UCB, GSK, Purina institute
RL reports grants from GSK, grants and personal fees from AZ, Novartis, Chiesi
MM reports personal fees from Menarini, Mylan, GSK, Astra Zeneca, Novartis, Chiesi, Sanofi, Pfizer
RM reports personal fees from ALK, allergopharma, Allergy Therapeutics, Friulchem, Hexal, Servier, Klosterfrau, Bayer, FAES, GSK, MSD, Johnson&Johnson, Meda, Stada, UCB, Nuvo, Menarini, Mundipharma, Pohl-Boskamp,grants from ASIT biotech, Leti, Optima, BitopAG, Hulka, Ursapharm, Inmunotek, grants and personal fees from Bencard, Stallergenes, grants, personal fees and non-financial support from Lofarma, non-financial support from Roxall, Atmos, Bionorica, Otonomy, Ferrero, personal fees and non-financial support from Novartis
JM reports personal fees and other from SANOFI-GENZYME & REGENERON, NOVARTIS, ALLAKOS, grants and personal fees from MYLAN Pharma, URIACH Group, personal fees from Mitsubishi-Tanabe, Menarini, UCB, AstraZeneca, GSK, MSD
OP reports grants and personal fees from ALK-Abelló, Allergopharma, g Stallergenes Greer, HAL Allergy Holding B.V./HAL Allergie GmbH, Bencard Allergie GmbH/Allergy Therapeutics, Lofarma, grants and personal fees from ASIT Biotech Tools S.A., Laboratorios LETI/LETI Pharma, Anergis S.A., GlaxoSmithKline, personal fees from Astellas Pharma Global, personal fees from EUFOREA, ROXALL Medizin, Novartis, Sanofi-Aventis and Sanofi-Genzyme, Med Update Europe GmbH, streamedup! GmbH, Mobile Chamber Experts (a GA2LEN Partner), Indoor Biotechnologies, MEDA Pharma/MYLAN, John Wiley and Sons, AS, Paul-Martini-Stiftung (PMS), Ingress-Health HWM, Regeneron Pharmaceuticals Inc., grants from Pohl-Boskamp, Inmunotek S.L., Biomay, Circassia
FSR reports speaker and advisory fees from AstraZeneca, Novartis, Sanofi, GSK, Teva and Lusomedicamenta, all outside the submitted work.
JS reports grants and personal fees from SANOFI, personal fees from GSK, NOVARTIS, ASTRA ZENECA, MUNDIPHARMA, FAES FARMA
ATB reports grants and personal fees from Novartis, Mundipharma, Teva Pharma, GSK (GlaxoSmithKline), AstraZeneca, grants from Leti, personal fees from Bial
STS reports personal fees from ERT, Roche products, Novartis, Sanofi Pharma, AstraZeneca, ALK-Abelló, grants from Glaxo Smith Kline,
IT reports personal fees from Honoraria for educational activities, speaking engagements, advisory boards from Boehringer Ingelheim, Astra Zeneca, GSK, Novartis, MSD and grants from GSK Hellas Astra Zeneca, and Elpen
DW reports personal fees from ALK, Optinose, and was a primary author on the JTFPP Rhinitis Practice Parameter Update 2020.
TZ reports Organizational affiliations: Commitee member: WHO-Initiative "Allergic Rhinitis and Its Impact on Asthma" (ARIA), Member of the Board: German Society for Allergy and Clinical Immunology (DGAKI), Head: European Centre for Allergy Research Foundation (ECARF) President: Global Allergy and Asthma European Network (GA2LEN), Member: Committee on Allergy Diagnosis and Molecular Allergology, World Allergy Organization (WAO)

Author contribution statement:

BSP, ASS, RJV, RA performed the analyses
LK, OP, VK, MTV, KCB, LB, GWC, VC, PCM, LC, CC, AAC, GDF, WJF, BG, TH, JCI, PK, HK, DELL, RL, MM, RM, MMA, RM, JM, YO, NGP, VP, NPT, FSR, SR, PWR, BS, MS, ATB, LTB, PVT, STS, SJ, AV, SW, AY, MZ participated to the patients recruitment
JB, WC, JMA, AB, TZ, JAF designed the study

467 JB and BSP wrote the paper

468 IJA, TC, TC, DKC, EMC, PD, MG, ZI, MJ, IK, DL, BL, MO, IT, [OV], DW are members of the think tank MAKK-air

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471 **Fundings : MASK**

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Tables

Table 1. Characteristics of observations/days under each medication scheme.

Medication scheme	*N* observations (%)	VAS Global Symptoms – median [95%CI] (IQR)	VAS Work – median [95%CI] (IQR)
No medication	119,823 (54.0)	7 [7-7] (22) [a]	4 [4-4] (16) [b]
Monotherapy	63,887 (28.8)	14 [14-14] (23) [a]	10 [9-10] (23) [b]
INAH [c]	529 (0.2)	26 [25-28] (43)	20 [18-22] (27)
Ocular AH [c]	637 (0.3)	19 [17-22] (32)	13 [10-15] (27)
OAH [c]	34,481 (15.5)	16 [15-16] (31)	11 [10-11] (24)
INCS	13,050 (5.9)	11 [11-12] (20)	9 [9-10] (19)
Oral steroid	575 (0.3)	33 [31-35] (26)	22 [16-28] (39)
AzeFlu formulation	8928 (4.0)	13 [12-13] (23)	7 [7-8] (21)
Remaining classes [d]	5687 (2.6)	15 [15-16] (28)	9 [9-10] (24)
Co-medication	38,315 (17.3)	21 [20-21] (36) [b]	15 [15-15] (30) [c]
Involving only OAH and INCS	10,974 (4.9)	16 [16-17] (33)	12 [11-12] (28)
Involving OAH, INCS and drugs of other classes	6900 (3.1)	22 [22-23] (33)	17 [16-18] (28)
Involving only oral OAH and AzeFlu	5813 (2.6)	17 [17-18] (25)	12 [11-13] (24)
Involving OAH, AzeFlu and drugs of other classes	1516 (0.7)	28 [27-29] (28)	25 [24-28] (29)
Involving only OAH and drugs of the "remaining classes" [d]	8180 (3.7)	27 [27-27] (44)	17 [16-19] (36)
Involving only INCS and drugs of the "remaining classes" [d]	2271 (1.0)	20 [18-21] (33)	16 [14-18] (31)
Involving only AzeFlu and drugs of the "remaining classes" [d]	1241 (0.6)	21 [20-22] (28)	20 [19-23] (26)
Any co-medication scheme involving oral steroids	1540 (0.7)	45 [42-48] (45)	30 [27-35] (46)
Other co-medication schemes	1420 (0.6)	27 [25-29] (43)	19 [16-23] (41)
Number of simultaneous medications in co-medication days	***N* observations**	**VAS Global Symptoms – median [95%CI] (IQR)**	**VAS Work – median [95%CI] (IQR)**
2 medications	28,154	19 [18-19] (34)	13 [13-14] (29)
3 medications	8231	24 [24-25] (35)	19 [18-20] (29)
4 medications	1483	26 [24-29] (41)	18 [16-22] (40)
>4 medications	447	57 [51-63] (47)	45 [35-52] (51)

AH=antihistamine; AzeFlu=Azelastine-Fluticasone; CI=Confidence interval; INAH=Intranasal antihistamine; INCS=Intranasal steroid; IQR=Interquartile range; OAH=Oral antihistamine; VAS Global Symptoms = MASK-air® visual analogue scale assessing the severity of overall allergic symptoms on that day; Work VAS = MASK-air® visual analogue scale assessing the work impact of allergic symptoms on that day; [a] $p<0.001$ for the comparison of VAS Global Symptoms between no medication, monotherapy and co-medication days; [b] $p<0.001$ for the comparison of VAS Work between no medication, monotherapy and co-medication days; [c] There were 35,647 observations with AH1 use of any type in monotherapy (median VAS Global Symptoms=16; median VAS Work=11); [d] Including any non-antihistamine non-steroid formulation (namely, decongestants, mast cell stabilizers, antileukotrienes, saline solutions), or any antihistamine of unspecified route of administration, or any unspecified respiratory steroid in patients not reporting asthma.

Table 2. Number of different drugs and drug groups used throughout a period of 12 months by patients who had reported medication use at least four times.

***N* different drugs**	***N* (%)**
1	196 (20.1)
2	317 (32.5)
3	256 (26.3)
4	114 (11.7)
5	47 (4.8)
6	27 (2.8)
≥7 [a]	18 (1.8)
***N* different drug groups**	***N* (%)**
1	246 (25.2)
2	409 (41.9)
3	249 (25.5)
4	54 (5.5)
5	13 (1.3)
6	4 (0.4)

[a] Includes use of 7 different drugs (*N*=11), 8 different drugs (*N*=3), 9 different drugs (*N*=2), and 10 different drugs (*N*=2).

Figure legends

Figure 1. Monthly absolute number of observations under different medication schemes throughout the years. AH: Antihistamines; INCS: Intranasal corticosteroids.

Figure 2. Monthly frequency of observations under different medication schemes (2A) and co-medication schemes (2B). Results are expressed as a percentage of the total number of days under medication for each geographical region. Combined data for the 2016-2020 period for each month are presented. AH: Antihistamines; INCS: Intranasal corticosteroids.

Figure 3. Monthly frequency of observations under different medication schemes (left panel) and relative search volumes on "allergy", "allergic rhinitis" and "pollen" (as assessed by Google Trends) (right panel) for three individual countries. AH: Antihistamines; AzeFlu: Azelastine-Fluticasone; INCS: Intranasal corticosteroids.

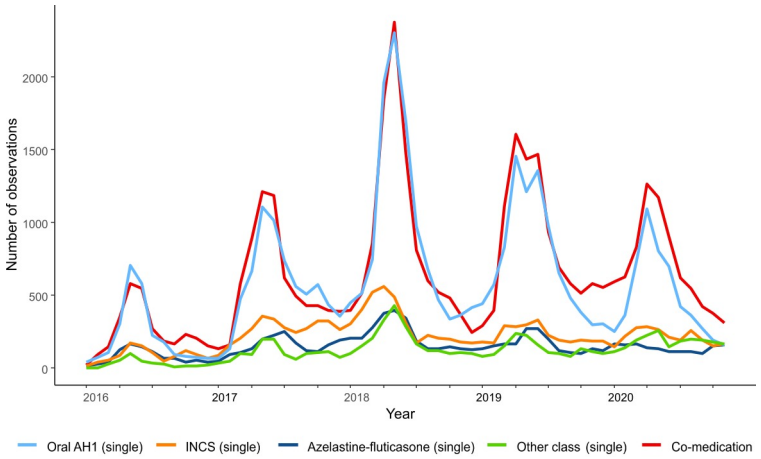

Figure 1

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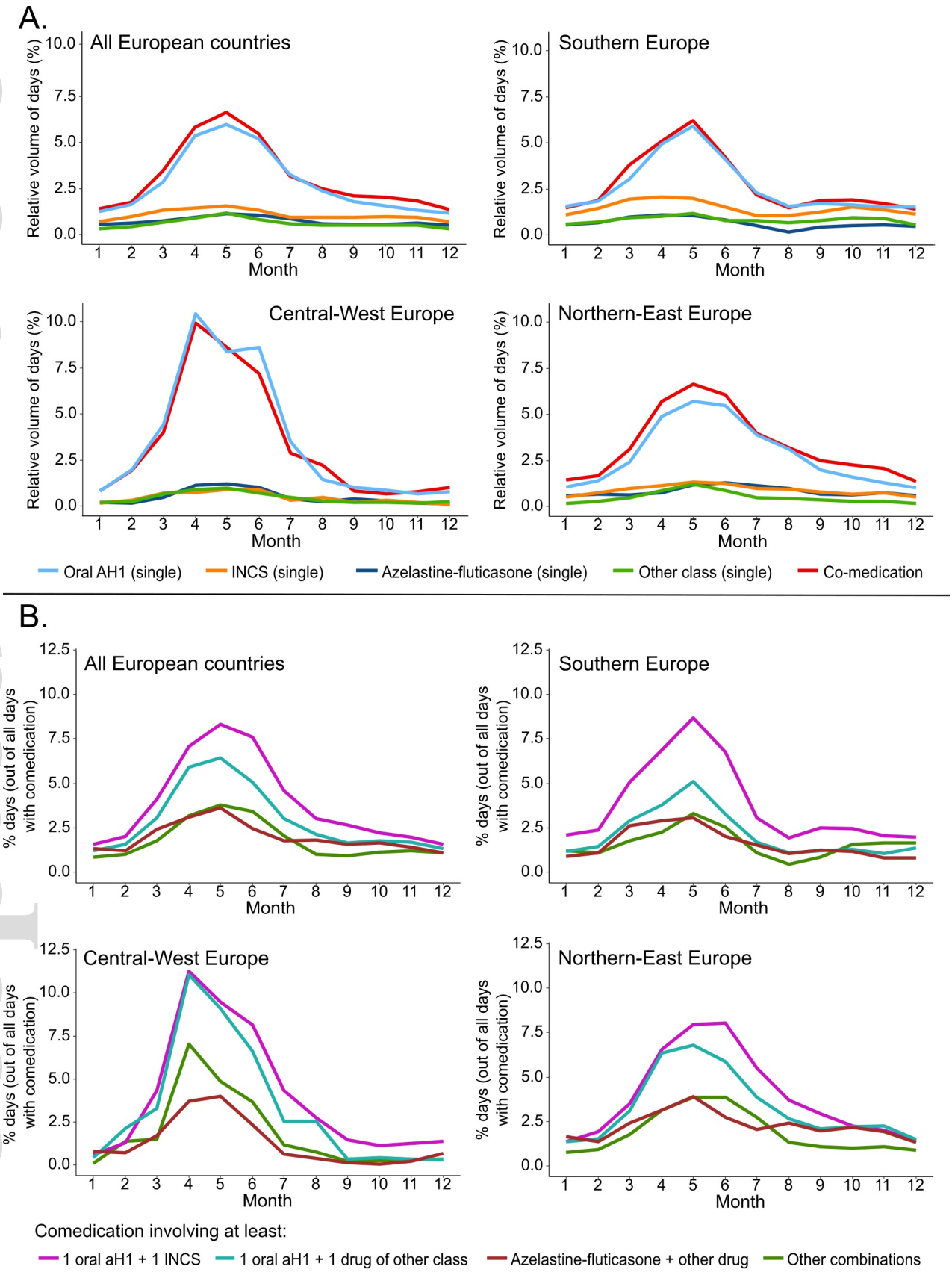

Figure 2

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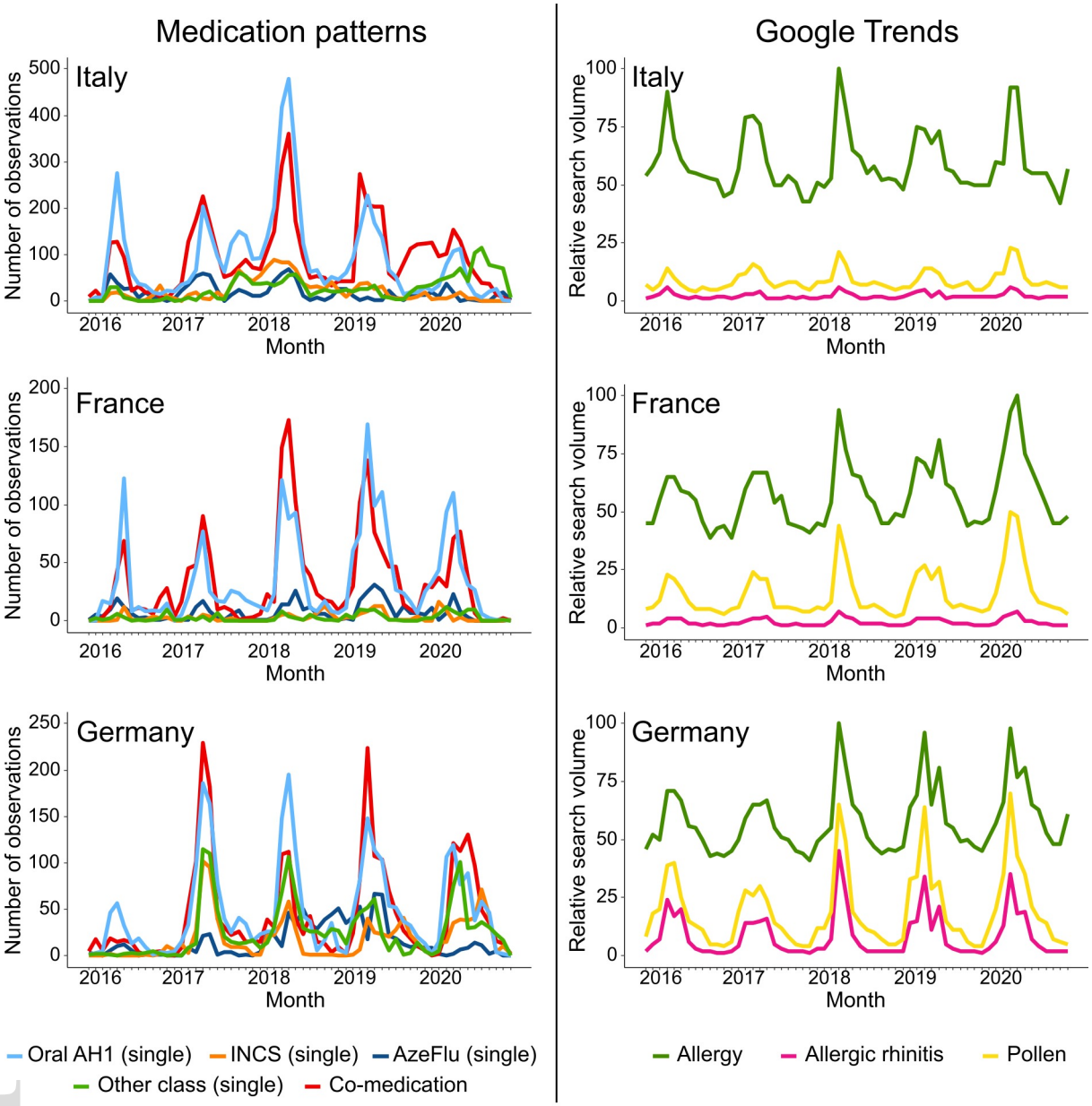

Figure 3

all_15275_f3.png