

ORIGINAL ARTICLE

Airway Diseases

New European Academy of Allergy and Clinical Immunology definition on pollen season mirrors symptom load for grass and birch pollen-induced allergic rhinitis

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Abstract

Background: The use of allergen immunotherapy (AIT) for allergic rhinitis and its clinical efficacy in clinical trials depends on the effective determination of pollen allergen exposure time periods. We evaluate pollen data from Germany to examine the new definitions on pollen season and peak pollen period start and end as proposed by the European Academy of Allergy and Clinical Immunology (EAACI) in a recently published Position Paper. The aim was to demonstrate the ability of these definitions to mirror symptom loads for grass and birch pollen-induced allergic rhinitis based on real-life data.

Methods: Data coming from four pollen monitoring stations in the Berlin and Brandenburg area in Germany and for 3 years (2014-2016) were used to investigate the correlation of season definitions, birch and grass pollen counts and total nasal symptom and mediation scores as reported by patients in "Patients Hay fever Diaries" (PHDs). After the identification of pollen periods on the basis of the EAACI criteria, a statistical analysis was employed, followed by a detailed graphical investigation.

Results: The analysis revealed that the definitions of pollen season as well as peak pollen period start and end as proposed by the EAACI are correlated to symptom loads for grass and birch pollen-induced allergic rhinitis reported by patients in PHDs.

Conclusion: Based on our analysis, the validity of the EAACI definitions on pollen season is confirmed. Their use is recommended in future clinical trials on AIT as well as in daily routine for optimal patient care.

KEYWORDS

allergic rhinitis, pollen counts, pollen season definition, symptom onset, symptom variation

1 | BACKGROUND

Allergic rhinitis (AR) is a symptomatic disorder of the nose having negative impacts to quality of life, affecting school and work productivity.¹ AR is generally caused after exposure to allergens due to hypersensitivity reactions which are IgE-mediated.² Allergen

immunotherapy (AIT) is a causal treatment option for AR as it induces immune tolerance to allergens.³⁻⁶ The demonstration of clinical efficacy of pollen AIT for hay fever sufferers in clinical trials depends on the effective definition of pollen seasons and thus defining time periods when allergic patients are exposed to pollen allergens in a clinically relevant way is crucial in clinical trials. A

comprehensive and harmonized definition of pollen seasons has been proposed by an EAACI Position Paper,⁷ summarized for birch (*Betula*) and grass (Poaceae) in Table 1, and the robustness of these definitions for grass (Poaceae) pollen has been verified for Germany on the basis of 5-year measurements coming from up to 40 monitoring stations in the country.⁸

In the next step, it is important to investigate the usefulness of these definitions from the clinical point of view. Therefore, the aim of our study was to demonstrate the correlation of season definitions, pollen counts and actual symptom loads as reported by patients using Pollen Hay fever Diaries PHD.⁹ In this article, we present the relationship between birch (*Betula*) and grass (Poaceae) pollen levels on the one hand, and actual symptom and medication use data on the other, for the Berlin and Brandenburg area in Germany for 3 years (2014–2016).

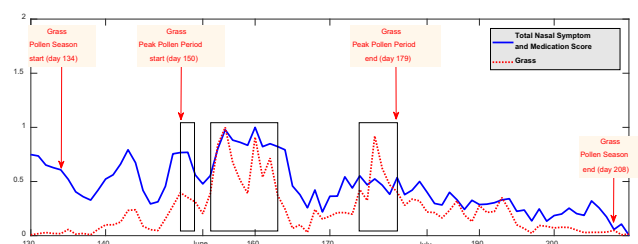
2 | MATERIALS AND METHODS

2.1 | Pollen, symptom, and medication data used

In an effort to analyze the temporal variation of birch and grass pollen levels in parallel with the variation of symptoms, data coming from pollen monitoring stations operating in the Berlin and Brandenburg area were studied. The stations that were considered to be representative are as follows: Berlin, Neustrelitz, Potsdam, and Treuenbrietzen (Figure 1). The Euclidian distance between the stations varies from 23 km between Berlin and Potsdam to 143 km

TABLE 1 Definitions of pollen seasons for Birch and Grass according to the EAACI Position Paper⁷ (nota bene: The “high pollen days” criterion is not shown as it has not been analyzed in this study)

Pollen season		High pollen season (or “Peak pollen period”)
Birch	Start: 1st day of 5 d (of 7 consecutive days) each of these 5 d with ≥ 10 pollen/m ³ and with a sum of these 5 d of ≥ 100 pollen/m ³ End: last day of series of 5 d (of 7 consecutive days) with ≥ 10 pollen/m ³ and with a sum of these 5 d of ≥ 100 pollen/m ³	Start: 1st day of 3 consecutive days, each with at least ≥ 100 pollen/m ³ End: last day of at least 3 consecutive days, each with ≥ 100 pollen/m ³
Grass	Start: 1st day of 5 days (of 7 consecutive days) each of these 5 d with ≥ 3 pollen/m ³ and with a sum of these 5 d of ≥ 30 pollen/m ³ End: last day of series of 5 d (of 7 consecutive days) with ≥ 3 pollen/m ³ and with a sum of these 5 d of ≥ 30 pollen/m ³	Start: 1st day of 3 consecutive days, each with at least ≥ 50 pollen/m ³ End: last day of at least 3 consecutive days, each with ≥ 50 pollen/m ³



- The new EAACI definition of pollen season allows to pinpoint pollen season and peak pollen period start and end.
- Pollen season characteristics are correlated to symptom loads for grass and birch pollen-induced allergic rhinitis symptoms reported by patients in Pollen Hay fever Diaries in Germany.
- The use of the new EAACI definition of pollen season is recommended in future clinical trials on allergen immunotherapy as well as in daily routine for optimal patient care.

between Neustrelitz and Treuenbrietzen. In all four areas, pollen monitoring is performed by seven-day volumetric spore traps (Burkard) located on rooftop levels. The pollen taxa that were included in the analysis are as follows: birch (*Betula*) and grass (Poaceae) and covered the years 2014, 2015, and 2016. The Pearson correlation coefficient between pollen counts of all four stations and for both pollen taxa studied was calculated, and it varies between 0.75 and 0.85.

Daily symptom data as well as medication use data are reported on a voluntary basis through a web-based Pollen App, which includes the Patient's Hay fever Diary (PHD). It should be emphasized that those reporting symptoms via the PHD are not patients by definition (ie, diagnosed with allergy), as anybody can report symptoms through the system. With other words, allergic patients have not been enrolled clinically by a physician. The PHD data are based on voluntary participation, anonymously and driven by own interest and allergies against the two pollen taxa addressed (birch and grass) cannot be specifically checked due to the anonymously participation. The number of symptom reports throughout the pollen season is highly variable: The mean number of PHD users (rounded to the closest integer) reporting symptoms is 84 for year 2014, 147 for year 2015, and 272 for year 2016. The PHD was developed taking into account the European Medicines Agency guidelines and allows for the structured and continuous reporting of pollen-induced symptoms and relevant medication use by allergy sufferers, being available in a variety of European languages.^{10–12} In the following, we report data on nasal symptoms, which are predominant in allergic patients throughout the season.¹³

We proceeded by calculating the mean pollen count levels per day in pollen grains/m³,¹⁴ from all aforementioned stations, resulting in a mean daily pollen count level for birch and grass for the area of interest. We then made use of the PHD data (which have been anonymized thus excluding any personal identification information) to extract the Total Nasal Symptom and Medication Score (TNSMS) for those patients that had stated their current daily location to be in the Berlin and Brandenburg area. This score was calculated on the basis of:

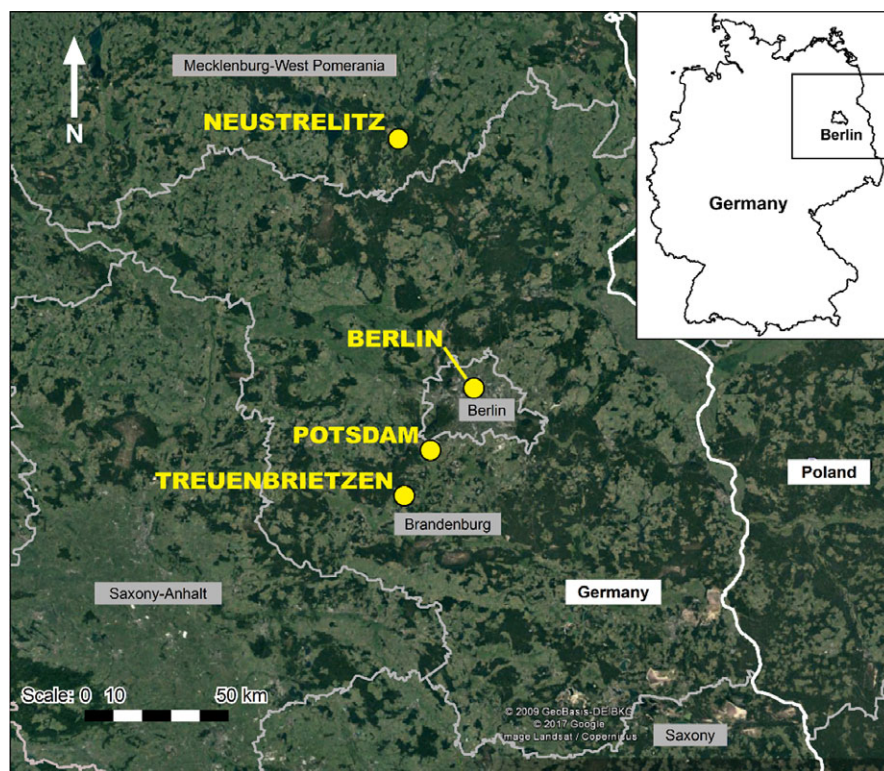


FIGURE 1 The Berlin and Brandenburg area of study indicating the location of the four pollen monitoring stations used. (source: GeoBasis-DE-BKG [© 2009], Google [© 2017]) [Colour figure can be viewed at [wileyonlinelibrary.com](#)]

- An overall severity symptom score ranging from zero (no discomfort and no health-related problems) up to three (strong discomfort with severe health-related problems) and
- The four specific nasal symptoms identified (itching, sneezing, running, and blocked nose), each one reported of being present or not (and thus receiving one or zero points, respectively).

On this basis, the Total Nasal Symptom Score (TNSS) varies between zero (minimum) and seven (maximum) as described in¹¹ and ¹⁵. It should be mentioned that the TNSS used in our study is not validated against other AR symptom scores used to evaluate the severity of the disease, but it results from the use of the PHD for collecting seasonal AR scores. On this basis, its use is considered valid, as already suggested by a study evaluating Internet platforms for AR symptom reporting.¹⁶

Allergic patients report symptoms that are influenced by the medication they receive.¹⁷ The medication intake therefore reversely affects the grade of severity of symptoms. However, different medication classes have different effects in improving patients' allergic symptoms. On this basis, a Weighted Nasal Medication use Score (WNMS) comprising a total of 2.05 points for treating nasal symptoms was adopted, as suggested by¹⁵: 1.0 point for the use of "Nose drops" or "Tablets" or both, 0.25 points for the use of "Eye drops," 0.5 points for the use of "Others," and 0.3 points for the use of "Homeopathic" medication. On this basis, the TNSMS is a sum of the TNSS and the WNMS and ranges from 0 to 9.05.

All available data were averaged per day to represent the mean daily pollen as well as the mean TNSMS levels in the Berlin and Brandenburg area. In order to provide with an overview of the data, their basic descriptive statistics for a period of 150 consecutive days starting on the 91st calendar day (approx. beginning of April till the end of August) and for the three years of study are presented in Table 2.

2.2 | Analysis of correlation

The estimation of the relationship of pollen counts and other environment-related parameters such as meteorological conditions has been carried out with the aid of several correlation coefficients,¹⁸ while the same approach has been employed in the analysis of relationships between pollen levels and related symptoms.¹⁹⁻²¹ For this reason, the investigation of the relationship between pollen levels and TNSMS in our study firstly employs the Pearson's correlation coefficient, which was used as a relative measure of association, calculated according to the following formulae:

$$rr = \frac{\sum_{i=1}^N (x_i - \bar{x}) \cdot (y_i - \bar{y})}{\sqrt{\sum_{i=1}^N (x_i - \bar{x})^2} \cdot \sqrt{\sum_{i=1}^N (y_i - \bar{y})^2}} \quad (1)$$

where x represents the TNSMS, y represents pollen concentration levels, and N the number of available data records per year of study.

The Pearson's correlation coefficient is an expression of the linear relationship (if any) between the studied parameters. In addition,

TABLE 2 Basic descriptive statistics (minimum [min], maximum [max], mean, and standard deviation [SD]) for daily averaged birch and grass pollen levels and Total Nasal Symptom and Medication Score (TNSMS) in the Berlin and Brandenburg area, for a period of 150 consecutive days starting on the 91st calendar day for every one of the 3 y under investigation (2014, 2015, and 2016)

	Min	Max	Mean	SD
Year 2014				
Birch	0.00	3042.00	132.57	480.60
Grass	0.00	159.50	17.78	28.40
TNSMS	1.28	3.74	2.26	0.51
Patient data	15 users had no missing data for 150 consecutive days; range of observations: 5-150 d			
Year 2015				
Birch	0.00	721.25	27.68	102.22
Grass	0.00	173.75	20.14	31.50
TNSMS	1.52	4.19	2.44	0.60
Patient data	12 users had no missing data for 150 consecutive days; range of observations: 3-150 d			
Year 2016				
Birch	0.00	2037.33	107.44	301.15
Grass	0.00	163.00	20.40	32.68
TNSMS	1.42	3.43	2.33	0.55
Patient data	9 users had no missing data for 150 consecutive days; range of observations: 1-150 d			

Pollen levels are calculated as the average of the four monitoring stations employed, thus having decimal values instead of integers. Additionally, we report the number of patients per year with available TNSMS for 150 consecutive days as well as the relevant range of available observations (in calendar days).

and to investigate how well a monotonic function can describe the relationship between the studied parameters, the Spearman correlation coefficient was also applied, calculated as follows:

$$r_s = 1 - \frac{6 \sum_{i=1}^N D_i}{n(n^2 - 1)} \quad (2)$$

where D_i represents the difference between the two sets of data, ranked (x) and ranked (y), ranked denoting that both datasets are ranked from higher to lower values,²² and x and y represents TNSMS and pollen levels, respectively.

To complement the correlation coefficient calculations, the P values for a significance level of $\alpha = .001$ were calculated. Therefore, if the P value is smaller than α , then the association resulting from the corresponding correlation coefficient is considered statistically significant.

As we wanted to check whether pollen levels and pollen season definitions are reflected on patient symptoms, we created relevant plots covering the time period of study for each one of the 3 years under investigation. The differences in the descriptive statistics of the parameters of interest (as reported in Table 2) led to a data

normalization step before plotting: For each one of the initial parameters of interest, a normalized parameter was estimated, calculated as follows:

$$Z' = \frac{z - \bar{z}}{\sigma} \quad (3)$$

where $\bar{z}$ is the mean value and σ is the standard deviation for each one of the pollen and symptom data included in the analysis.

3 | RESULTS

The pollen grains/m³ together with the TNSMS as well as with the total number of PHD reports per day were plotted for the period starting from the 91st day (1st of April for years 2014 and 2015 and 31st of March for year 2016) and for 150 consecutive days for each of the 3 years (2014-2016), in order to focus on the basic pollen season for birch and grass and to study nasal symptoms in particular during birch and grass pollen season (Figures 2,3,4). In addition, the pollen season (PS) and peak pollen period (PPP) start and end for both taxa were calculated on the basis of the EAACI definitions (7, Table 3). The basic descriptive statistics of pollen levels and TNSMS for each one of the PS start and end periods and for all years of study are presented in Table 4. Moreover, the correlation coefficients and the associated P values between the TNSMS and the pollen levels (for birch and grass) were calculated for the period characterized from the PS start and end per pollen type and year (Tables 5, 6).

For the year 2014, the TNSMS reaches its highest value at the beginning of the season (5th of April), a week after the birch PS starts (27th of March, Figure 2 and Table 3). This maximum is followed by the maximum number of patient reports for this year (155 reports at the 7th of April). The overall TNSMS diminishes till the second half of May, when it again starts to grow, following the grass PS start (13th of May, Table 3) and an increase in the daily grass pollen counts. From there on, the TNSMS follows the overall grass pollen count fluctuation, until the grass PS end (at 27th of July).

Birch pollen concentrations at their highest are one order of magnitude greater than the concentrations of grass, surpassing a value of 3000 grains/m³, while grass maximum roughly reaches 160 grains/m³ (Table 4). Corresponding TNSMS levels for the birch season are higher in comparison with the ones recorded for the grass season (3.00 vs 2.70). Moreover, birch pollen levels result in the definition of three PPP start and end periods, while the relevant period for grass is only one (Table 3). The total number of users reporting symptoms per day within the whole studied period ranges from 41 to 155.

For the year 2015, high birch pollen levels at the beginning of the season (721 grains/m³ for the 15th of April) seem to "trigger" the generation of symptom reports by PHD users (Figure 3). The maximum number of PHD user reports (329 reports for the 20th of April) follows the first PPP start for birch (19th of April, Table 3) and

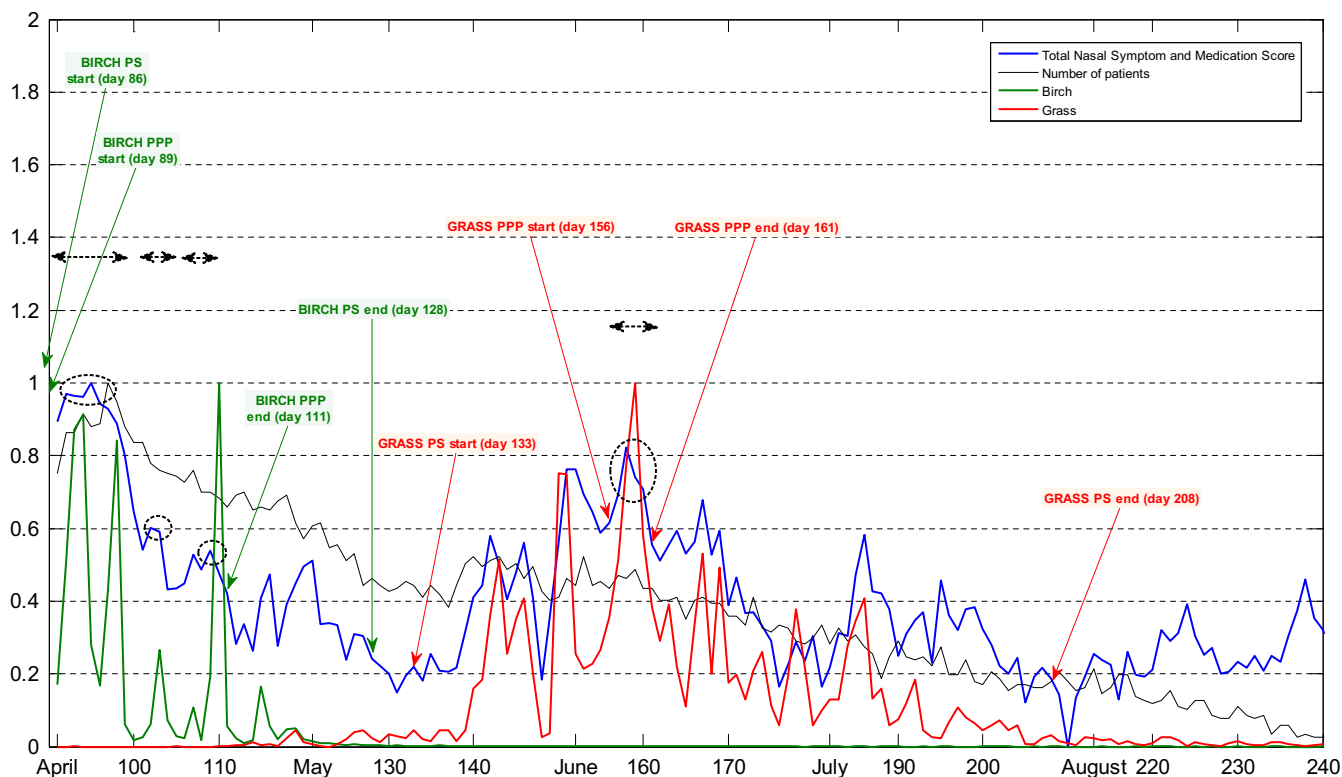


FIGURE 2 Temporal variation of the Total Nasal Symptom and Medication Score (TNSMS) from April 1, 2014 (91st calendar day of the year) up to August 28, 2014 (240th calendar day of the year, ie, for 150 consecutive calendar days) and for the Berlin and Brandenburg area. The multiple peak pollen period (PPP) starts-ends and the corresponding TNSMS are denoted with double arrows and dotted ellipses, respectively, for both birch and grass, according to Table 3. The horizontal axis reports month start and calendar day number. All values are normalized [Colour figure can be viewed at wileyonlinelibrary.com]

the same level of reports (332 for the 12th of May) appears just after the grass PS start (9th of May, Table 3). The later event also marks the increase in the TNSMS which follows, to a great extent, that of grass pollen levels: The three highest pollen count levels of the year (141 grains/m³ for the 3rd of June, 154 grains/m³ for the 6th of June, and 113 grains/m³ for the 11th of June) coincide with three peaks of the TNSMS.

Birch pollen concentrations at their highest are higher than the concentrations of grass (721.25 vs 173.75). Corresponding TNSMS levels for the birch season are lower in comparison with the ones recorded for the grass season (2.75 vs 3.51). Birch pollen levels also result in the definition of two PPP start and end periods, while the relevant periods for grass are three (Table 3). The total number of users reporting symptoms per day within the studied period ranges from 58 to 332.

The year 2016 is characterized by the largest number of PHD reports (>400), with a temporal variation that is very similar to the one of the TNSMS (Figure 4). The first increase in the TNSMS and the number of PHD user reports is observed after birch PS start and first PPP start (4th and 5th of April, respectively, Table 3) with two characteristic “peaks” of reports just before and after the mid of April: 358 reports for the 13th of April and 366 reports for the 18th of April, the latter being the date with the maximum TNSMS. At the same time, birch pollen concentration levels are high presenting two

relevant local maxima: 2038 grains/m³ at the 12th of April and 1919 grains/m³ at the 19th of April. After this period, the symptom curve as well as the number of symptom reports per day varies around lower values until the 13th of May when the grass PS start occurs (Table 3). From there on, the number of symptom reports increases reaching the maximum value of 424 reports on the 21st of May and at the same date when the first peak of the grass pollen levels appear (reaching 176 grains/m³). After this point, and until the last PPP end for grass (27th of June, Table 3), both symptoms and reports reflect the variation in the grass pollen levels with a maximum value reached again on the 7th of June. The same behavior is observed even until the grass PP end (26th of July, Table 3).

Birch pollen concentrations at their highest are more than an order of magnitude higher than the concentrations of grass pollen (2037.33 and 163 grains/m³, respectively). Corresponding TNSMS levels for the birch season are lower in comparison with the ones recorded for the grass season (2.75 vs 2.86). Birch pollen levels also result in the definition of two PPP start and end periods, while the relevant periods for grass are three. The total number of users reporting symptoms per day within the studied period ranges from 135 to 424.

The Pearson's correlation coefficient between pollen levels and TNSMS for the PS start to PS end period (Table 5) is high for both pollen types for the years 2014 and 2016 while being low for birch

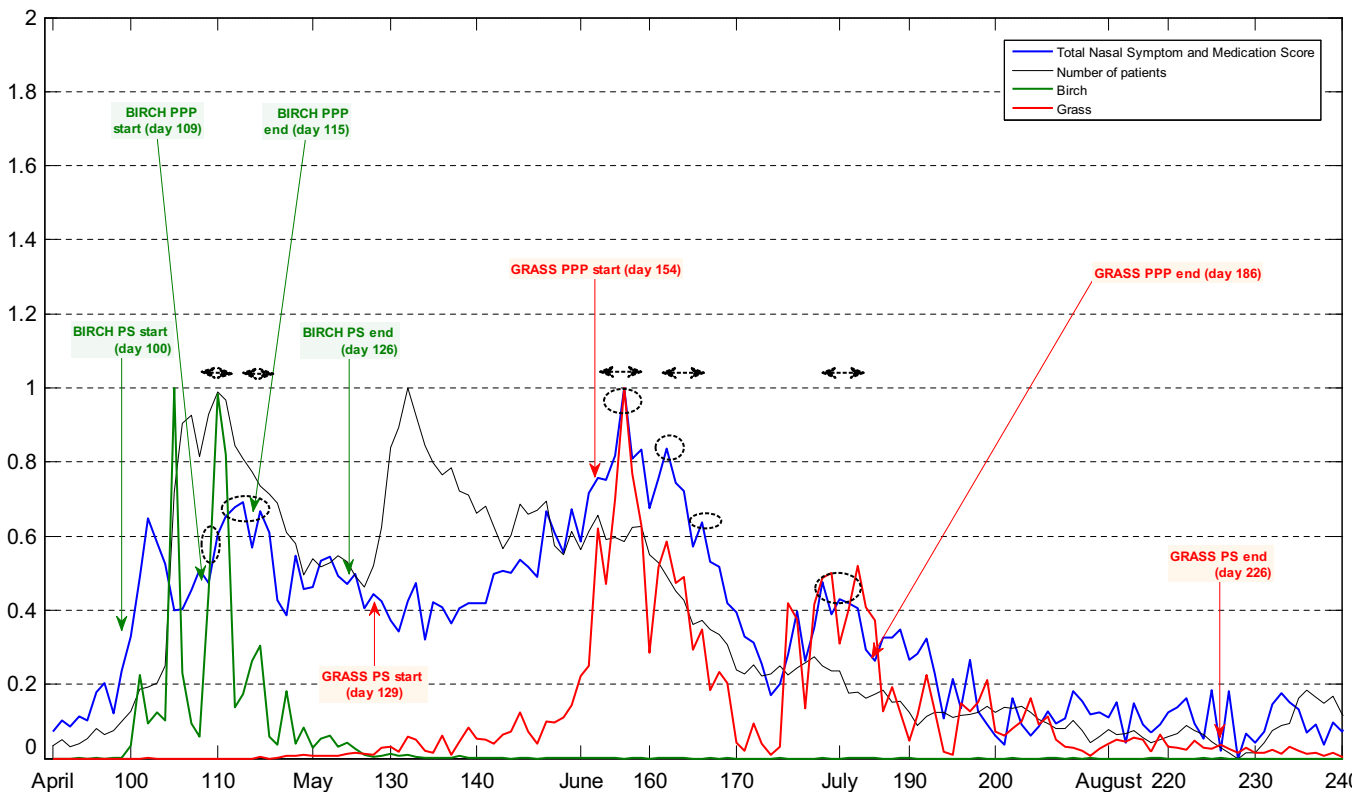


FIGURE 3 Temporal variation of the Total Nasal Symptom and Medication Score (TNSMS) from April 1, 2015 (91st calendar day of the year) up to August 28, 2015 (240th calendar day of the year, ie, for 150 consecutive calendar days) and for the Berlin and Brandenburg area. The multiple peak pollen period (PPP) starts-ends and the corresponding TNSMS are denoted with double arrows and dotted ellipses, respectively, for both birch and grass, according to Table 3. The horizontal axis reports month start and calendar day number. All values are normalized [Colour figure can be viewed at wileyonlinelibrary.com]

and high for grass for the year 2015. When taking the Spearman correlation coefficient into account (Table 6), then values for the PS start to PS end period are also high for birch and grass for the year 2014, while being low for birch and high for grass for 2015 and the opposite for 2016. Overall, both correlation coefficients suggest that the pollen season definitions result in high correlations in the majority of cases (nine of twelve of total coefficients calculated) between pollen and TNSMS levels.

4 | DISCUSSION

The onset, the severity, and the temporal variation of symptoms of pollen allergic patients are important for the diagnosis and management of AR, having a direct impact on their quality of life.

The correlation of pollen levels and daily symptoms has already been well established. In addition, the differentiation of symptom levels between pollen season start and end, under similar pollen levels, has been identified and attributed to the “priming effect”: The early exposure seems to lower the threshold for subsequent symptom triggering.^{21,23,24} Levels of symptoms can be characterized by the criteria of *Allergic Rhinitis and its Impact on Asthma Guidelines*,¹³ but one step missing is to identify levels of daily symptoms as a

response to pollen season onset and variation as well as to high pollen season days.

In all three studied years, in this analysis, it is evident that the TNSMS is influenced by the PS start and end for birch and grass, as suggested by the graphical comparison of the variables. Correlation coefficients (mainly Pearson but also Spearman) support this finding, the year 2015 being the one with the weakest correlation between TNSMS and PS start-end. The latter may be attributed to 2015 being the “weakest” year among three concerning mean birch pollen levels in terms of mean as well as maximum values (Table 4) and also to the possible influence of other pollen species that could cause nasal symptoms as well. The same stands for the period just before the beginning of the grass pollen season for 2016, where possibly other pollen species cause nasal symptoms.

Moreover, the level of symptoms reported seems to directly correlate especially with the PPP start and end for all 3 years: According to Figures 2,3,4, local TNSMS peaks are only included within the PPP for birch and grass. Moreover, the number of patients using the PHD mainly follows the level of TNSMS as expected: Patients have the tendency to report especially high symptom levels and may lose their interest in reporting should their symptom levels drop.

Another interesting aspect refers to the symptom levels and their relationship with especially PPP duration. Although TNSMS levels

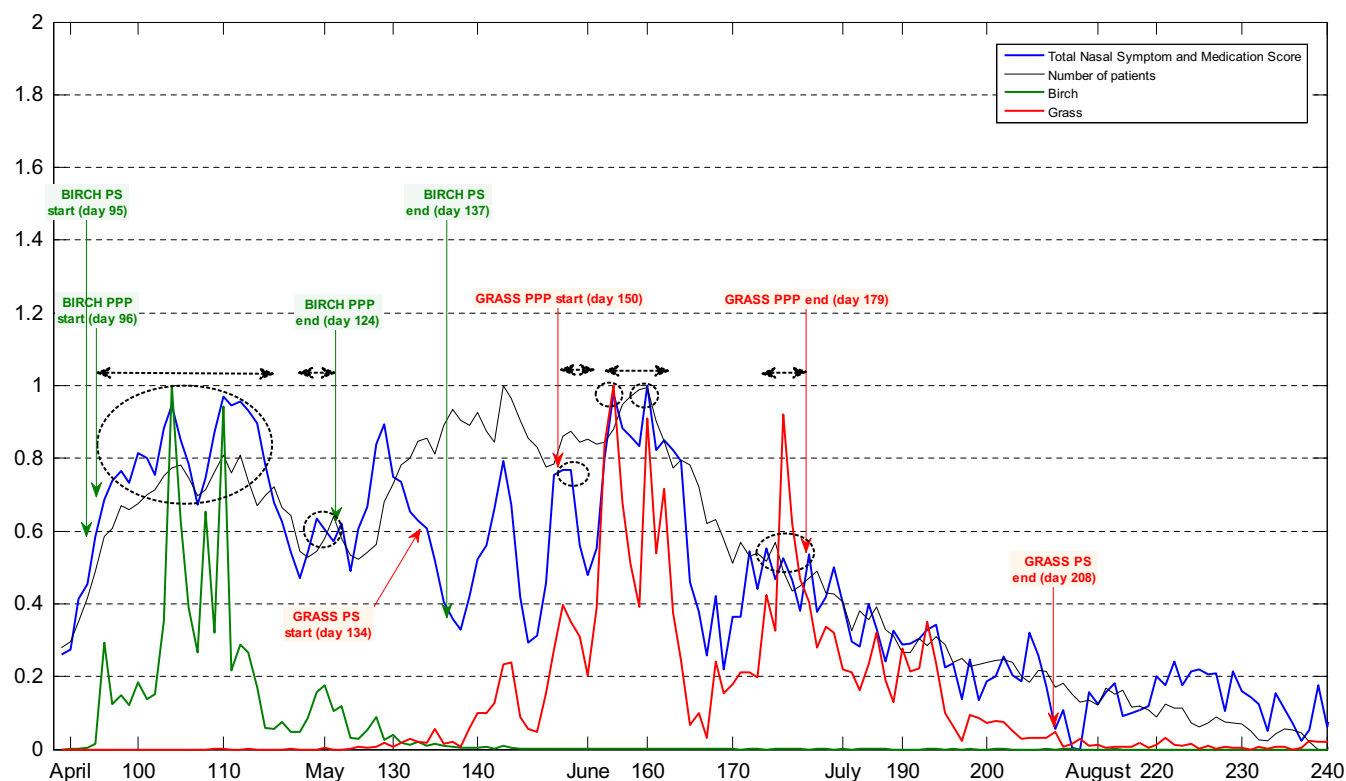


FIGURE 4 Temporal variation of the Total Nasal Symptom and Medication Score (TNSMS) from March 31, 2016 (91st calendar day of the year) up to August 27, 2016 (240th calendar day of the year, ie, for 150 consecutive calendar days) and for the Berlin and Brandenburg area. The multiple peak pollen period (PPP) starts-ends and the corresponding TNSMS are denoted with double arrows and dotted ellipses, respectively, for both birch and grass, according to Table 3. The horizontal axis reports month start and calendar day number. All values are normalized [Colour figure can be viewed at wileyonlinelibrary.com]

TABLE 3 Pollen season (PS) and Peak pollen period (PPP) start and end for birch and grass and for the 3 y of study in the Berlin and Brandenburg area

	PS start-PS end		PPP start-PPP end	
	Birch	Grass	Birch	Grass
2014	86-128 (27.03-05.05)	133-208 (13.05-27.07)	89-99 (30.03-09.04) 102-104 (12.04-14.04) 109-111 (19.04-21.04)	156-161 (05.06-10.06)
2015	100-126 (10.04-06.05)	129-226 (09.05-14.08)	109-111 (19.04-21.04) 113-115 (23.04-25.04)	154-159 (03.06-08.06) 161-166 (10.06-15.06) 179-186 (28.06-05.07)
2016	95-137 (04.04-16.05)	134-208 (13.05-26.07)	96-117 (05.04-26.04) 120-124 (29.04-03.05)	150-152 (29.05-31.05) 154-163 (02.06-11.06) 174-179 (22.06-27.06)

Numbers indicate calendar days.

generally correlate with the pollen levels of either birch or grass (depending on the time of the year), there are cases (like the high birch levels at the 2014 pollen season) where the initially high symptoms seem to “lose” their ability to follow repeated high pollen levels like the highest birch levels recorded in our study (>3000 grains/ m^3 on the 20th of April 2014). A similar situation occurred also concerning grass, where the increase in pollen levels at the end of June 2016 was not followed by an analogous increase in the TNSMS. Results

are in line with allergen exposure chamber trials,²⁵ as well as results about early and late pollen season-related symptoms under natural (seasonal) exposure reported in^{23,24,26}.

These findings indicate that the pollen season criteria as harmonized by the EAACI⁷ are able to map symptom reports and symptom levels onset and variation. Therefore, the application of these criteria can lead to a homogeneous identification of PS and PPP start-end regardless of geographic location and can be used as an early

TABLE 4 Basic descriptive statistics (minimum [min], maximum [max], mean, and standard deviation [SD]) for daily averaged birch and grass pollen levels and Total Nasal Symptom and Medication Score (TNSMS) in the Berlin and Brandenburg area, for the PS start and end periods and for the years 2014, 2015, and 2016

	Min	Max	Mean	SD
Year 2014				
Birch	9.3	3042.0	570.8	876.98
Grass	1.0	159.5	34.1	32.93
TNSMS (birch PS start-end)	1.4	3.0	2.1	0.50
TNSMS (grass PS start-end)	1.2	2.7	1.8	0.38
Year 2015				
Birch	17.75	721.25	153.11	202.02
Grass	1.00	173.75	30.61	35.11
TNSMS (birch PS start-end)	1.85	2.75	2.36	0.24
TNSMS (grass PS start-end)	1.23	3.51	2.01	0.54
Year 2016				
Birch	12.67	2037.33	376.74	471.71
Grass	1.33	163.00	40.29	37.23
TNSMS (birch PS start-end)	1.76	2.75	2.32	0.27
TNSMS (grass PS start-end)	1.20	2.86	1.91	0.38

Pollen levels are calculated as the overall average among the four monitoring stations.

TABLE 5 Pearson's correlation coefficient between the Total Nasal Symptom and Medication Score and the pollen count levels and *P* value for birch and grass, calculated for the years 2014, 2015, and 2016 and for the pollen-specific season (PS start to PS end period per year and per pollen type)

Year	2014		2015		2016	
	<i>r</i>	<i>P</i>	<i>r</i>	<i>P</i>	<i>r</i>	<i>P</i>
Birch (PS start to PS end)	.63	1.6×10^{-5}	.13	.53	.64	4×10^{-5}
Grass (PS start to PS end)	.78	7×10^{-17}	.63	2×10^{-9}	.43	1.2×10^{-4}

TABLE 6 Spearman correlation coefficient between the Total Nasal Symptom and Medication Score and the pollen count levels and *P* value for birch and grass, calculated for the years 2014, 2015, and 2016 and for the PS start to PS end period per year

Year	2014		2015		2016	
	<i>r</i>	<i>P</i>	<i>r</i>	<i>P</i>	<i>r</i>	<i>P</i>
Birch (PS start to PS end)	.79	2×10^{-9}	.23	.24	.79	5×10^{-7}
Grass (PS start to PS end)	.80	5×10^{-18}	.47	2×10^{-5}	.25	.038

warning for patients as well as medical practitioners concerning relevant symptom onset and rise. Moreover, the aforementioned definitions allow for the accurate identification of the points in time where symptoms are expected to increase, vary (in accordance with

pollen levels) and decline, thus providing with a useful instrument in patient management especially for the indication of AIT.

The described changing correlations between pollen counts and levels of symptoms in allergy sufferers and users of PHD in different years are not surprising: Not only the amount of pollen in the air but also environmental factors and changing major allergen amounts (Bet v 1/Ph p 5) may have a strong but regionally dependent impact on the symptom load.^{27,28}

Finally, and in terms of representativeness of the PHD data used in our study, it should be mentioned that the voluntary input of personal complaints related to AR symptoms into a diary presupposes a certain amount of interest in one's own illness. It is possible, but by no means certain, that the interest in using the diary depends on the severity of the complaints; with stronger symptoms, the interest might be higher. The willingness to use the diary may also depend on the level of education. It is conceivable that the PHD users are not representing the general population of hay-fever sufferers and in this respect, should the findings of this study be interpreted and used.

5 | CONCLUSIONS

Accurate management and treatment of patients with allergic rhinitis are highly depending on the exact knowledge of their exposure to the respective pollen allergens during the season. The latter presupposes the continuous monitoring of airborne pollen and the estimation of pollen counts and requires for a clinically effective definition of the start, end, and duration of pollen exposure times. The new definitions on pollen season (PS) start and end as well as peak pollen period (PPP) start and end as recently proposed in a Position Paper of the EAACI were applied for the Berlin and Brandenburg area in Germany, for a period of 3 consecutive years (2014-2016), and were compared with symptoms and medication use data as prospectively reported by allergic patients in PHDs. The results indicate that (i) the definitions are robust with regard to measured birch and grass pollen concentrations and (ii) they also correlate to the onset and variations of rhinitis symptoms. This analysis underlines the validity of the EAACI definitions of pollen seasons and as such recommends their use in daily routine for optimal patient care as well as in future clinical trials on AIT.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

AUTHOR CONTRIBUTIONS

K.K., K.C.B., and O.P. conceived and initiated the study; B.W. and M.W. prepared the pollen and the symptom data; K.K. designed the study framework; K.K., N.K., and M.R. made the computations; K.K., O.P., and K.C.B. drafted the manuscript; U.B. provided with expert support; O.P. and K.C.B. provided with expert advice and support.

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