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ORIGINAL PAPER

# The patient's hay-fever diary: three years of results from Germany

**K. Karatzas · D. Voukantsis · S. Jaeger · U. Berger · M. Smith · O. Brandt · T. Zuberbier · K. Ch. Bergmann**

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**Abstract** The patient's hay-fever diary (PHD) is a newly developed, internet-based tool for self-documentation of pollen-induced symptoms (eyes, nose and airways), general well-being and medication use. In Germany, more than 1,600 users made over 60,500 reports in 3 years (2009–2011). An analysis of these reports reveal that the nose symptom "sneezing" is the most commonly reported (3/10 of reports), followed by eye symptom "itching" and nose "blocked". In addition, medication use follows a similar pattern every year, with tablets being the most commonly used medication type (up to 60 % of the reports made in the years 2009 and 2011). Temporal variations in overall symptoms and organ-specific symptom scores are found to be associated with atmospheric concentrations of birch and grass pollen. Data from the PHD can be analysed with the aid of various mathematical methods and may provide information about symptoms and their severity for pollen-allergic sufferers. They may also be valuable for clinical studies in immunotherapy with pollen extracts.

**Keywords** Pollen · Symptoms monitoring · Pollen hay-fever diary

## 1 Introduction

Pollen grains are a component of the so-called biological weather (Klein et al. 2012) and are carriers of allergens, that is, proteins that cause a number of

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symptoms in the sensitized part of the population. One common allergic reaction is hay-fever. The disorder can impact significantly on a person's quality of life (Aït-Khaled et al. 2009; Kovats et al. 2003; Laatikainen et al. 2011) and has high socio-economic costs, either directly through treatment or indirectly through decreased productivity caused by absence from education, work or by impaired performance (Blaiss 2003; Bousquet et al. 2001; Ferguson 2004; Meltzer 1998).

The severity of hay-fever symptoms depends on several factors, such as genetic disposition and individual threshold: what might be considered to be a high amount of aeroallergen exposure for some individuals could be a low amount for others (Traidl-Hoffmann et al. 2009). Thus, a more personalized approach, which addresses symptoms rather than airborne pollen concentrations, would be more appropriate to model pollen-induced symptoms (Voukantsis et al. 2013). This personalized approach could also help in taking into account how the use of medication affects symptom severity (Wallace et al. 2008), as well as whether patients receive a more effective and positively perceived treatment improving their quality of life (Marple et al. 2007).

Collecting data from individual patients is a key aspect in understanding pollen-induced symptoms. If information about symptoms is collected in a systematic way, particularly in relation to the timing, the quantity of airborne pollen and the medication used, then these data may help us improve the overall quality of life and manage allergies as a disease.

A system that allows people to report on their symptoms and the medication they use in a common for all users, structured way, has been developed for the first time in Europe (Berger et al. 2011). The patient's hay-fever diary (PHD) system has been developed in cooperation with the Austrian Pollen Information Service, the Stiftung Deutscher Polleninformationsdienst, the Réseau National de Surveillance Aérobiologique in France, the ORL Department at the Medical University of Vienna and the Allergy-Centre-Charité in Berlin and is operated by the Medical University of Vienna.

In this study, we present data that the PHD users (located in Germany) have reported during the time period January 2009–October 2011. Our goal is to understand the users' profile, to compare their symptoms with pollen concentration levels, and to discuss the potential use of these data.

## 2 Materials and methods

### 2.1 Presentation of the PHD and of data being used

This study has been based on two distinct databases: (a) symptoms and medication use data from the PHD and (b) pollen count data (pollen concentration data) from the European Aeroallergen Network (EAN).

#### *2.1.1 The patient's hay-fever diary*

The PHD (www.pollendiary.com/Phd/ and www.pollenstiftung.de) has been developed in order to allow for the structured and continuous reporting of pollen-induced symptoms and relevant medication use by allergy sufferers throughout Europe and is currently available in a variety of European languages. The PHD was developed taking into account the European Medicines Agency guidelines (EMEA 2008). The PHD users were informed about the possibility to learn about the relationship between their symptoms and pollen counts by entering the website of the German Pollen Information Service (www.pollenstiftung.de), while there have also been various press releases about the service. It should be noted that it is unknown to us whether the PHD users have a physician-diagnosed or a "self-diagnosed" pollen-sensitivity, the latter possibly based on their knowledge of pollen season and occurrence of pollen.

Patient's hay-fever diary users can link their nasal, ocular and respiratory symptoms with the pollen levels at the places where they have been and thus identify the aeroallergens they are likely to have been exposed to. The PHD provides each user with information on his/her history of symptoms (as reported in the past), as well as with information on the pollen count levels for the monitoring site closer to his/her location. PHD data consist of recordings of symptoms that are reported by the users with the aid of an easy to use graphics interface (Fig. 1) on the basis of the following way:

For each one of three organs (eyes, nose and airways (lungs)), a discomfort index from zero (0) to three (3) is applied, in an analogy with problems reported by PHD users, as follows:

- No discomfort (no problems) = 0
- Low discomfort (mild problems) = 1

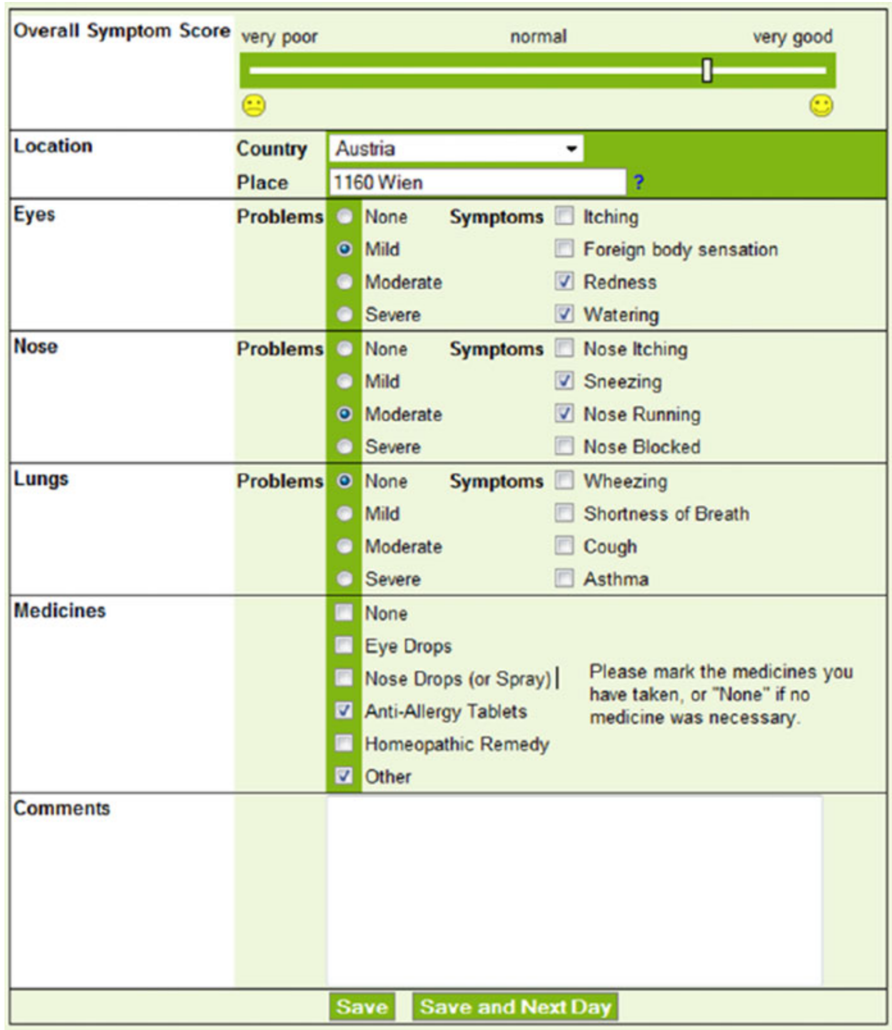
Overall Symptom Score very poor normal very good
Location Country Austria
Place 1160 Wien ?
Eyes Problems None Mild Moderate Severe Symptoms Itching Foreign body sensation Redness Watering
Nose Problems None Mild Moderate Severe Symptoms Nose Itching Sneezing Nose Running Nose Blocked
Lungs Problems None Mild Moderate Severe Symptoms Wheezing Shortness of Breath Cough Asthma
Medicines None Eye Drops Nose Drops (or Spray) Anti-Allergy Tablets Homeopathic Remedy Other
Please mark the medicines you have taken, or "None" if no medicine was necessary.
Comments
Save Save and Next Day

**Fig. 1** The data entry form in the PHD that is voluntarily filled by each participant on a daily basis. In this specific example, the language used is English, while the PHD user input resulted in 7 points for symptoms plus 2 points for medication being used

- Moderate discomfort (moderate problems) = 2
- Strong discomfort (severe problems) = 3

Then, for each organ, four (4) specific types of symptoms may be reported as follows (each symptom receives one point):

- Eyes: itching, foreign body feeling, redness, watering
- Nose: itching, sneezing, running, blocked
- Airways (Lungs): wheezing, shortness of breath, cough, asthma

Each organ-specific symptom can thus receive a maximum of 3 points (for severe problems) plus 4 points (for demonstrating all organ-specific symptoms), that is, a total (maximum) of 7 points. This leads to an overall total symptom score (maximum) of 21 points for all three organs. As in a previous study by Voukantsis et al. (2013), up to five additional points could be added as a result of the medication being used (one point per medication type: eye drops, nose drops, tablets, homeopathic and other). Thus, the total number of points related to the symptoms and medication that a user can report may vary from zero (no symptoms) up to 26. It should be noted that instead of simply adding five additional points as a result of the medication being used, the medication points can be "weighted" in terms of importance (e.g. medication for the nose is given more weight than medication for the eyes because of the affect it has on the symptoms), yet this approach has not been applied in the current paper.

In addition to the organ-specific symptoms, an overall symptom score is recorded, ranging from "very poor" to "very good" and corresponding to a scale of integer values from ten to zero (10–0).This score is meant to represent the overall symptom severity and feeling of quality of life from the users' point of view.

The PHD users have a number of services available, including the history of all their symptoms and graphs that combine their symptoms with relevant pollen count data. The data made available for analysis in the frame of this study consisted of PHD reports in Germany dated from the first of January 2009 up to the twentieth of October 2011.

#### 2.1.2 Pollen concentration data

Daily average pollen data for the years 2009, 2010 and 2011 were collected at pollen-monitoring stations in Germany ($n = 46$ stations) using volumetric spore traps of the Hirst design (Hirst 1952) situated at roof level. Pollen samples were analysed by light microscopy, and raw data were converted to airborne pollen concentrations per cubic metre of air according to recommended protocols (Hecht and Winkler 1994). The pollen data are used in the following manner: The pollen-monitoring stations are grouped into regions. Each data entry by a PHD user is assigned to a region on the basis of the Zip code information that he/she provides. The pollen count values used are the average over all pollen concentration values of the stations in the region. If a station does not provide data for a day, it is not taken into account for average calculation (so the average is only calculated over all data providing stations). A station may be member of more than one region. The data are stored in the EAN database (https://ean.polleninfo.eu/Ean/) and are linked to the PHD.

### 2.2 Methods of data analysis

The PHD data were normalized to allow for a seamless analysis for all available years, as described in the rest of this chapter. For this purpose, detailed queries were performed with the aid of proper data analysis tools and computational procedures (including clustering), in order to extract the information of interest. Then, a number of descriptive media (graphs and tables) were chosen as the way to describe the findings of the analysis of the PHD data related to years 2009, 2010 and 2011. Moreover, combined graphs were constructed, in order to visualize and investigate symptoms as well as related parameters. The analysis was conducted with the aid of the Matlab computational environment (The MathWorks, Inc., Natick, MA, USA).

#### 2.2.1 Data normalization

Normalizing data is a data analysis step usually applied to change the range of values for certain variables. In this case, we have applied the min–max scaling to transform pollen symptoms and pollen concentrations into the same range of values, that is, [0, 1]. The min–max scaling, over a variable $x$, is described by the formula:

$$x\mathrm{hat} = (x - x\mathrm{min})/(x\mathrm{max} - x\mathrm{min}) \quad (1)$$

where $x$min and $x$max are the minimum and maximum values of the variable $x$. Thus, the new variable, $x$hat, will have a minimum value of zero and a maximum value of one.

### 2.3 Hierarchical clustering

Clustering is an unsupervised learning technique capable of identifying structures in large datasets and representing the results in the form of data groups of similar characteristics (Mirkin 2005). Similarity is measured in terms of certain metrics, in this case, Euclidean distance in N-dimensional space (where N is the number of variables in the dataset). Therefore, the data groups (clusters) express specific associations among the variables of a dataset—in this case, the temporal distribution of the severity of allergic symptoms during the year 2011—and could represent interesting patterns that are worthy of further investigation.

In this case, we have applied the average linkage clustering algorithm (Murtagh, 1984). The latter one belongs to a family of clustering algorithms called *hierarchical clustering*. The main characteristic is the separation of data into groups over a variety of scales in order to create a cluster tree. The resulting tree is not a single set of clusters, but rather a multilevel hierarchy of clusters. The application of this method in the current paper has provided with the results presented with the aid of Fig. 5.

## 3 Results

### 3.1 PHD use

The total number of records (reports) for the 3-year period for Germany was found to be 60,784, and the total number of people that made use of the PHD was 1,686, out of which 789 were female, 888 were male and 9 had no gender identification in the database. The distribution of users per year and the associated number of reports are presented in Table 1; Figs 2, 3. It should be noted that knowledge on the specific areas of Germany from which users come from is limited to the Zip code of their location, which is the only area-specific information that they are asked to include in the PHD. This information was not used in the current analysis. The Zip code based information is being used by the PHD to provide with pollen count data as previously described in Section. 2.1.2.

From Fig. 2, it is evident that there is a small number of users (less than 50), in comparison to the overall number of PHD users, that contributed more than 200 daily reports in the 3-year period, that is, for more than approximately 20 % of the total time. In addition, a large number of users (approx. 1,300) reported symptom data for <50 days of the whole reporting period, that is, for not more than 5 % of the days of the study period. The demography of PHD users is presented in Table 2, from which it is evident that their majority comes from the age group 25–44, followed by age groups 45–64 and 16–24. These results should be interpreted in parallel with other parameters like the demography of internet users in Germany (DESTATIS 2013). On this basis, it is evident that the majority of the PHD users in Germany for the years 2009–2011 belong to the age group that has a mean daily access to the internet of 84 % (the second highest in the country), while the age group with the highest daily internet usage is represented by only 10.5 % of the PHD users. This shows that the technological platform of the PHD does not favour the participation of those characterized as the more persistent internet users, but is rather influenced by the allergy symptoms experienced and the willingness to actively get involved. Concerning any relationship between the age of the users and the symptoms, it should me mentioned that there may be a different severity of allergic symptoms in children, adults and the elderly, but the PHD documents their perception of the symptoms, which may also be individually different.

**Table 1** Number of PHD users and their reports per year

| Years | Users | Reports |
|---|---|---|
| 2009 | 353 | 4,295 |
| 2010 | 486 | 16,296 |
| 2011 | 982 | 40,193 |

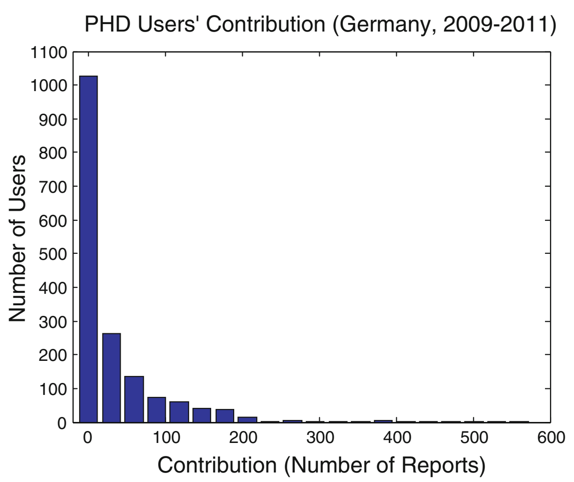


**Fig. 2** PHD users' contribution for the years 2009–2011. The *x-axis* describes the total number of (daily) reports and the *y-axis* the overall number of users

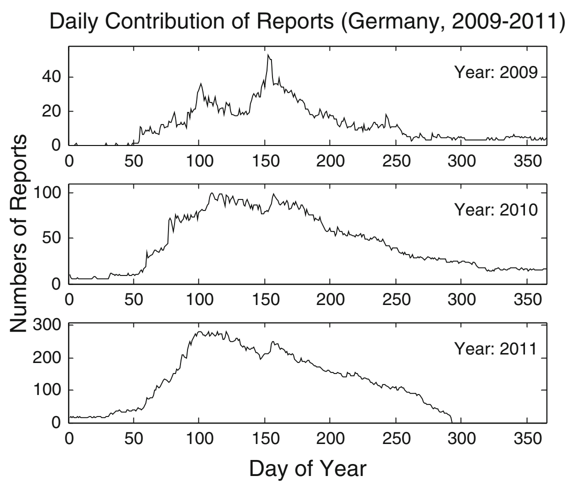


**Fig. 3** Daily contributions (reports) to the PHD, per year. The *x-axis* corresponds to the day of the year from January first and the *y-axis* to the number of reports per day (the contribution of reports extends to twentieth October in 2011)

**Table 2** Age distribution of the PHD users in Germany 2009–2011 on the basis of data provided by user reports

| Age group | Number of users and their percentages over the total PHD users per age group (%) | Percentage of internet users in Germany (on daily basis) per age group (%) |
|---|---|---|
| 1–15 | 41 (3.1) | 63 |
| 16–24 | 141 (10.5) | 90 |
| 25–44 | 770 (57.6) | 84 |
| 45–64 | 355 (26.6) | 71 |
| 65+ | 30 (2.2) | 59 |

The percentage of internet users is derived from DESTATIS (2013)

With the aid of Fig. 3, we can have an overview of the temporal variation of reports. It is therefore evident that the profile of daily contributions for the 3 years of study was similar, with two peaks appearing approximately at the same time per year (around days 110 and 156, corresponding to the twentieth of April and the fifth of June). It should be noted that reports were provided by users throughout the year, indicating that some of them might be attributed to allergic reactions not related to the pollen season (the exception is 2011, for which the database that we had available included no reports after day 292, i.e. twentieth of October; we intend to provide with mode data in a future paper).

The total score of symptoms per organ (as reported by each user and per year) varied. The mean value of the overall organ symptoms reported gives an indication of the most "common" symptoms. This can also be interpreted as the mean weight or severity of symptoms.

Nasal symptoms were found to be the most severe, followed by ocular and airway symptoms (Table 3). On this basis, we investigated the organ-specific symptoms and their frequency of appearance in the overall symptoms reported. Thus, "nose sneezing" (29 %) was followed by "nose blocked" (26 %) and "eye itching" (also 26 %). Nasal symptoms are included in at least 21 % of the reports, while ocular symptoms are found in 10–26 % of reports and airway symptoms in 4–13 % of reports (Fig. 4). Overall, "nose sneezing", "nose blocked" and "eye itching" are the three symptoms most frequently reported by the PHD users in Germany within the three studied years.

**Table 3** Total mean value of reported symptoms per organ (minimum value equals zero, and maximum equals three)

| Years | Symptoms | | |
|---|---|---|---|
| | Eye total | Nose total | Airway total |
| 2009 | 1.26 | 1.98 | 0.81 |
| 2010 | 0.87 | 1.66 | 0.52 |
| 2011 | 1.13 | 1.79 | 0.64 |

### 3.2 Medication use and symptoms reported

Emphasis was put on identifying the medication type on the basis of reported data, as well as the diurnal variation of its use. Thus, we calculated the number of reports that included at least one medication type, as the basis for the estimation of the percentages of medication usage per year. On this basis, it was found that the majority of the PHD reports mentioned the use of anti-allergic tablets (from 56 % in 2010 up to 60 % in 2009 and 2011) and that medication use followed a similar pattern every year in terms of percentages of medication types (Table 4). In addition, we calculated the correlation coefficient between the overall total symptoms (symptom score ranging from 0 to 21) and the medication type being used (Table 5). The highest correlation was found to be with tablets ($r = 0.86$), followed by nose drops and eye drops, the latter two corresponding to organs that demonstrate the highest percentage of symptoms.

### 3.3 Symptoms and pollen

The most common aeroallergens in Germany (and in central and northern Europe) are *Betula* (birch), *Poaceae* (grasses) and *Artemisia* (e.g. mugwort) (D'Amato et al. 2007). On this basis, the relationship between those three pollen types and the symptoms reported via the PHD were investigated using the 2011 dataset, as this is the richest in symptom records, consisting of a total of 982 users and 40,193 reports. Symptom data were considered to be more reliable if they had no temporal gaps. We therefore assumed that the criterion for selecting the PHD users to be investigated should be a number of seven (7) consecutive days of reports (at least), and thus, we identified a total of 491 users. For each user, the overall symptoms score was employed. This score was plotted for every day a report was recorded, in a graph where the

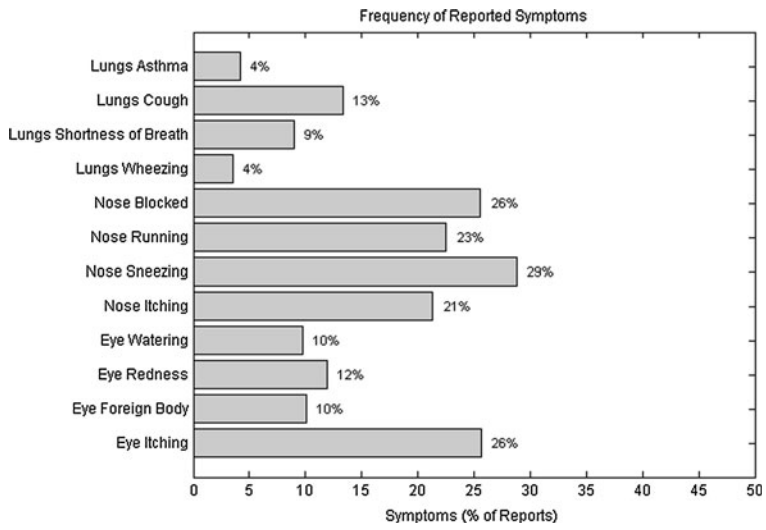


**Fig. 4** Symptoms being reported for all 3 years, as a percentage of the total number of reports included in the PHD for Germany. The term "lungs" refers to airways and is used because of its inclusion in the current version of the PHD

**Table 4** Medication type used as reported by the PHD users

| Years | Medication type used | | | | | |
|---|---|---|---|---|---|---|
| | Eye drops (%) | Nose drops (%) | Tablets (%) | Homeopathic (%) | Other (%) | Overall |
| 2009 | 285 (13) | 618 (27) | 1,362 (60) | 276 (12) | 643 (28) | 2,262 |
| 2010 | 1,274 (19) | 1,949 (29) | 3,717 (56) | 625 (9) | 2,204 (33) | 6,654 |
| 2011 | 4,365 (25) | 6,446 (37) | 10,498 (60) | 2,221 (13) | 5,451 (31) | 17,348 |

Parenthesis indicated the percentage in comparison with the overall number of reports that included medication types per year

**Table 5** Correlation coefficient between medication type and overall total symptoms (aggregated data over all PHD users per year)

| | Overall total symptoms |
|---|---|
| Eye drops | 0.64 |
| Nose drops | 0.68 |
| Tablets | 0.86 |
| Homeopathic | 0.21 |
| Other | 0.15 |
| Overall total symptoms | 1 |

horizontal axis represents calendar time and the vertical axis is the integer-ID corresponding to each user (i.e. a number between 1 and 491). The PHD users were clustered as described in chapter 2.3 on the basis of the temporal variation of the overall symptom score that they reported. In the same graph, the pollen seasons for birch, grass and mugwort pollen were introduced on the basis of the first and last non-zero values of pollen concentration (Fig. 5).

Figure 5 demonstrates that the three pollen seasons under consideration include the majority of reported symptoms for the related time periods, provided that we do not take into account PHD users that report symptoms for a wider time frame (represented by horizontal lines in the graph). In addition, the same figure reveals the existence of clusters of high overall symptoms during the combined period of birch, grass and mugwort flowering (red areas in the symptom levels).

The next step in the description of the relationship between symptoms and pollen types was achieved by plotting: (a) the temporal variation of the overall symptoms, together with the total symptom scores for the three organs; (b) the temporal development of the overall symptom score accompanied by the concentration for the three pollen taxa included in the investigation. All these are included in Fig. 6.

By inspecting Fig. 6a, it is evident that the patterns of the temporal variation of the overall symptoms as well as of the total ocular, nasal and airway symptoms are very similar. On this basis, the overall symptom

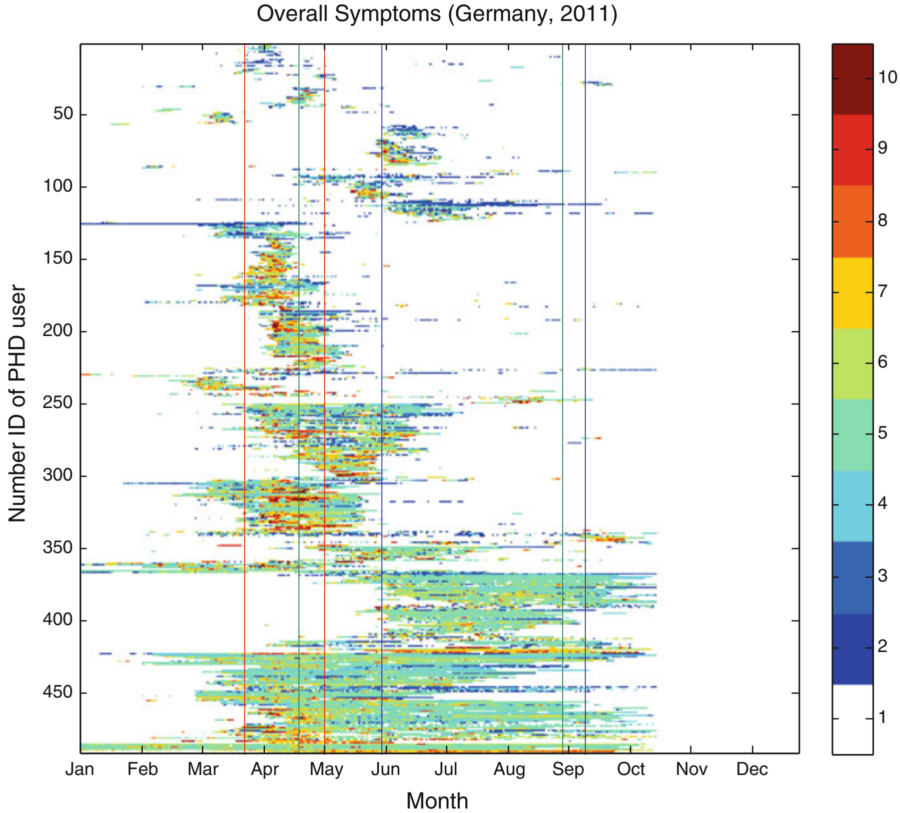


**Fig. 5** Overall symptoms score (1–10 with a different colour scale), for each one of the 491 different PHD users (*y-axis*) who reported symptoms for at least 7 consecutive days. PHD users were clustered on the basis of the temporal variation of their overall symptoms score. The pollen periods are identified with the aid of two vertical lines of the same colour (start–end) as follows: birch = *red lines*, grass = *green lines*, mugwort = *blue lines*. Reports for the year 2011 end on the twentieth of October due to data availability. (Color figure online)

score may be used as the basis for the identification of increasing/decreasing trends for the specific organ-based score of symptoms.

The three most frequent organ-specific symptoms demonstrate similar development with maxima at the beginning of April and June. The normalized pollen counts (linearly transformed values to the scale [0, 1]) for birch, grass and mugwort pollen (Fig. 6b) show that overall symptoms scores generally follow the birch and grass pollen seasons.

## 4 Discussion

The PHD was developed to overcome unsophisticated methods for documenting symptoms in pollen-induced allergy sufferers, for example, self-written diaries in paper form, and has evolved to a data driven service. Such a service can support a large number of affected individuals, providing with a database of symptoms and related information. Multilingual support, compatibility with the rapidly emerging Smartphone markets and innovative services that result by combining linked databases are some of the key characteristics of the PHD system.

In this paper, we analysed part of the PHD system database that corresponds to users located in Germany and for the period 2009–2011. We identified several user profiles with distinct habits in contributing reports and using medication. Some of the key findings of this study are summarized below:

- There is a great discrepancy between PHD users in terms of the frequency of symptom reports. The majority of users report symptoms for a small overall time frame, while less than 5 % of the users report symptoms for more than 20 % of the years of study.
- The temporal variation of reports demonstrated two peaks in specific time frames regardless of the year (twentieth of April and fifth of June).
- Nasal symptoms were found to be the most severe, followed by ocular and airways symptoms. “Nose sneezing”, “nose blocked” and “eye itching” are the most common organ-specific symptoms. This finding is in line with previous studies, reporting

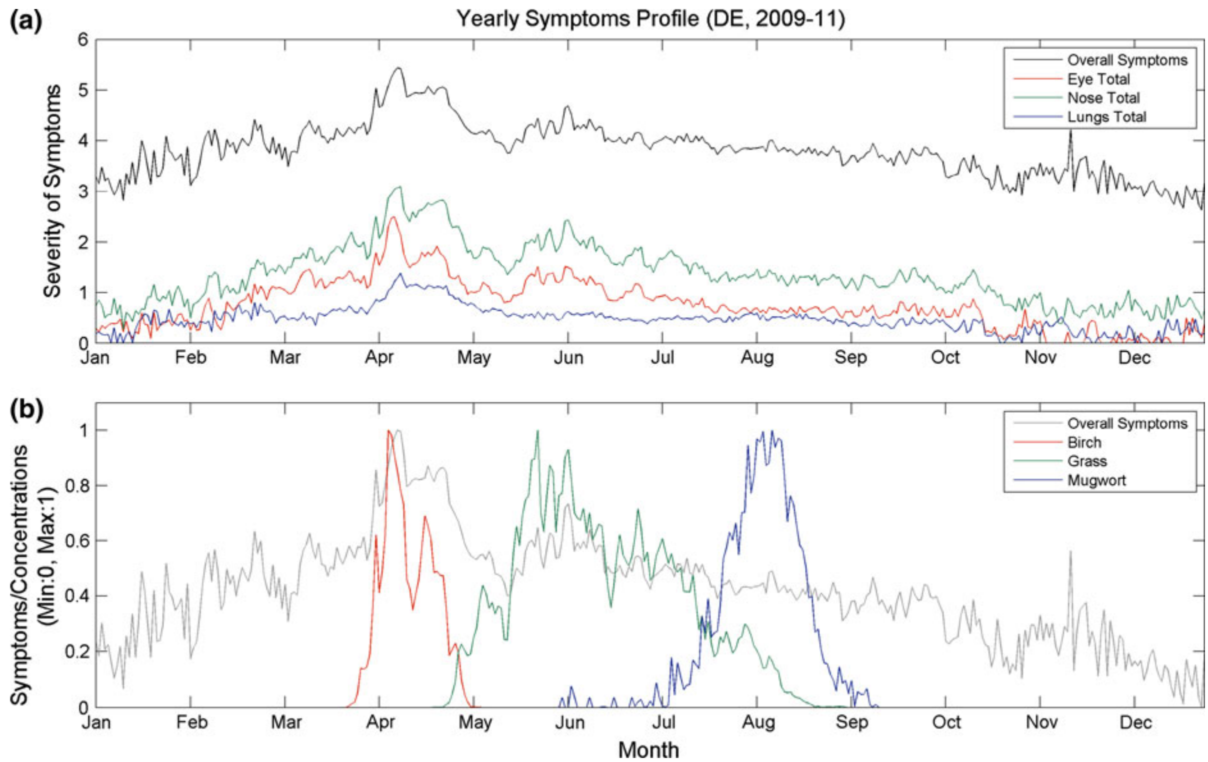


**Fig. 6** Temporal resolution of symptoms and pollen counts. The data were aggregated over the years 2009–2011, resulting to the yearly profile. *Upper graph* **a** Overall symptom score vs total symptoms for the three organs (average values of all users in Germany, 2009–2011). *Lower graph* **b** normalized overall symptoms and pollen concentrations of birch, grass and mugwort (values between Min: 0 and Max: 1, see Sect. 2.2.1). The data are average values over all PHD users in Germany and all pollen concentrations (from all stations), for 2009–2011

that nasal congestion was the most common moderate or severe nasal symptom (55 %) and that 44 % of patients suffered moderate or severe ocular symptoms (1,494 patients with allergic rhinitis, Meltzer 2007).

- Concerning medication use, the most common medication being used is tablets, while the percentage of medication types does not vary significantly per year.
- The overall symptoms reported peak during the pollen season of birch and grass, while there was no increase in overall symptoms during mugwort season. The reason for the latter is unknown to us. It may be that mugwort is inducing more nasal and eyes symptoms than overall symptoms. The importance of mugwort in the identification of allergy reactions has risen recently, as suggested by Heinzerling et al. (2013), who propose the inclusion of this specific taxon in the "European standard" prick test. It should be noted that a clarification concerning the role of each pollen taxon to symptom development will be subject to another, more detailed publication, after threshold values will have been determined for different regions on the continent.
- The overall symptom scores generally follow the normalized birch and grass pollen seasons. It should be noted that a similar behaviour has been reported for grass pollen-induced symptoms in the Netherlands (de Weger et al. 2011), thus verifying a similarity in the pattern that may exist in central Europe.

In addition, the PHD combines symptom data with knowledge about atmospheric concentrations of pollen provided by the European Aerobiology Network. As a result, it will be possible to examine the type and amount of airborne pollen attributing to an individual's symptoms and thereby identifying dose–response relationships (threshold values).

On this basis, it is evident that the most prominent way for the analysis of pollen-induced symptoms and the provision of information services for quality of life support a personalized approach. Voukantsis et al. (2013) recently showed that it is possible to construct a model with acceptable performance for predicting pollen-induced symptoms at a personal level. In contrast, the authors were unsuccessful at developing a unique model for all users. This suggests that predictions for atmospheric concentrations of aeroallergens have a limited value on their own and that it should be more beneficial to predict an individual's symptoms instead.

The results presented here also indicate that it could be possible to develop an information service, based on forecasts of atmospheric pollen concentrations, which would provide PHD users with an early warning of the type and severity of symptoms that they are likely to experience during the forthcoming days (expressed as the level of risk). In addition, the identification of personal threshold levels for symptom induction and development may be examined as a next step in the improvement of information provision for patients and for the support of the everyday operations of physicians as well as health administrators and governmental officers.

## 5 Conclusions

The PHD is a suitable and easy to understand tool for documentation of pollen-induced symptoms and medication. The number of users in Germany has been increasing in the 3 years of operation of the system (2009–2011).

The PHD may give new insights into the individual threshold level of pollen species and their required number for inducing symptoms thereby taking into account drug influences. Furthermore, it may be an ideal tool for clinical studies in immunotherapy using pollen extracts.

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**Ethical standard** The authors of this paper state that they have taken into account the ethical standards laid down in the 1964 Declaration of Helsinki. All users of the PHD have given their consent prior to their inclusion in the PHD while in addition they had the option to give information anonymously. Details that might disclose the identity of the subjects participating in the study have been omitted. All data related to persons that have registered their symptoms and medication use to the PHD have been treated anonymously in this paper. On this basis, no ethical issues arise from this study and from the use of PHD data.

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