



Impact of air pollution on symptom severity during the birch, grass and ragweed pollen period in Vienna, Austria: Importance of O₃ in 2010–2018[☆]

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ABSTRACT

Air pollution is a threat to the general population, especially to pollen allergy sufferers in urban environments. Different air quality parameters have hitherto been examined which add to the burden of pollen allergy sufferers. Parameters such as NO₂, SO₂, PM₁₀, PM_{2.5}, and O₃ are supposed to have additional impact, not only on health in general (increase in asthma, allergy sensitization frequency), but also on pollen grains (increase of allergenicity). However, it remains unknown if those air quality parameters increase symptom severity during the pollen season. We selected the birch, grass, and ragweed pollen seasons as different time periods throughout the year and analyzed the relationship of symptom data to pollen, air quality, and meteorological data (temperature, relative humidity) for the metropolis of Vienna (Austria). A linear regression model was computed based on different symptom data, and both pollen and air quality data were tested simultaneously. Ozone was positively and significantly associated with symptom scores in all three seasons, whereas this was only rarely the case with other pollutants. Therefore, only ozone was selected for further analysis in a model including meteorological parameters. In this model, effect estimates of ozone were attenuated but remained significant for the grass pollen season. The lack of significance in the other seasons may be attributed to the less numerous symptom data entries and the shorter duration of the pollen seasons for birch and ragweed. All other air quality parameters usually showed lower concentrations during the pollen seasons and displayed little variation. This might explain the lack of a clear signal. Our results suggest that today's allergic population is already affected by air quality (rising O₃ levels). Air quality should be considered as well in pollen information and pollen allergy studies in general because of its increasing importance in the light of global warming.

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1. Introduction

The prevalence of allergies has been rising in recent decades (D'Amato et al., 2015). Allergic rhinitis affects the global population, namely 10–30% of adults and up to 40% of children accounting for 400 million people worldwide (Pawankar et al., 2013). Estimations of sensitization rates of pollen allergies themselves vary, but approximately 20% of the population in Austria are affected by an allergy (Dorner et al., 2006); as an example of a Central European country. In the Vienna area, sensitization rates amount to 56.3% for grass, 41.7% for birch, and 11.1% for ragweed pollen based on the skin prick tests of more than 13 000 pollen allergy sufferers (Hemmer et al., 2010). The socioeconomic impact of allergies is

Abbreviations: APIn, Annual Pollen Integral; EAN, European Aeroallergen Network (<https://ean.polleninfo.eu/>); PHD, Patient's Hay-fever Diary (www.pollen-diary.com/); SLI, symptom load index; ZAMG, Austrian National Weather Service (Zentralanstalt für Meteorologie und Geodynamik); BETU, *Betula*; POAC, Poaceae; AMBR, *Ambrosia*.

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tremendous with, e.g. estimations of direct and indirect costs for an untreated patient of €2400 per year in the European Union (EU) (Zuberbier et al., 2014). Pollen allergies and their impact are therefore a considerable burden for the population concerned, the health-care system, and the economy. The definitive mechanisms and causes for the increase of allergies are still not understood in detail. The effect of air pollution has been increasingly in focus in addition to the hygiene hypothesis, that aims to explain the increased occurrence of allergies due to the reduced confrontation of the immune system with natural allergens and infections in urban environments (Okada et al., 2010). Urban areas are concerned in particular due to their denser populations on the one hand and, on the other hand, the correlation with a higher prevalence of pollen allergies in those areas (Nicolaou et al., 2005). Air pollution is discussed as a possible multifactorial cause and is of relevance for more than one pathway. The effects of air pollutants were shown for: (1) human health in general (Dauchet et al., 2018; Lehtomäki et al., 2018); (2) asthma patients in particular (Barck et al., 2005; D'Amato et al., 2018; Kreit et al., 1989); (3) hospital admissions, outpatient visits, and medication sales (Grundström et al., 2017; Zhang et al., 2015); and (4) pollen and its allergenicity (Beck et al., 2013; Majd et al., 2004; Sénéchal et al., 2015; Zhu et al., 2018). Hitherto evidence thus suggests that air pollution impacts prevalence and symptom severity of pollen allergies (D'Amato, 2000; D'Amato et al., 2001; Kim et al., 2013), although the latter has not been the focus in most studies.

Various air pollutants have been included in epidemiological and experimental studies, among them particulate matter with a small aerodynamic diameter in a range of 2.5–10 µm (PM_{2.5}, PM₁₀), sulfur dioxide (SO₂), nitrogen dioxide (NO₂), and ozone (O₃). All of these aforementioned air pollutants negatively impact human health. PM₁₀ and PM_{2.5} mostly originate from combustion processes. PM_{2.5}, in particular, causes significant health problems: it is estimated that PM_{2.5} is responsible for 3% of mortality from cardiopulmonary diseases and 5% of mortality from cancer concerning the respiratory system worldwide (Cohen et al., 2005). NO₂ is formed by combustion processes. It is not only a precursor for ozone but can also exacerbate asthma symptoms (D'Amato et al., 2018). Additionally, studies suggest that NO₂ increases pollen allergenicity (Frank and Ernst, 2016). SO₂ is emitted by the combustion of fossil fuels. It causes increased airway inflammation (Liu et al., 2009) and altered allergen expression (Rogerieux et al., 2014). Tropospheric ozone formation increases during hot and sunny weather, as the gaseous air pollutant is formed by UV-radiation (Atkinson, 2000) depending on the concentration of the precursor pollutants, nitrogen oxides and volatile organic compounds, originating mostly from industrial and traffic sources. Ozone not only affects pollen and its allergenicity (e.g. Zhu et al., 2018), but also serves as an indicator for reactive species and photochemical smog, respectively (World Health Organization, 2000).

With ongoing research in the field of air pollution, the term

“multi-pollution” became increasingly popular. New studies indicate that especially urban air consists of multiple air pollutants and harm human health even more than single air pollutants (Brunekreef et al., 2019).

The best way to discover a measurable impact of air pollutants on the daily life of pollen allergy sufferers is via symptom data. The use of symptom data arises from clinical trials for immunotherapy (European Medicines Agency, 2009). Feedback by allergy sufferers is needed for dose finding and control of efficacy of the immunotherapy. However, working with patients directly is time and cost consuming, especially when studying a large sample size. The advances in technology made electronic symptom-diaries increasingly popular and crowd-sourced symptom data became available (e.g. Bastl et al., 2020).

This study aims to analyze crowd-sourced allergy symptom data in a metropolis in combination with pollen, weather, and air quality data for the first time on a large spatial scale to gain insights into the relevance of different air pollution parameters and a possible measurable effect.

2. Material and methods

2.1. Pollen data

Daily pollen concentrations of the three major aeroallergens birch (*Betula*), grasses (Poaceae) and ragweed (*Ambrosia*) for Vienna (years 2010–2018) were obtained from the European Aeroallergen Network database (EAN; www.ean-net.org). The monitoring station in Vienna is a Hirst-type pollen and spore trap (Hirst, 1952) and is located on the rooftop of the Karl–Kreil building (coordinates: 48.248889, 16.356250) at an elevation of 14 m, at the Austrian National Weather Service (Zentralanstalt für Meteorologie und Geodynamik). Air samples were evaluated adhering to the minimum requirements of the European Aerobiology Society and EAN (Galán et al., 2014), whereas the terminology for aerobiology follows Galán et al. (2017). We applied the 80% definition for the pollen season, defined to start at 10% of the Annual Pollen Integral (APIn) (Galán et al., 2017) and to end at 90% of the APIn. This definition was chosen to minimize the overlap between the analyzed time periods and to reduce the impact of other pollen types of relevance for pollen allergy sufferers in the beginning/end of the respective pollen periods (e.g. alder at the start of the pollen season of birch or mugwort during the start of the pollen period of ragweed). The defined time periods are given in Table 1.

2.2. Symptom data

Symptom data were requested from the Patient's Hay-fever Diary (PHD) (www.pollendiary.com). This is a free web-based tool for the documentation of pollen allergy symptoms and comparison to regional pollen concentrations and is also available as a mobile

Table 1
Start and end dates and APIn of the 80% season definition of the birch, grass, and ragweed pollen seasons as well as the SLI values respectively from 2010 to 2018.

Year	Season/APIn Birch	SLI Birch	Season/APIn Grass	SLI Grass	Season/APIn Ragweed	SLI Ragweed
2010	03.04–25.04/10936	5.44	05.06–15.07/2817	4.25	20.08–03.10/711	2.88
2011	02.04–19.04/3210	5.55	19.05–13.07/2440	3.69	22.08–10.09/1329	3.61
2012	26.03–14.04/9512	5.37	11.05–18.07/1388	3.93	20.08–18.09/354	3.34
2013	17.04–27.04/4748	6.45	16.05–24.07/3299	3.87	18.08–09.09/857	3.59
2014	23.03–09.04/7262	5.47	19.05–07.07/2154	4.57	18.08–20.09/371	3.37
2015	10.04–23.04/5262	5.64	17.05–07.07/3467	4.43	23.08–17.09/645	4.58
2016	02.04–23.04/9731	5.80	22.05–15.07/2677	4.36	26.08–14.09/1411	4.70
2017	29.03–11.04/3684	5.25	19.05–10.07/2678	4.54	10.08–28.09/714	4.18
2018	09.04–23.04/5791	6.22	02.05–10.07/2925	4.13	09.08–28.09/720	3.87
Mean	03.04–19.04/6150	5.70	18.05–13.07/2649	4.20	19.08–20.09/790	3.80

application for iOS and Android. While it has been introduced to several European countries, it was developed in Austria and started in 2009. Therefore, it is a pool for crowd-sourced symptom data that operates in line with the latest EU regulations on data protection and security. This implies that a minimum of personal data is collected. The symptom score calculation and its modification to the symptom load index (SLI) as normalized values on a scale from 0 to 10 is described in detail in Bastl et al. (2014). Data on the organs eyes, nose, lungs, and specific symptoms, degree of severity as well as medication are included in these scores. Asthma is included due to its importance and connection to allergies, although it is not a symptom, but a chronic disorder (Global Asthma Network, 2018). Not all available symptom data were processed. Only data entries from users of Vienna (Austria) and users with a significant positive background correlation (positive correlation coefficient sign. level below 0.05) to the respective pollen types were used to process data most likely deriving from pollen allergy sufferers without having access to a medical diagnosis. It was already shown that such filtering techniques as well as the use of the SLI lead to robust results and that the spatial distribution pattern of symptom data within Vienna is stable (Bastl et al., 2014, 2015; 2018; Kmenta et al., 2017). The user numbers as well as the seasonal data entries are displayed in Table 2. Additional crowd-sourced user information (yearly and seasonal user numbers/data entries; daily user numbers within the season; possible polysensitized users) is included as supplementary material.

2.3. Air quality and meteorological data

Air quality data were obtained from the Municipal Department 22 (Environmental Protection) in Vienna. Data were collected for O₃, PM₁₀, PM_{2.5}, NO₂, and SO₂ from 17 measuring stations distributed across Vienna. All measuring stations included are managed according to the Austrian Ambient Air Quality Act (Immissionschutzgesetz-Luft) and the Ozone Act (Ozongesetz). Not all parameters are measured at all stations. The measuring stations are located in areas with varying degrees of urbanization, in traffic affected or oriented as well as in recreation or industrial areas to capture the diversity of Vienna's habitats. More details and information on individual stations can be retrieved from the air quality reports of Vienna (e.g. Augustyn et al., 2019). Herein, we summarize the data for the whole of Vienna by calculating a mean from all stations measuring the respective parameters based on daily mean values per station. Ozone values were calculated differently as a mean of all stations and as a maximum eight-hour mean as proposed by the World Health Organization guidelines (World Health Organization, 2005), based on half-hour concentrations amounting to hourly mean concentrations. Data were calculated as a mean from all stations providing values (ignoring stations with missing

values).

The parameters of temperature and relative humidity were chosen for inclusion from the meteorological data obtained from the ZAMG (www.zamg.ac.at). The data were derived from a semi-automatic weather station (station number: 5904) situated directly at the ZAMG. Temperature is calculated herein as mean value of the daily maximum and minimum temperature and relative humidity is calculated as mean value of the values recorded at different times during the day (07:00, 14:00, 19:00 UTC).

2.4. Statistics

Simple linear regression models using the SLI as the dependent variable and the square root of the pollen concentration as the independent variable were computed. These regression models are used twofold:

- to illustrate the correlation and the relationship between SLI and the respective square root of the pollen concentration and
- to use the residuals of these models for explorative analysis steps.

The regression lines in the scatterplots for birch, grasses, and ragweed for all years (2010–2018) illustrate the model. The box-plots were grouped and used to visualize the residuals from the linear regression and to gain insights into the variations of different ozone concentration groups. The residuals of the linear regression were normally distributed. The days were grouped into those with ozone concentrations at or below 100 µg/m³ and those above 100 µg/m³. This threshold is based on WHO air quality guidelines (World Health Organization, 2005) and was exceeded regularly during the examined time period.

The next step in the analysis was to examine the relationship between the SLI and a certain air pollution parameter. We call this "Method 1" which can be described by the equation $SLI_d = \sqrt{Pollen_d} + O_{38md}$. SLI data, pollen concentrations, and air pollution parameters were used as differenced values (by subtracting the value of the previous day from the current day) in "Method 1". We have chosen this approach to remove autocorrelation from the time series and to better display and process the variability of daily values. The resulting values represent the daily change in absolute terms. The SLI was used as a total and in addition, as the respective proportion of eyes, nose, lungs, and medication scores. The direction of the effect (regression coefficient) and its significance in analysis of variance (ANOVA) were computed together with the R² in "Method 1". The starting point for the second method was a full factorial model and non-significant factors were sequentially eliminated. This second linear regression approach (absolute SLI as

Table 2

Number of PHD users (sign. pos. correlation to the respective pollen types) and number of seasonal data entries per year and for the whole time period (averaged for 2010–2018) during the birch, grass and ragweed pollen seasons defined as 80% of the annual pollen concentrations of birch, grass, and ragweed.

Year	Birch			Grasses		Ragweed	
	# of users	# of entries	# of users	# of entries	# of users	# of entries	
2010	59	740	84	1852	16	411	
2011	104	1235	107	3017	21	238	
2012	78	1062	95	3305	13	165	
2013	189	1231	185	5083	30	402	
2014	155	1572	131	2937	12	161	
2015	81	727	120	2606	21	290	
2016	165	1944	89	1825	18	210	
2017	63	556	73	1305	31	758	
2018	49	458	73	1934	12	280	
Mean of 2010–2018	105	1058	106	2652	19	324	

the dependent variable and air pollution and meteorological parameters as independent variables) was used to test and correct for the potential influence of the respective meteorological parameters ("Method 2"). Based on this method, an ANOVA was computed to identify any significant air pollution parameter effect if basic meteorological parameters were also included in the calculation. This is of importance since meteorological parameters influence pollen, symptoms, and air pollution during the season. Autocorrelation of the residuals (tested with the Durbin–Watson test (Fox, 2016)), was removed by including further (the meteorological) parameters in combination with the ozone concentrations (chosen based on the results of "Method 1"). "Method 2" used lagged values (the values of the previous day instead of the current day). The independent variables' square root of the pollen concentrations, the lagged square root of the pollen concentrations, the logarithm of the temperature, the lagged relative humidity, the ozone concentration, and the lagged SLI were tested for the dependent variable (SLI).

The explicit equations for "Method 2" are:

- Birch: $SLIBETU = \sqrt{BETU} + \sqrt{BETU}_1 + SLIBETU_1 + O_{38m} + \log t + rel_1 + \varepsilon$
- Grass: $SLIPOAC = \sqrt{POAC} + \sqrt{POAC}_1 + SLIBPOAC_1 + O_{38m} + \log t + rel_1 + \varepsilon$
- Ragweed: $SLIAMBR = \sqrt{AMBR} + \sqrt{AMBR}_1 + SLIAMBR_1 + O_{38m} + \log t + rel_1 + \varepsilon$

To look for problematic multicollinearity in the methods the variance inflation factor was computed (Fox and Weisberg, 2018). The maximum value for the set of "Method 2" was three and only values above five can be considered problematic in the calculations (Gareth et al., 2014).

No values were missing for symptom, pollen, and weather data as well as for ozone. For the other air quality parameters, a few values were missing randomly. The complete dataset for the statistical analysis is attached as supplementary material excluding daily pollen concentration data (no open data source). Statistical analyses were performed in the computing environment R 3.6.1 (R Core Team, 2019) and graphs were generated using the R package ggplot2 (Wickham, 2016).

3. Results

The air pollution parameters NO₂, SO₂, PM₁₀, PM_{2.5}, and O₃ are briefly characterized:

PM₁₀ and PM_{2.5} exceeded their target values on a regular basis from 2010 to 2018, but the highest values occurred during wintertime (outside the analyzed pollen seasons). The lowest values were recorded usually in summer time. NO₂ and SO₂ rarely exceeded their target values (mean 2010–2018: 1–2 days) with the latter occurring in low concentrations that were within the measurement error of the used devices. The target value of O₃ was exceeded frequently during the summer months (on 25 days as a mean for 2010–2018) with the eight-hour mean exceedance ranging from 131 µg/m³ to 196 µg/m³ (the Austrian target values are still set at 120 µg/m³ in comparison to the WHO target value which is 100 µg/m³) (World Health Organization, 2005). In addition, Austria recommends avoiding physical stress for people at risk at one hour mean concentration values above 180 µg/m³ and the same for healthy people at values above 240 µg/m³. The latter high exceedances were recorded rarely (only in 2015). All relevant data are published in detail in the Vienna air quality reports (e.g. Augustyn et al., 2019).

Duration and intensity in terms of the APIn of the pollen seasons and the mean SLI values throughout the investigated time frame

are summarized in Table 1 to reflect the seasonal variation.

Meteorological data are briefly described for the three analyzed pollen seasons. The mean temperature in the birch pollen season ranged from 10.1 °C to 17.7 °C (mean 2010–2018: 13.4 °C) and the mean relative humidity ranged from 48% to 66% (mean 2010–2018: 60%). In the grass pollen season, the mean temperature ranged from 18.9 °C to 21.8 °C (mean 2010–2018: 20.3 °C), whereas the mean relative humidity ranged from 52% to 66% (mean 2010–2018: 60%). The mean temperature in the ragweed pollen season ranged from 15.7 °C to 21.8 °C (mean 2010–2018: 19.5 °C) and the mean relative humidity ranged from 61% to 78% (mean 2010–2018: 67%).

The linear regression with the SLI as the dependent variable and the square root of daily pollen concentrations as the independent variable ("Method 1") shows an equal distribution of the data points and a significant linear trend for all pollen seasons (Fig. 1), although less for the ragweed pollen season (higher occurrence of zero days as well). For the birch pollen season, the correlations between the square root of the daily pollen concentrations and total SLI was 0.57. For the symptoms, the correlations were: 0.59 for the nose, 0.59 for the eyes, 0.30 for the lungs, and 0.06 for medication. The same correlations for the grass pollen concentrations amounted to a total SLI of 0.64 and symptom correlations were: 0.64 for the nose, 0.60 for the eyes, 0.37 for the lungs, and 0.49 for medication. For the ragweed pollen concentration, these correlations were 0.41 for the total SLI and 0.42 for the nose, 0.41 for the eyes, 0.10 for the lungs, and 0.10 for medication.

In "Method 1" only O₃ concentrations gave a consistent result with significant values for all three pollen types (Table 3). Significant results could be detected for the total SLI, eyes and nose, but not for lungs and in some cases (birch and grass pollen season) for medication. All air quality parameters except for ozone led to non-significant results in most of the cases (only on occasion; see Table 3).

The boxplots (Fig. 2) for the three respective pollen seasons from 2010 to 2018 illustrate the differences between the two O₃ concentration groups, especially for the birch and ragweed pollen seasons.

Since there was no significance for other pollution parameters during the respective time period, only O₃ was analyzed in "Method 2" including meteorological data. Temperature and humidity gave significant values for the birch and grass pollen seasons (only temperature was significant for the ragweed pollen season; Table 4). O₃ itself gave no significant result after taking pollen data and meteorological data for the birch and ragweed pollen seasons into account but was still highly significant for the grass pollen season (Table 4). In "Method 2", an increase of the O₃ level would behave in the following way: If O₃ rises from the 1% quantile to the 99% quantile (from 55 to 145 µg/m³), the SLI would rise on average about 0.29. Based on data from all grass pollen seasons, this would be an increase of 6% of the mean SLI for all years (2010–2018) due to O₃.

4. Discussion

4.1. Impact of air pollution on symptom data

An increase in O₃ concentration leads to an increased symptom severity during the birch, grass, and ragweed pollen season, when the trend component from pollen concentrations is removed. This result can be reproduced for the grass, but not for the birch and ragweed pollen seasons, when temperature and relative humidity are included in addition. This may be attributed to the shorter time periods for analysis due to a shorter pollen season (for birch and ragweed) as well as to less numerous PHD data entries than for the grass pollen season (see 2.2.). The problem of low PHD user

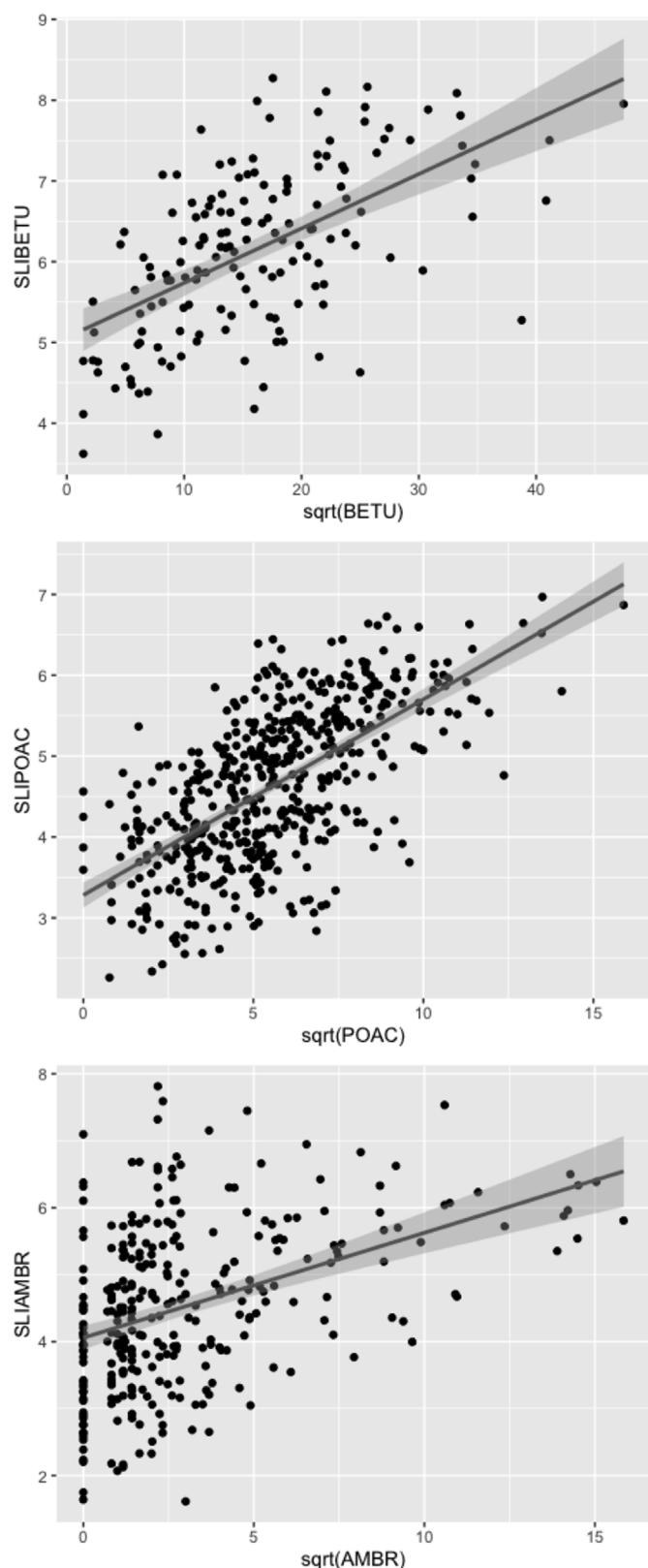


Fig. 1. Simple linear regression model with the SLI values (y-axis) and the square root of pollen concentrations (x-axis) for birch (first), grasses (middle), and ragweed (lower) pollen seasons. Data derived from the years 2010–2018. Note the homogenous distribution and thus the pollen concentration trend inherent in the SLI data.

Table 3

The corresponding R^2 (in percent) of “Method 1” including the significance levels and direction of the regression coefficient for the air quality parameters on the total SLI and the symptoms: eyes, nose, lungs, and medication during the birch, grass, and ragweed pollen seasons 2010–2018.

Birch	PM ₁₀	PM _{2.5}	O ₃	NO ₂	SO ₂
SLI total	29.3 NS/+	28.4 NS/+	32.8 **/+	28.5 NS/-	29.1 NS/-
Eyes	29.7 NS/-	30.1 NS/-	32.3 */+	32.5 */-	31.6 */-
Nose	22.9 NS/+	22.5 NS/+	26.1 **/+	22.7 NS/-	22.9 NS/-
Lungs	17.4 **/+	16.0 */+	14.4 NS/+	13.5 NS/+	13.0 NS/-
Medication	4.7 **/+	3.6 */+	5.1 **/+	1.8 NS/+	0.4 NS/-
Grasses	PM ₁₀	PM _{2.5}	O ₃	NO ₂	SO ₂
SLI total	25.2 NS/-	25.4 */-	29.7 ***/+	25.0 NS/-	24.8 NS/-
Eyes	20.6 NS/-	20.6 NS/-	22.1 ***/+	21.0 */-	20.2 NS/-
Nose	20.2 */-	20.5 **/-	23.2 ***/+	19.7 NS/-	19.5 NS/+
Lungs	5.0 NS/-	5.0 NS/-	5.5 NS/+	5.1 NS/-	4.9 NS/-
Medication	5.6 NS/+	5.3 NS/+	10.7 ***/+	6.0 */+	5.2 NS/+
Ragweed	PM ₁₀	PM _{2.5}	O ₃	NO ₂	SO ₂
SLI total	7.6 NS/+	7.1 NS/+	9.4 **/+	7.2 NS/+	7.8 NS/+
Eyes	6.3 **/+	4.7 NS/+	5.5 */+	6.5 **/+	6.0 */+
Nose	5.1 NS/+	5.1 NS/+	6.9 */+	5.0 NS/+	5.3 NS/+
Lungs	0.3 NS/+	0.3 NS/-	1.1 NS/+	0.4 NS/-	0.6 NS/-
Medication	0.7 NS/-	0.7 NS/-	0.29 NS/-	1.0 NS/-	0.4 NS/+

Significance levels: *** $p < 0.001$, ** $p < 0.01$, * $p < 0.05$, NS no significant correlation.

numbers during the season have been described in several other publications (Bastl et al., 2018; Kmenta et al., 2015; Kmenta et al., 2017). Another possible explanation is the occurrence of the highest O₃ concentrations during the grass pollen season in the months of May, June, July, and August due to the importance of UV-radiation for its formation. The grass pollen season is thus the dataset with the longest pollen period, the highest amount of symptom data entries, and the highest O₃ concentrations showing the highest additive effect of ozone on the symptoms of pollen allergy sufferers during this time period. Moreover, the grass pollen season consists of many grass species contributing to the pollen and symptom load which leads to a longer pollen period and maybe also higher sensitization rates (Kmenta et al., 2016; Kmenta et al., 2017).

However, there are other possible obstacles when including meteorological data: O₃ concentrations and temperature are tightly connected with each other and temperature itself can have a significant impact on human health (Baccini et al., 2008). Furthermore, temperature influences pollen data as well as symptom and O₃ data. Pollen production is triggered by temperature but also water availability (Cabrera et al., 2019; Gentili et al., 2019). Therefore, finding an effect besides other parameters such as pollen and meteorological data is difficult (birch and ragweed pollen season of this study). Our positive results herein for the grass pollen season are in line with previous findings, that O₃ has an effect on health apart from temperature (Zanobetti et al., 2012). The boxplot for the grass pollen seasons (Fig. 2) mirrors possible pitfalls due to the connection of O₃ concentrations and temperature. The highest O₃ concentrations occur together with the highest SLI values (although lower in comparison to the SLI of the birch pollen seasons) – thus reducing the box with above 100 $\mu\text{g}/\text{m}^3$. This could be attributed to the fact that high temperatures and O₃ concentrations occur during the summertime, when the pollen season of grasses is already fading, and the burden of grass pollen allergy sufferers already decreases.

Moreover, O₃ concentrations showed a relationship to increased eye and nose symptoms during all three pollen seasons analyzed

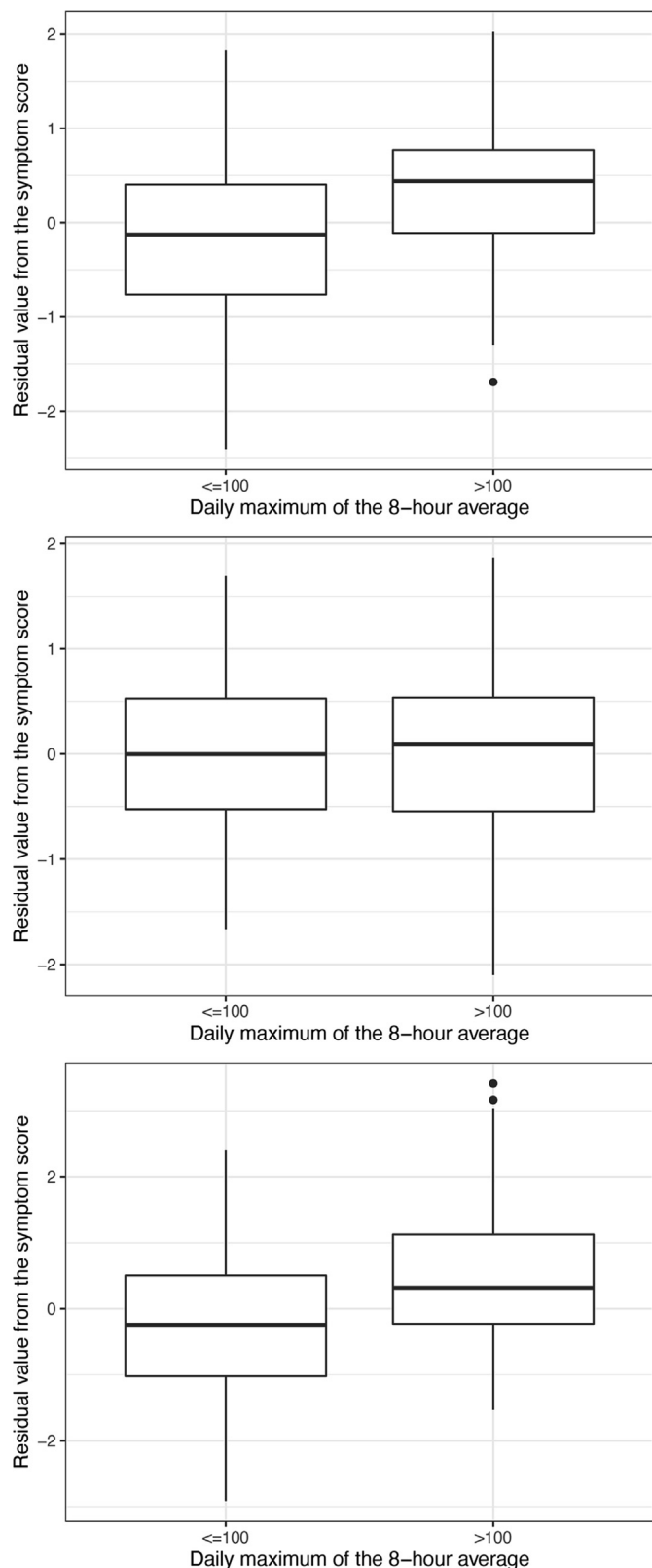


Fig. 2. Box plots for the residual of the SLI with ozone concentrations below or equal (left) and above $100 \mu\text{g}/\text{m}^3$ (right) for the birch (upper), grass (middle), and ragweed (lower) pollen season. The box represents 50% of the data and is limited by the 25% and 75% quantiles, respectively. The bold line represents the median of the data from 2010 to 2018. The length of the whiskers is defined by the observation with a maximum distance of 1.5 times the box width from the box border. All dots are outside of this range and can be considered as extreme observations..

and to increased medication intake for birch and grass pollen seasons. The missing relationship with lung symptoms could be explained by the far less common occurrence of lung symptoms including asthma in the general population (Zuberbier et al., 2017). This result might be surprising in the light of the known health effects of O_3 on lung function (Kulle et al., 1982), inflammation of lung tissues (Jörres et al., 2000), and an increased responsiveness to allergens (Jörres et al., 1996). While the results concerning eyes and nose are consistent, those for medication should be interpreted with caution. Values for medication intake could be influenced by recommendations from allergologists/medical doctors, who would advise taking allergy medication on a regular/daily basis and/or already before the pollen season starts. Hence, a certain fraction of users might not take medication according to their experienced symptoms but try to suppress them before they arise. Eye and nose symptoms could be indirectly triggered by O_3 concentrations: O_3 is the most important contributor to photochemical smog, which contains several types of gases among them peroxyacyl (PAN), which is known to cause eye and nose irritations (Altshuler, 1977). However, these gases are not measured by the Environmental Agency in Vienna and therefore, their occurrence remains unknown. Finally, O_3 also has an impact on the allergenicity of pollen (Beck et al., 2013; Majd et al., 2004; Zhu et al., 2018).

Other analyzed air quality parameters (NO_2 , SO_2 , PM_{10} , and $\text{PM}_{2.5}$) did not show a significant influence on the SLI. PM_{10} and $\text{PM}_{2.5}$ occur in higher concentrations mainly during the winter months due to increased heating in households and poorer air exchange, especially during inversion layer conditions. Therefore, most exceedances for particulate matter are recorded outside of the analyzed time period, namely the pollen season. NO_2 and SO_2 were recorded in low concentrations in Vienna and in low variation during the season. In particular, SO_2 was measured only in values within the measurement errors of the measuring stations and can be thus considered as irrelevant (Augustyn et al., 2019). Therefore, only O_3 is a parameter of the air quality data included herein with a regular exceedance of target values on a regular basis within the pollen season and thus, a parameter that can be analyzed deeply. A high data quantity is necessary to draw conclusions on a broad scale. Therefore, crowd-sourced tools like the PHD will gain importance as data pools. Increasing user numbers will push further research and lead to more robust results. Digitalization as well as mHealth and eHealth should be promoted to enable similar studies for other cities and even rural areas.

4.2. Limitations

Certain factors represent limitations to this study and the interpretation of our results. The crowd-sourced symptom data used herein are user data from the PHD and generated from potential, but not medically diagnosed pollen allergy sufferers. Users record their symptoms on a voluntary basis, but it remains unknown if they are real patients suffering from pollen allergies. In addition, a cumulative effect on symptom data due to co- and multi-sensitization of not well characterized users could affect the results. Moreover, users only enter symptoms if they experience allergic burden. Therefore, not all users enter data during the whole time period (pollen season). Other human factors such as location changes (e.g. holiday periods) or days with low pollen concentrations could affect daily user entries as well. However, the user filtering methods applied before the SLI calculation as well as the pollen season definition decrease these risks to a minimum and therefore, the data can be seen as a proxy for allergy symptom data.

Air quality data were averaged for the whole city of Vienna. Real-life conditions include the movement of persons between

Table 4

Significance levels and sign of the regression coefficient for the birch, grass, and ragweed pollen seasons 2010–2018 for O₃ analyzed in “Method 2” considering temperature and relative humidity. The corresponding R² is displayed (in percent) as well.

Parameters	significance, and sign for birch 2010–2018	significance, and sign for grasses 2010–2018	significance, and sign for ragweed 2010–2018
O ₃ (8h)	NS/+	***/+	NS/+
Temperature	**/+	***/+	*/+
Rel. humidity	**/+	***/+	NS/+
R ²	85.2	90.0	80.5

Significance levels: *** p < 0.001, ** p < 0.01, *p < 0.05, NS no significant correlation.

different locations during the day. Mean values of air quality parameters might thus not be accurate for every user or for every single day. In addition, O₃ was not measured near heavy-traffic roads, because it would skew the results due to the reaction of O₃ with NO reducing it to O₂ and NO₂ in the presence of vehicle emissions. However, it was already proven for Vienna that the symptom pattern does not vary within the city and that at least the SLI values (Bastl et al., 2018) and pollen data (Bastl et al., 2019) are representative for the whole city area.

The increase of symptom data could not only be attributed to air pollution parameters but also to viral infections since a recent study found that pollen causes a reduced pro-inflammatory response to rhinovirus in airway epithelia, leading to increased numbers of viral infections during times with high pollen concentrations. (Gilles et al., 2019). However, this effect will more likely affect the wintertime and the interim periods of the seasons and therefore, is only a possible explanation for higher symptom data during the season of the early flowering trees (e.g. birch).

The statistical models and methods performed in this study cannot imply direct causation in this single study. Although all parameters analyzed have been tested statistically and support the results, spurious correlation due to hidden factors not included might exist and could be reported in future studies.

Finally, an adaptation effect has to be discussed that may occur in the short-term. The effect of O₃ on lung function can be reduced or absent, while inflammatory markers decrease, but airway inflammation persists after repeated O₃ exposure (Jörres et al., 2000). The development and duration of this adaptation effect is highly individual. It may develop between the second to fifth day of repeated exposure and may last seven to 20 days (Horvath et al., 1981). This effect and its individuality in persons concerned may further complicate the interpretation of the effect of O₃ concentrations on symptom data and human health in general.

5. Conclusions

Air pollution is presumed to be one of the major causes for the rising prevalence of allergies in recent years. In addition, it is known, that air pollution has an effect on the human body and pollen itself. The results of our research suggest that especially O₃, has an effect on the severity of symptoms of pollen allergy sufferers during the pollen season.

Therefore, the inclusion of O₃ concentrations should be considered for pollen forecasts and pollen information on a broad scale. Future services for pollen allergy sufferers and pollen forecast models should include air pollutants with a special focus on O₃ to increase the forecast quality and should try to improve the quality of pollen forecasts this way. Moreover, the importance of O₃ as an important factor for pollen allergy sufferers might have an impact on clinical and allergological studies which rate air pollution as a possible relevant factor, especially when data from different regions are compared.

In the light of global warming and climate change air pollution already affects today's population and will affect future generations

even more. Therefore, reducing tropospheric O₃ is a challenge for human health in a global context.

Declaration of competing interest

No conflicts of interest are reported.

CRediT authorship contribution statement

Markus Berger: Conceptualization, Methodology, Formal analysis, Investigation, Writing - original draft, Writing - review & editing, Visualization. **Katharina Bastl:** Writing - original draft, Writing - review & editing, Supervision, Visualization. **Maximilian Bastl:** Writing - original draft, Writing - review & editing. **Lukas Dirr:** Resources, Data curation. **Hans-Peter Hutter:** Methodology, Writing - original draft, Validation, Data curation. **Hanns Moshammer:** Methodology, Writing - original draft, Validation, Data curation. **Wolfgang Gstöttner:** Supervision, Project administration, Funding acquisition.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.envpol.2020.114526>.

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