RESEARCH

Clinical response to varying pollen exposure in allergic rhinitis in children in The Netherlands

Ellen Tameeris[1*], Arthur M. Bohnen[1], Patrick J. E. Bindels[1] and Gijs Elshout[1]

Abstract

Background Allergic rhinitis (AR) affects 10–15% of children. Symptoms in seasonal AR are influenced by pollen exposure. Pollen counts vary throughout the pollen season and therefore, symptom severity fluctuates. This study investigates the correlation between pollen concentration and symptom load in children with AR in The Netherlands.

Methods A secondary analysis was performed in a study determining the most effective treatment for children with seasonal AR. Symptoms were measured during three months in 2013 and 2014 using a daily symptom diary. The pollen concentration was measured with a Hirst type volumetric spore trap sampler. A correlation coefficient was calculated for the correlation between the pollen concentration and the mean daily symptom score. The study protocol was approved by the medical ethical review committee of the Erasmus MC and is incorporated in the International Clinical Trials Registry Platform (EUCTR2012-001,591–11-NL).

Results In 2014, the correlation coefficient for birch pollen concentration and symptom score was 0.423 ($p = 0.000$). The correlation coefficient for grass pollen concentration and symptom score was 0.413 ($p = 0.000$) and 0.655 ($p = 0.000$) in 2013 and 2014, respectively. A delayed correlation between the birch pollen concentration and the symptom scores was seen up to two days after the pollen measurement (0.151, $p = 0.031$). For grass pollen this effect lasted up to three days after the pollen measurement (0.194, $p = 0.000$).

Conclusion We found comparable correlations between symptom score and pollen concentration as found by EAACI. Birch and grass pollen have an elongated influence on symptom score of several days. This implies patients need to continue on demand medication longer after a measured pollen peak.

Keywords Allergic Rhinitis, Pollen counts, Pollen season definition, Symptom variation, Children

Introduction

Allergic rhinitis (AR) is a common disorder of the upper airways [1]. 10–15% of children in the UK are affected [2]. Symptoms in seasonal AR can be nasal or ocular and arise when patients become sensitized to aeroallergens such as pollen.

Antihistamines (AH) or intranasal corticosteroids (INCS) [1] are safe and an effective treatment options for children with AR [3]. Standard treatment of allergic rhinitis is continuous use of INCS throughout the pollen season [1, 4]. However, adherence to this advice is limited [5]. Intermittent use of intranasal corticosteroids has proven to be equally effective in treating AR symptoms, hereby limiting total steroid intake [3, 6]. This limitation in steroid intake could minimise side-effects.

AR symptoms are directly influenced by patients' exposure to pollen [7]. Pollen counts vary throughout the pollen season (PS), dependent on weather conditions and flowering period of plants [8]. The European Academy of Allergy and Clinical Immunology (EAACI) formed a

*Correspondence:
Ellen Tameeris
e.tameeris@erasmusmc.nl
[1] Department of General Practice, Erasmus Medical Center Rotterdam, Doctor Molewaterplein 40, 3066GD Rotterdam, The Netherlands

Tameeris *et al. BMC Pediatrics*   (2023) 23:258

Page 2 of 8

definition of PS and peak pollen periods (PP) [9]. A correlation between birch and grass pollen concentration and symptom score was found for adult patients with AR in European countries during the defined PS an PP [10]. Predictions of pollen concentrations can help individuals to adapt their medication use to expected pollen concentration and symptom load. Additionally, activities could be adjusted. The definition for PS and PP has not been verified in children. This study aims to investigate the correlation between PS, pollen concentration and symptom load in children with AR.

Methods

Patients

A secondary analysis was performed in a study determining the most effective treatment for children with seasonal AR, for details see Wartna et al [3]. In this single-blinded trial children aged 6–18 years were randomized (after signing informed consent) into three treatment groups during the PS of 2013 and 2014. The treatment options were: INCS (fluticasone) on a daily basis, INCS on demand and AH (levocetirizine) on demand. Patients with an International Classification of Primary Care code for AR or a previous prescription for AR-medication registered in the electronic medical file were selected. Patients needed a mean total symptom score (TSS) over the last season high enough to be classified as symptomatic (7 or more out of 21 points). The screening score consisted of recalling four nasal and three ocular symptoms from the previous season on a 0 to 3 scale (Appendix I). A positive radioallergosorbent test (RAST) for grass pollen was required. The study protocol was approved by the medical ethical review committee of the Erasmus MC and is incorporated in the International Clinical Trials Registry Platform (EUCTR2012-001,591–11-NL).

Symptom measurement

Included children had to rate their ocular and nasal symptoms daily during the PS from April until July in 2013 or 2014. This symptom diary was previously used in a study on the effectiveness of sublingual immunotherapy in children with AR [11]. Symptoms were rated from 0 (no burden) to 3 (very high burden) (Appendix II). Symptoms scored were sneezing, nasal itch, congestion or rhinorrhea and ocular itch, redness or teary eyes and wheezing, shortness of breath and nighttime coughing. The TSS range was 0 to 30. Available symptom scores were averaged to a mean daily TSS.

The summer holidays started at July 1st. During this period participants went on holiday and were residing further away from the pollen counting station. Data between July 1st and July 31st in both observed years were not used in the correlation analysis.

Pollen counts

Pollen concentration was determined using pollen counts from the Leiden University Medical Center (LUMC). The LUMC uses a Hirst type volumetric spore trap sampler to assemble daily pollen from the air. The assembled pollen samples are then microscopically identified. Pollen counts are reported daily as grains/m3 [12].

PS was defined following the criteria stated by EAACI. Birch PS starts at the first of five consecutive days with the birch pollen concentration ≥ 10 grains/m^3 and if the sum of the pollen count on these five days is ≥ 100 grains/m^3. The season ends at the last day of five days with a pollen concentration of ≥ 10 grains/m^3. Grass PS starts on the first day of five consecutive days on which the grass pollen concentration rises to or above 3 grains/m^3, and if the sum of the pollen count on these five days is ≥ 30 grains/m^3. The season ends on the last day of a series of five consecutive days with a pollen concentration of ≥ 3 grains/m^3, with a sum of these days of ≥ 30 grains/m^3. Peak pollen concentrations were defined as a pollen count > 100 grains/m^3 for at least three consecutive days for birch pollen and > 50 grains/m^3 for at least three consecutive days for grass pollen [9].

Statistical analysis

Spearman correlation coefficients between daily pollen concentrations and mean TSS were calculated [13]. For birch pollen correlations only birch sensitive patients were analysed and the period of analysed measurements included days with grass pollen load < 5 grains/m3. For grass pollen correlations the period included days with birch pollen load < 5 grains/m3. As the relationship between pollen concentration and symptom score was nonparametric, a Spearman correlation coefficient was calculated.

To determine a possible delayed effect of birch pollen concentration on TSS, the subsequent days were investigated using lagged pollen concentration. The pollen concentrations were compared to TSS one to four days later.

A sub analysis was performed for the correlation between birch pollen concentration and TSS in patients with birch pollen polysensitisation. In addition, a sub analysis was performed for peak pollen concentration, type of symptoms (nasal or ocular), children/adolescents and distance from the study subjects to the pollen counting station. The postal codes of the patients' address were collected to investigate if the distance from the pollen counting site influenced the correlation. Differences in baseline characteristics were calculated using the

Tameeris *et al. BMC Pediatrics* (2023) 23:258

Page 3 of 8

Chi-square test for categorical variables and the ANOVA test for continuous variables [14].

Missing data were analysed and imputed using multiple imputation. Analysis on the pooled data was reported. Statistical analyses were performed using SPSS statistics version 25.

Results

Baseline characteristics

One hundred fifty children were included in the PS of 2013 and 2014. The participants were randomised to three treatment groups: INCS daily (N=50), INCS on demand (N=52) and AH on demand (N=48). 52% of the participants were boys (N=78), mean age was 11.6 years. There were no significant baseline differences in patient characteristics (Table 1). Of the birch sensitised patients 69.4% were adolescents (p=0.021). 16.7% of the diary entries was missing. There was no significant difference in the percentage of symptom free days between the randomisation groups [3].

Mean distance from the pollen counting station was 22.26 kms (KM) (SD 10.59).

Pollen seasons and peaks

The birch PS in 2013 lasted from April 23rd until May 13th, the grass PS lasted from May 27th until July 31st. In 2014 the birch PS lasted from April 1st until April 23rd, the grass season lasted from May 15th until June 28th. Mean grass pollen concentration differed significantly between 2013 and 2014 (Table 2). In 2013 birch PP concentrations occurred from May 2nd until May 4th grass PP did not occur during the study period. In 2014 a birch PP occurred from April 2nd until April 4th, grass PP occurred from June 1st until June 3rd and from June 6th until June 9th. The PP were too short for analysis of correlation.

Table 2 Pollen concentrations per year (grains/m3)

	Min	Max	Mean	SD
2013				
Birch Pollen	0.00	305.00	18.84	55.76
Grass Pollen	0.00	171.00	14.11*	29.68
2014				
Birch Pollen	0.00	1203.00	22.27	114.15
Grass Pollen	0.00	168.00	19.16*	28.64

* $p < 0.05$ for 2013 compared to 2014

Symptom scores

The mean TSS in 2013 was 10.97 (SD 1.67), the mean nasal symptom score (NSS) was 6.82 (SD 1.01), the mean ocular symptom score (OSS) was 4.15 (SD 0.82). In 2014, the mean TSS was 10.72 (SD 1.07), the mean NSS was 6.31 (SD 0.65) and the mean OSS was 4.41 (SD 0.47). Mean TSS, NSS and OSS differed significantly between the two cohorts (p=0.001). However, this difference is probably not clinically relevant. Pollen concentration levels and mean TSS per PS are graphically represented in Fig. 1A-C.
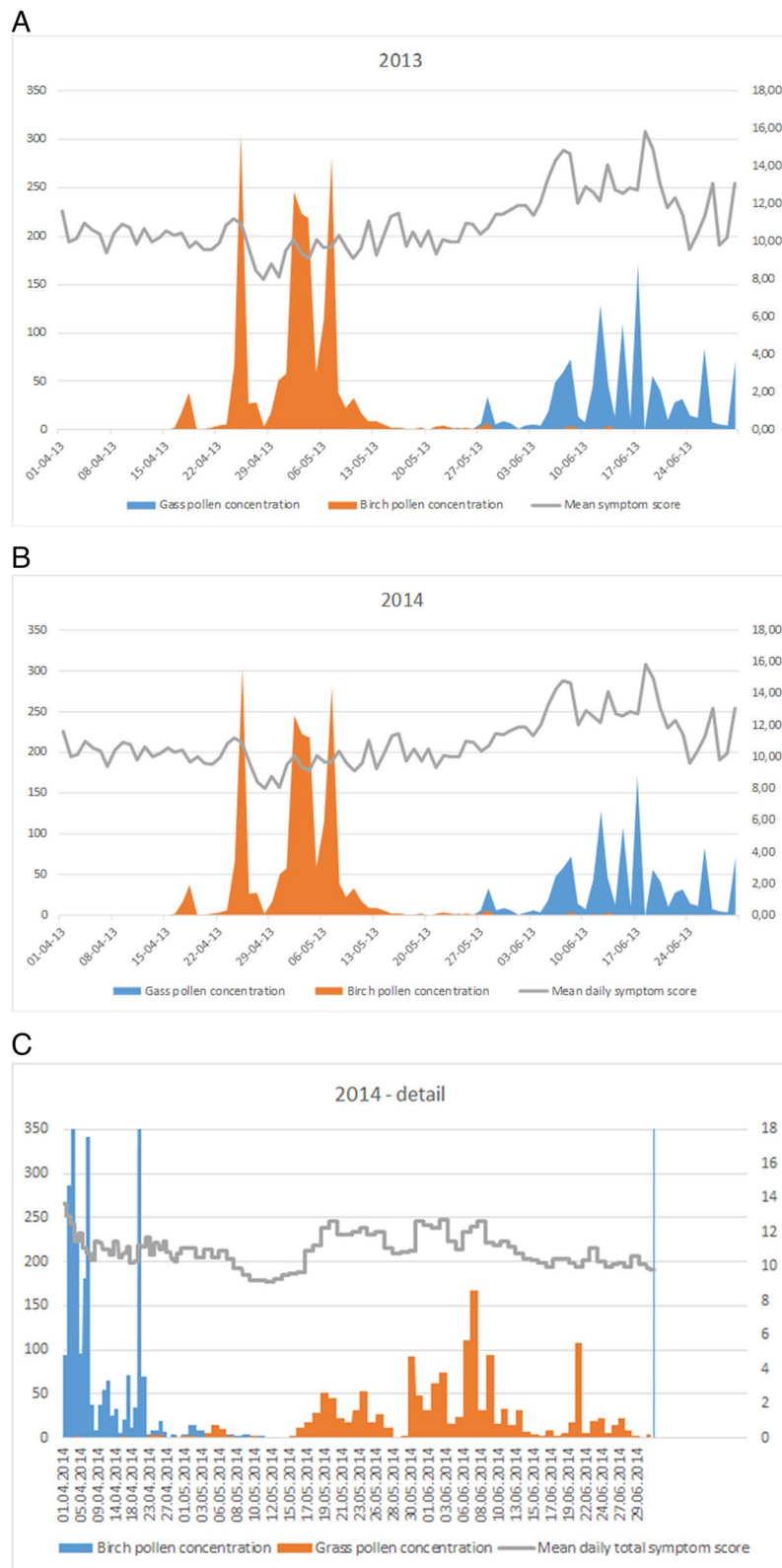
Correlation between pollen concentration and symptom scores

The correlation coefficients between TSS and birch pollen concentration in birch sensitive patients during birch PS in 2013 were not significant. In 2014, this correlation was 0.423 (p=0.000) (Table 3).

There is a stronger correlation between TSS and birch pollen concentration in birch sensitive adolescents compared to children < 10 years (Table 4).There was no difference in correlation coefficients between the treatment groups (Appendix II).

Table 1 Baseline characteristics per cohort

	2013 (*n*=51)	2014 (*n*=99)	*P*-value
Sex (boys), *N (%)*	24 (47.1)	54 (54.5)	0.385
Age (years), *mean (SD)*	11.85 (0.54)	11.57 (0.31)	0.634
Asthma, *N (%)*	8 (15.7)	15 (15.1)	0.931
Grass sensitisation, *N (%)*	51 (100)	99 (100)	0.471
Birch sensitisation, *N (%)*	29 (56.9)	60 (60.6)	0.658
HDM sensitisation, *N (%)*	26 (51.0)	49 (49.5)	0.863
Monosensitisation, *N (%)*	11 (21.6)	24 (24.2)	0.712
Current use of secondary care for AR, *N (%)*	2 (3.9)	12 (12.1)	0.127
Grass sensitisation class > 2, *N (%)*	38 (74.5)	59 (59.6)	0.043
Birch sensitisation class > 2, *N (%)*	29 (56.9)	62 (62.7)	0.367
Retrospective symptom score, *mean (SD)*	12.31 (3.10)	11.93 (3.18)	0.477
Baseline symptom score	11.47 (4.10)	10.34 (4.30)	0.319

Fig. 1 **A**—graphical presentation of pollen concentration & symptom score in 2013. **B**—graphical presentation of pollen concentration & symptom score in 2014. **C**—detail of pollen concentration & symptom score 2014

Table 3 Correlation between symptom score and birch pollen concentration for birch pollen sensitive patients

Variable	2013			2014		
	Spearman's Rho	95% CI	*P*-value	Spearman's Rho	95% CI	*P*-value
Daily score mean	0.248	0.110–0.377	0.201	0.421	0.347–0.490	0.000
Daily Ocular score mean	0.176	0.036–0.309	0.455	0.329	0.251–0.403	0.002
Daily Nasal score mean	0.210	0.071–0.341	0.110	0.412	0.337–0.482	0.000

Measurements performed during grass pollen load < 5 grains/m3

Table 4 Spearman correlation coefficients between pollen counts and the mean symptom scores in children < 10 years and adolescents

	Variable	Birch season	2013			2014			
			95% confidence interval (CI)	Grass season	95% CI	Birch season	95% CI	Grass season	95% CI
Children < 10 years	Mean total symptom score	0.175	-0.249–0.543	0.462*	0.256–0.628	0.380*	0.225–0.516	0.670*	0.630–0.706
	Mean ocular symptom score	0.076	-0.243–0.547	0.413*	0.201–0.588	0.312*	0.207–0.501	0.630*	0.587–0.669
	Mean nasal symptom score	0.181	-0.388–0.466	0.456*	0.225–0.623	0.363*	0.153–0.456	0.690*	0.652–0.724
Adolescents	Mean total symptom score	0.243	0.086–0.388	0.408*	0.315–0.493	0.423*	0.334–0.505	0.653	0.629–0.675
	Mean ocular symptom score	0.204	0.015–0.323	0.389*	0.274–0.457	0.414*	0.324–0.496	0.674	0.589–0.638
	Mean nasal symptom score	0.173	0.046–0.352	0.369*	0.295–0.475	0.330*	0.236–0.418	0.614	0.651–0.695

* $p < 0.05$

The correlation coefficients for lagged birch pollen concentration (the pollen concentration of one and two days prior to the recorded symptom score) became weaker and non-significant after two days. The correlation coefficient between grass pollen concentration and mean TSS during the grass PS in 2013 was 0.413 ($p = 0.000$). In 2014 this correlation was 0.655 ($p = 0.000$). The correlation coefficients for lagged grass pollen concentration decreased, but remained significant until three days after the measured pollen concentration (Table 5).

The correlation coefficient between mean TSS and the distance from the study subject's home address to the pollen measuring station was very small and not significant. There was no significant difference in correlation coefficient between subjects living within or further than 30 km from the pollen measuring station (Table 6).

Discussion

This study confirms the correlation between birch and grass pollen concentration and TSS in children and adolescents with AR in The Netherlands. In addition, it confirms a delayed effect of several days, which implies that patients need to take on demand medication for more days after a registered PP. We found variable correlations over the two studied seasons, which can be explained by seasonal variations in pollen concentration.

There is a stronger correlation between TSS and birch pollen concentration in birch sensitive adolescents compared to children < 10 years. This result could be influenced by the higher prevalence of birch and grass polysensitisation among adolescents [15]. The correlation coefficients between TSS and grass pollen concentration did not differ significantly between children and adolescents.

Tameeris *et al. BMC Pediatrics*   (2023) 23:258

Page 6 of 8

Table 5 Correlation between symptom score and lagged grass pollen concentration (number of days) during grass pollen season (birch pollen load < 5 grains/m3)

Variabele	Spearman's Rho (daily score)	P-value	Spearman's Rho (Ocular score)	P-value	Spearman's Rho (Nasal score)	P-value
2013						
Lag grass 1 day	0.321	0.000	0.350	0.000	0.232	0.000
Lag grass 2 days	0.147	0.000	0.179	0.000	0.078	0.000
Lag grass 3 days	0.194	0.000	0.250	0.000	0.031	0.129
2014						
Lag grass 1 day	0.626	0.000	0.581	0.000	0.627	0.000
Lag grass 2 days	0.490	0.000	0.488	0.000	0.473	0.000
Lag grass 3 days	0.296	0.000	0.303	0.000	0.292	0.000

Table 6 Correlation between mean total symptom score and grass or birch pollen concentration for children living < 30 KM and > 30 KM from the pollen measuring station

Variable	Spearman's Rho	95% Confidence interval	P-value
< 30KM Birch pollen	0.109	0.084–0.133	0.000
> 30KM Birch pollen	0.185	0.127–0.242	0.000
< 30KM Grass pollen	0.367	0.345–0.389	0.000
> 30KM Grass pollen	0.339	0.284–0.392	0.000

When analysing lagged correlation between mean TSS and pollen concentration, the correlation coefficient decreases, but remains significant for pollen concentrations from two (birch pollen) to three (grass pollen) days prior to the diary entries. This delayed effect can implicate that pollen concentrations might be of importance not only on the current day, but also subsequent days. The delayed influence of pollen concentration could be explained by pollen grains being trapped inside buildings, or a chronic state of inflammation of the nasal mucosa [16, 17]. This implies that patients might need to continue their on demand medication up to three days after a measured PP.

Better alignment between TSS and treatment can lead to improved symptom control, quality of life and decrease in steroid intake by optimising as-needed intake of medication. The EAACI proposed definitions for PS and peak pollen concentration for use in clinical trials [10]. This study confirms the correlation of the proposed pollen concentration levels to define grass and birch PS for children and adolescents with AR in The Netherlands.

Karatzas et al. confirmed the definitions of PS and peak pollen period as proposed in the EAACI position paper for two German areas [18]. During the study, pollen concentrations correlated to the observed rhinitis symptom scores. Pfaar et al. also confirmed these findings for regions in Austria, Finland and France [10]. Both studies are based on open-access hay-fever diaries, which leaves exact characteristics of the studied population unknown. The correlation coefficients between birch pollen concentration and mean TSS found in our study are weaker. Only part of our study population is sensitised to birch pollen. In addition, the birch pollen concentration in 2013 is too low to find a significant correlation between TSS and pollen concentration. The correlation between symptom score and grass pollen concentration is comparable to the levels of correlation found by Karatzas and Pfaar [10, 18].

The mean birch and grass pollen concentration differed significantly between the two observed PS. These findings could well be explained by annual variation in weather conditions and environmental factors and are therefore not surprising. These findings are also supported by the significant difference in mean TSS, differences in correlation coefficients between the two years and lack of a statistical significant correlation between birch pollen concentration and TSS in 2013. The relatively low levels of pollen concentration in 2013 resulted in a weaker correlation between pollen season and symptom score, and pollen concentration and symptom score.

The participants in this study were asked to fill in a symptom diary every day for a period of three months. Symptom scores were also reported in times of low pollen exposure. This gives a more fair insight in the correlation between pollen concentration and TSS compared to studies based on voluntary input of AR symptoms. The fact that participants did not only fill in the diaries in case of (severe) symptoms could explain the lower correlation found in this study compared to the results found by Karatzas & Pfaar [10, 18].

Tameeris *et al. BMC Pediatrics*   (2023) 23:258

Page 7 of 8

Participants lived a maximum of 66 km away from the pollen measuring location. The area is variable in environment, from farmland to urban, which could have resulted in local pollen concentrations that are different from the used measurements. The LUMC pollen measuring station is the nearest station to the study participants and is used as one of the Dutch reference stations to inform patients on PP. In previous research, pollen concentration estimations have been found reliable up to 30 km from the measuring station [19]. 29.4% of the study participants lived more than 30 km away from the station. However, we found no significant difference in the correlation between pollen concentration and mean TSS among study participants living within 30 km or further than 30 km from the pollen measuring station.

Study participants were randomised into three treatment groups: INCS continuous, INCS on demand and AH on demand. The amount of symptom free days did not differ significantly between the three treatment groups [3]. These results implicate that the correlation between symptom score and pollen concentration holds regardless of treatment for AR.

Our results enable the use of the proposed definition for PS and PP for both clinical trials and daily clinical routine in The Netherlands for children and adolescents with AR. Measured and predicted pollen concentrations can be used to predict an increase or decrease in symptom score and guide medication intake in children with AR. Weather and pollen concentration forecasts, improved by better knowledge of PS and peaks, can be used to anticipate outside activities of AR patients. As-needed use provides half of the corticosteroid exposure compared to regular, continuous treatment [6]. In addition, adherence to prescription of continuous use of INCS is often poor: 40–71.5% [20]. Adding as-needed medication use to the treatment options in shared decision making might improve adherence. In case of a PP, as-needed medication may be useful on the following 2–3 days due to a delayed development of nasal and ocular symptoms after pollen exposure. Even if locally expected pollen exposure is low in these days.

Abbreviations used

AR	Allergic Rhinitis
AH	Antihistamine
INCS	Intranasal Corticosteroids
EAACI	European Academy of Allergy and Clinical Immunology
LUMC	Leiden University medical Centre
KM	Kilometres
TSS	Total Symptom Score
NSS	Nasal Symptom Score
OSS	Ocular Symptom Score
PS	Pollen season
PP	Pollen peak

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12887-023-04021-1.

Additional file 1: eAppendix 1. Screening questionnaire. **eAppendix 2.** symptom diary. **eAppendix 3.** Pooled Spearman correlation coefficients. **eAppendix 4.** Abbreviations used.

Availability of data and materials
The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The study protocol was approved by the medical ethical review committee of the Erasmus MC and is incorporated in the International Clinical Trials Registry Platform on 19–07-2012 (EUCTR2012-001591–11-NL).
All experiments were performed in accordance with relevant guidelines and regulations. All participants > 12 years and/or their legal guardians signed informed consent prior to enrolment in the study.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

References

1. Sachs AP, Berger MY, Lucassen PL, Van der Wal J, Van Balen JA, Verduijn MM. NHG-Standaard Allergische en niet-allergische rhinitis: Eerste herziening. NHG-Standaarden voor de huisarts. 2009;2009:980-98.
2. Scadding GK, Kariyawasam HH, Scadding G, Mirakian R, Buckley RJ, Dixon T, et al. BSACI guideline for the diagnosis and management of allergic and non-allergic rhinitis (Revised Edition 2017; First edition 2007). Clin Exp Allergy. 2017;47(7):856–89.
3. Wartna JB, Bohnen AM, Elshout G, Pijnenburg MW, Pols DH, GerthvanWijk RR, et al. Symptomatic treatment of pollen-related allergic rhinoconjunctivitis in children: randomized controlled trial. Allergy. 2017;72(4):636–44.
4. Brozek JL, Bousquet J, Agache I, Agarwal A, Bachert C, Bosnic-Anticevich S, et al. Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines-2016 revision. J Allergy Clin Immunol. 2017;140(4):950–8.
5. Wang K, Wang C, Xi L, Zhang Y, Ouyang Y, Lou H, et al. A randomized controlled trial to assess adherence to allergic rhinitis treatment following a daily short message service (SMS) via the mobile phone. Int Arch Allergy Immunol. 2014;163(1):51–8.

Tameeris *et al. BMC Pediatrics*   (2023) 23:258

Page 8 of 8

6. Thongngarm T, Wongsa C, Phinyo P, Assanasen P, Tantilipikorn P, Som-pornrattanaphan M. As-needed versus regular use of fluticasone furoate nasal spray in patients with moderate to severe, persistent, perennial allergic rhinitis: a randomized controlled trial. J Allergy Clin Immunol Pract. 2021;9(3):1365–73.

7. Durham SR, Nelson HS, Nolte H, Bernstein DI, Creticos PS, Li Z, et al. Magnitude of efficacy measurements in grass allergy immunotherapy trials is highly dependent on pollen exposure. Allergy. 2014;69(5):617–23.

8. D'Amato M, Annesi-Maesano I, Molino A, Mormile M, Vitale C, Vatrella A, et al. [Thunderstorm and asthma outbreaks during pollen season] Temporali e attacchi d'asma durante le stagioni polliniche. Epidemiol Prev. 2017;41(3–4):208–11.

9. Pfaar O, Bastl K, Berger U, Buters J, Calderon MA, Clot B, et al. Defining pollen exposure times for clinical trials of allergen immunotherapy for pollen-induced rhinoconjunctivitis - an EAACI position paper. Allergy. 2017;72(5):713–22.

10. Pfaar O, Karatzas K, Bastl K, Berger U, Buters J, Darsow U, et al. Pollen season is reflected on symptom load for grass and birch pollen-induced allergic rhinitis in different geographic areas-An EAACI Task force report. Allergy. 2020;75(5):1099–106.

11. Röder E, Berger MY, Hop WC, Bernsen RM, de Groot H, GerthvanWijk R. Sublingual immunotherapy with grass pollen is not effective in symptomatic youngsters in primary care. J Allergy Clin Immunol. 2007;119(4):892–8.

12. de Weger LA, Beerthuizen T, Hiemstra PS, Sont JK. Development and validation of a 5-day-ahead hay fever forecast for patients with grass-pollen-induced allergic rhinitis. Int J Biometeorol. 2014;58(6):1047–55.

13. Lee SW. Regression analysis for continuous independent variables in medical research: statistical standard and guideline of Life Cycle Committee. Life Cycle. 2022;2.

14. Lee SW. Methods for testing statistical differences between groups in medical research: statistical standard and guideline of Life Cycle Committee. Life Cycle. 2022;2.

15. de Bot CM, Röder E, Pols DH, Bindels PJ, van Wijk RG, van der Wouden JC, et al. Sensitisation patterns and association with age, gender, and clinical symptoms in children with allergic rhinitis in primary care: a cross-sectional study. Prim Care Respir J. 2013;22(2):155–60.

16. Menzel A, Matiu M, Michaelis R, Jochner S. Indoor birch pollen concentrations differ with ventilation scheme, room location, and meteorological factors. Indoor Air. 2017;27(3):539–50.

17. Wang D, Clement P, Smitz J, De Waele M, Derde MP. Correlations between complaints, inflammatory cells and mediator concentrations in nasal secretions after nasal allergen challenge and during natural allergen exposure. Int Arch Allergy Immunol. 1995;106(3):278–85.

18. Karatzas K, Katsifarakis N, Riga M, Werchan B, Werchan M, Berger U, et al. New European academy of allergy and clinical immunology definition on pollen season mirrors symptom load for grass and birch pollen-induced allergic rhinitis. Allergy. 2018;73(9):1851–9.

19. Katelaris CH, Burke TV, Byth K. Spatial variability in the pollen count in Sydney, Australia: can one sampling site accurately reflect the pollen count for a region? Ann Allergy Asthma Immunol. 2004;93(2):131–6.

20. Baiardini I, Novakova S, Mihaicuta S, Oguzulgen IK, Canonica GW. Adherence to treatment in allergic respiratory diseases. Expert Rev Respir Med. 2019;13(1):53–62.

Publisher's Note