Final report

Control of the efficacy of the wearable air purifier Respiray Wear A+ in allergic rhinitis caused by birch pollen

Respiray OÜ

Respiray Wear A+

ECARF
For a Better Life with Allergies

Content

1. General information

1.1 Confidentiality notice

The contents of the protocol are to be treated confidentially and may not be passed on to uninvolved parties, either verbally or in writing, without the consent of Respiray and ECARF Institute GmbH

1.2 Responsibilities

Sponsor	Respiray OÜ, Moisa 4, 13522 Tallinn
Testing Institute	ECARF Institute GmbH, Robert-Koch-Platz 7, 10115 Berlin
Director of Studies	Prof. Dr. med. Dr. h. c. Torsten Zuberbier
Study doctor	Prof. Dr. med. Karl-Christian Bergmann, specialist in respiratory and bronchial medicine, internal medicine, allergology

Berlin, 16 December 2022

Torsten Zuberbier

Digital unterschrieben von Torsten Zuberbier
Datum: 2022.12.20 11:56:15 +01'00'

Prof. Dr. med. Dr. h. c. Torsten Zuberbier
Study director

Prof. Dr. med. Karl-Christian Bergmann
Study doctor

1.3 Summary

Title of the study	To demonstrate the efficacy of the wearable air purifier Respiray Wear A+ in a one arm monocentric study for patients with allergic rhinoconjunctivitis due to birch pollen and associated symptoms.
Short designation	Study 166-P-22
Indication	Allergic rhinoconjunctivitis due to birch pollen and associated symptoms.
Primary aim of the study	To investigate the efficacy of RESPIRAY WEAR A+ worn around the neck by patients with allergic rhinoconjunctivitis due to birch pollen and associated symptoms.
Secondary aim of the study	Reduction in Total Symptom Score (TSS) from baseline (exposure to birch pollen in the AEC at visit V1) without the device, compared to TSS with the device in a final exposure with birch pollen (V3).
Study population	At least 23 people with allergic rhinoconjunctivitis caused by birch pollen are to complete the study
Primary endpoint	Total Symptom Score (TSS) during 60 minutes of birch pollen exposure in the exposure chamber (AEC) at V3 (AEC exposure) vs. baseline AEC exposure (V1).
Secondary endpoints	Secondary endpoint at V3 (AEC exposure) vs. baseline AEC exposure (V1): a) Subjective parameters • Total Symptom Score (TSS) as sum of Total Eye Symptom Score (TESS) and Total Nasal Symptom Score (TNSS) • Total Eye Symptom Score (TESS) • Total Nasal Symptom Score (TNSS) • VAS well-being b) Objective parameters • Peak Nasal Inspiratory Flow (PNIF) every 30 minutes during and after exposure • Spirometry (FEV1) before and after exposure • amount of nasal secretions • Number of individuals with late reactions and use of emergency medication.
Biometrics	Data will be analysed based on descriptive statistics. Mean values of primary and secondary endpoints will be used to compare differences between baseline and final exposition.
Timetable	Duration of the study: December 2022
Test centre	ECARF Institute GmbH, Robert-Koch-Platz 7, 10115 Berlin
Ethics Committee	Charité - Universitätsmedizin Berlin, Ethics Committee CCM, Charitéplatz 1, 10117 Berlin Vote EA1/221/22

1.4 Course of study

The entire study (see table 1) is divided into a screening phase (V0) for the selection of suitable subjects, a baseline exposure (V1) incl. follow-up phone call (V2), and a further final exposure (V3) with the associated follow-up phone call (safety phone call, V4).

table 1: flow chart of the entire study

At least 7 days prior to V1	Day 1	Day 2	Day 7	Day 8
Screening V0	Baseline exposure V1	Safety Call V2	Final Exposure V3	Safety Call V4

2. Study design and study organisation

2.1 Method

The planned AEC exposures at visits 1 and 3 were carried out with the ECARF mobile exposure chamber. This chamber can be flexibly transported to each experimental site. It consists of two standard high-cube containers (24 feet and 7.32 metres respectively) that form a unit of 7.45 × 4.90 × 2.86 metres when placed side by side. One container houses an office and a changing room, while the other container houses the test chamber itself and the air-conditioning equipment. Both containers form an interconnected unit (Fig. 2). Access to the test chamber is provided via the changing room. The test chamber is monitored by a camera and microphones accessible via the control software in the observation room.

The test chamber can accommodate up to nine subjects in addition to a study nurse and/or doctor and is equipped with chairs with adjustable footrests and disinfectable surfaces. Each chair has its own holder for a tablet. The installed air conditioning allows the chamber temperature to be set at 10-38 °C with a relative humidity between 30-80 per cent.

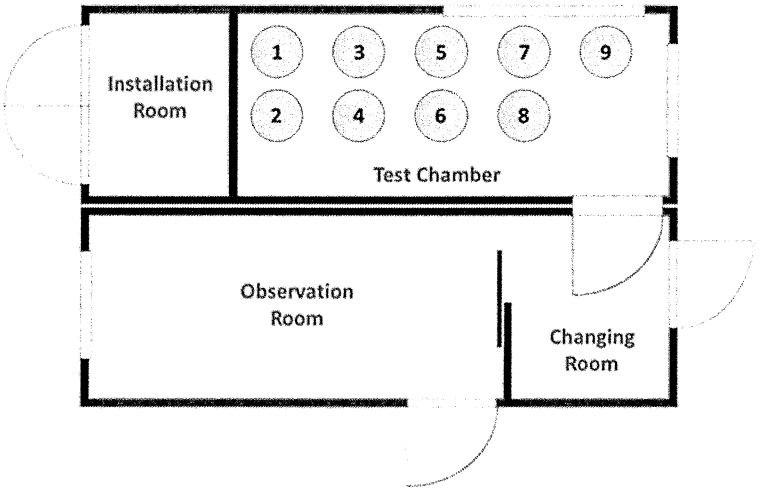

Figure 1: Sketch of the mobile exposure chamber

All tests in the chamber are performed under standardised conditions at 20 °C and 55 percent relative humidity. In the 60-minute exposure at V1 and V3, the average allergen concentration in the breathing air of each seated subject is 8000 birch pollen/m³.

Before the start of the test, the subjects in the chamber undergo an acclimatisation phase of 20 minutes without exposure.

2.1.1 Devices

1. Exposure Chamber, ECARF Institute GmbH, Berlin
2. Peak Nasal Inspiratory Flow Meter, Clement Clarke International Ltd, Harlow, Essex, United Kingdom
3. EasyOne™ Spirometer, ndd Medizintechnik AG, Zurich, Switzerland
4. Peak flow meter, PersonalBest, Philips GmbH, Herrsching, Germany

2.2 Test parameters

The time after acclimatisation but before the start of exposure is defined as time "0 min". The following data are collected before and after the subjects' stay in the chamber at visit V1 and V3:

- TSS: 0, 10, 20, 30, 40, 50, 60
- TESS: 0, 10, 20, 30, 40, 50, 60
- TNSS: 0, 10, 20, 30, 40, 50, 60
- PNIF: 0, 30, 60 min
- VAS 0, 30, 60 min
- Spirometry: before and after exposure

Total Symptom Score (TSS)

The TSS was used following the publication by Pfaar and colleagues (Pfaar et al. 2014).
The TSS is assessed by the subject at visits V1 and V3 before and every 10 minutes during the 60-minute exposure in the AEC. The TSS is the sum of 2 scores:

TSS = TESS + TNSS with a max. score of 24 points

The intensity of each symptom is rated on a scale from 0 to 3 and then added up:

0 = no symptoms
1 = mild symptoms (clearly present, but only very weakly pronounced, does not bother subjects/minimally)
2 = moderate symptoms (definite presence of symptoms that disturb the subject but are tolerable)
3 = severe symptoms (symptom is difficult to tolerate, restricts the subject's daily life)

Total Eye Symptom Score (TESS) is the sum of 4 eye symptoms with a maximum score of 12 points:

- Eye itching
- Foreign body sensation
- Eye watering
- redness (assessment by the study nurse)

Total Nasal Symptom Score (TNSS) is the sum of 4 nasal symptoms with a maximum score of 12 points:

- Itching
- Sneeze
- runny nose
- nasal congestion

Visual analogue scale (VAS)

The VAS is a psychometric response scale that is used to determine the subject's well-being during the exposure. It ranges from 0 to 100 in intervals of 1. Whereas 0 means very good and 100 means very bad. The well-being is determined by each subject at t0, t30 and t60.

Peak Nasal Inspiratory Flow (PNIF)

Using PNIF (nasal inspiratory airflow measurement method), the allergic reactions at the nasal mucosa are checked to be able to determine the degree of obstruction. All test persons are instructed in the correct use of the PNIF measuring device. After a complete exhalation, the subject holds the PNIF meter horizontally and places the face mask airtight around the nose. With the mouth closed, a strong nasal pull is applied. PNIF is determined during exposure at V1 and V3 in the AEC and at times of 0, 30, 60, 90 and 60 minutes. At all measurement times, the highest value is documented from 2 measurements per time point.

2.3 Characterisation of probands

In study 166-P-22, a total of 31 interested subjects were screened. Of these, 26 subjects with allergic rhinoconjunctivitis with or without asthma caused by birch pollen could be included for study participation. 5 interested subjects did not fulfil the inclusion criteria or could not be included due to the exclusion criteria. Another 3 subjects also failed to show up for the final exposition. In total, 23 subjects completed all visits.

Tables 1 and 2 below describe the overall collective in terms of the significant independent variables

Table 2 Subject data

Age (y), Mean (SD)	39.6 (12.3)
Female, n (%)	17 (73.9)
Male, n (%)	6 (26.1)
Weight (kg), Mean (SD)	74.7 (27.2)
Prick test (mm), Mean (SD)	9.3 (3.4)

2.3.1 Inclusion Criteria

- Persons of either sex aged > 18 to < 65 years
- Oral and written consent
- Persons with clinically relevant birch pollen allergy for at least 2 years.
- Positive skin prick test (SPT) for birch pollen (wheal diameter: ≥ 3 mm) not older than 8 months
- Persons who are fully conversant in the German language

2.3.2 Exclusion Criteria

- Persons under the age of 18 yrs.
- Lack of verbal and written consent
- Persons who do not speak German
- Acute infections

- People with severe and/or uncontrolled asthma within the last 3 months before screening
- Individuals with serious chronic medical conditions and/or any condition for which, at the investigator's discretion, study participation would pose a risk to the patient.
- Contraindications to adrenaline and/or other emergency medicines (especially cetirizine)
- Mental illness (e.g., depression) in the last 2 years
- Eating disorders (e.g., bulimia, anorexia nervosa) in the last 2 years
- Pregnant or breastfeeding female subjects
- Alcohol or drug abuse
- Participation in clinical trials in the last 3 months
- Placement in an institution due to court or official orders
- Allergen immunotherapy within the last 5 years against birch pollen
- Heavy smokers (according to WHO definition more than 20 cigarettes daily)

2.3.3 Medication abstentions

The following restrictions apply to the use of medicines:

- Decongestant nose drops (3 days)
- Antihistamines (5 days)
- Anti-allergic eye drops and nasal sprays (1 week)
- Topical steroids (2 weeks)
- Systemic corticosteroids (3 weeks)
- Probiotics (4 weeks)
- Antibiotics (4 weeks)

2.3.4 Admission/Registration

At the beginning of the study, interested persons are informed about the study procedure and possible risks, including emergency medicine, in a detailed discussion with the study doctor. The study doctor must give the person sufficient time to think about the information and the opportunity to ask questions (at least 24 hours) and must make sure that the person has understood the information. All of the subject's questions must be answered and any ambiguities clarified.

The consent of the subjects must also explicitly refer to the collection and processing of personal data. Therefore, the subjects must be explicitly informed about the purpose and scope of the collection and the use of these data, especially health data.

Written reference must be made to the storage of full names, dates of birth, addresses, telephone numbers or also the storage of initials in the study centre if this is necessary in the planned study. In addition, it must be described when these data will be finally destroyed (completion of the study, closing of the database, after ten years, etc.). This information must be formulated in the data protection passage in the consent form of the subjects.

The subjects can withdraw their consent and discontinue the study at any time and without giving reasons. The information on when and for what purpose the subjects were selected and when consent was withdrawn must be retained in the documentation.

The subjects are to be informed that in the event of a revocation of the declaration of consent, the stored data may continue to be used insofar as this is required by law.

It must be ensured that the subjects independently sign and date the consent to participate in the study. One copy of the subject information and consent form is given to the subject, another remains at the trial centre.

All subjects receive a subject identification code to pseudonymise the collected data. This identification code is maintained throughout the study.

3. Evaluation oft the study

3.1 Total Symptom Score (TSS)

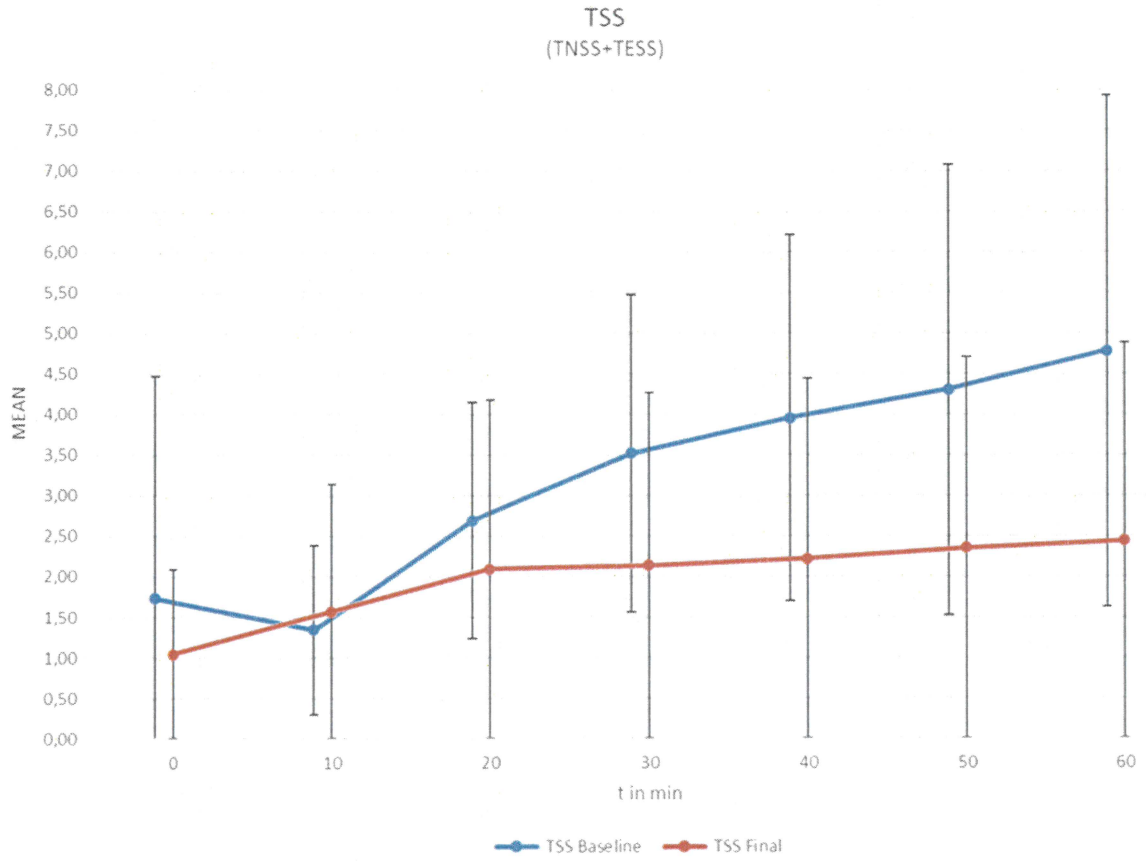

Figure 2: Mean values of the sums of all symptom scores for eyes and nose (TNSS+TESS) for baseline and final exposure. Error bars represent standard deviations.

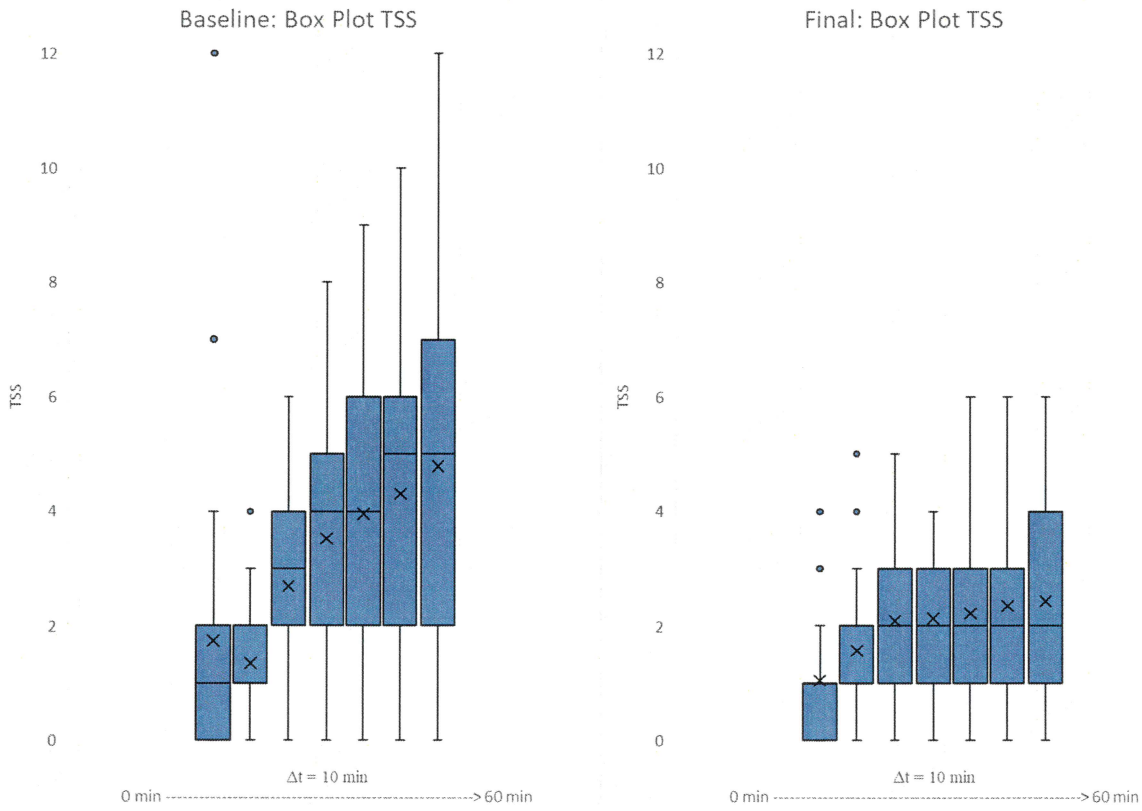

Figure 3 and 4: TSS-Scores at each interval for baseline and final exposure. The boxes indicate the median, the 25th and 75th percentiles, whereas the extremes represent the minimum and maximum values. The cross represents the mean value.

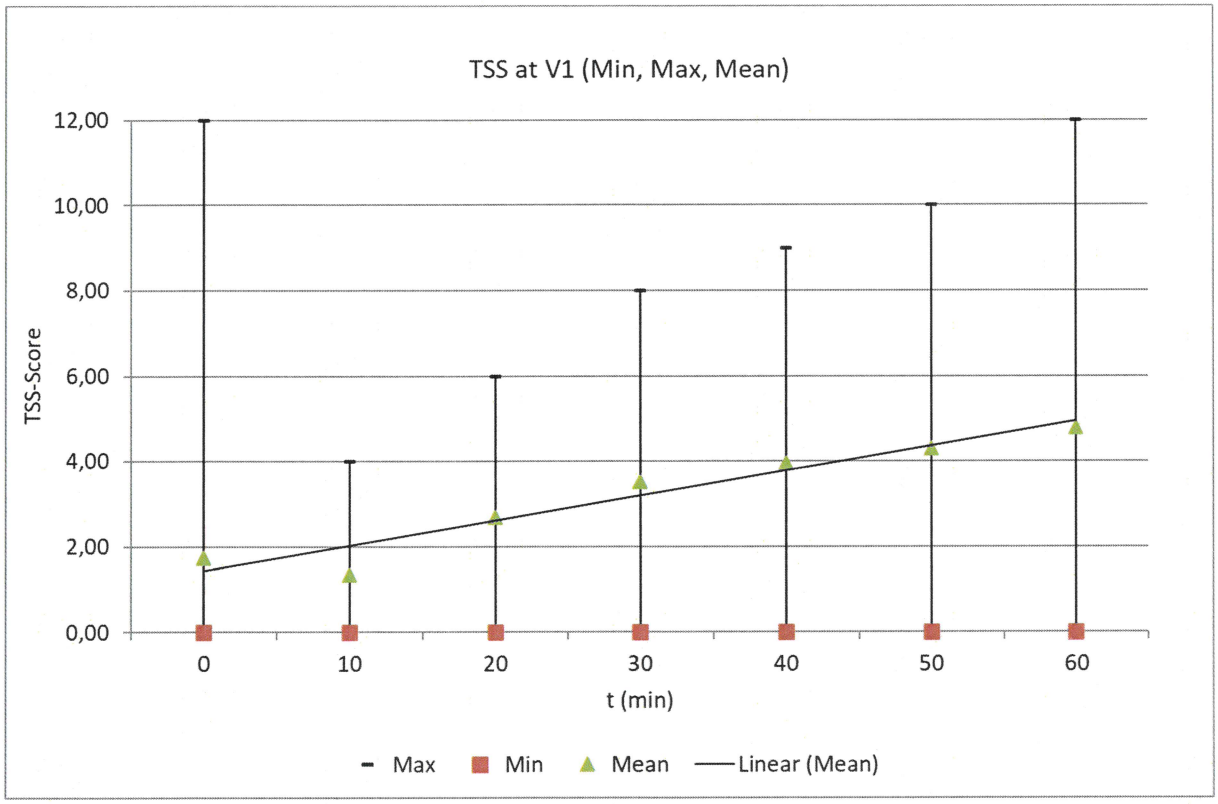

Figure 5: Maximum, minimum, and mean values oft baseline TSS-Scores

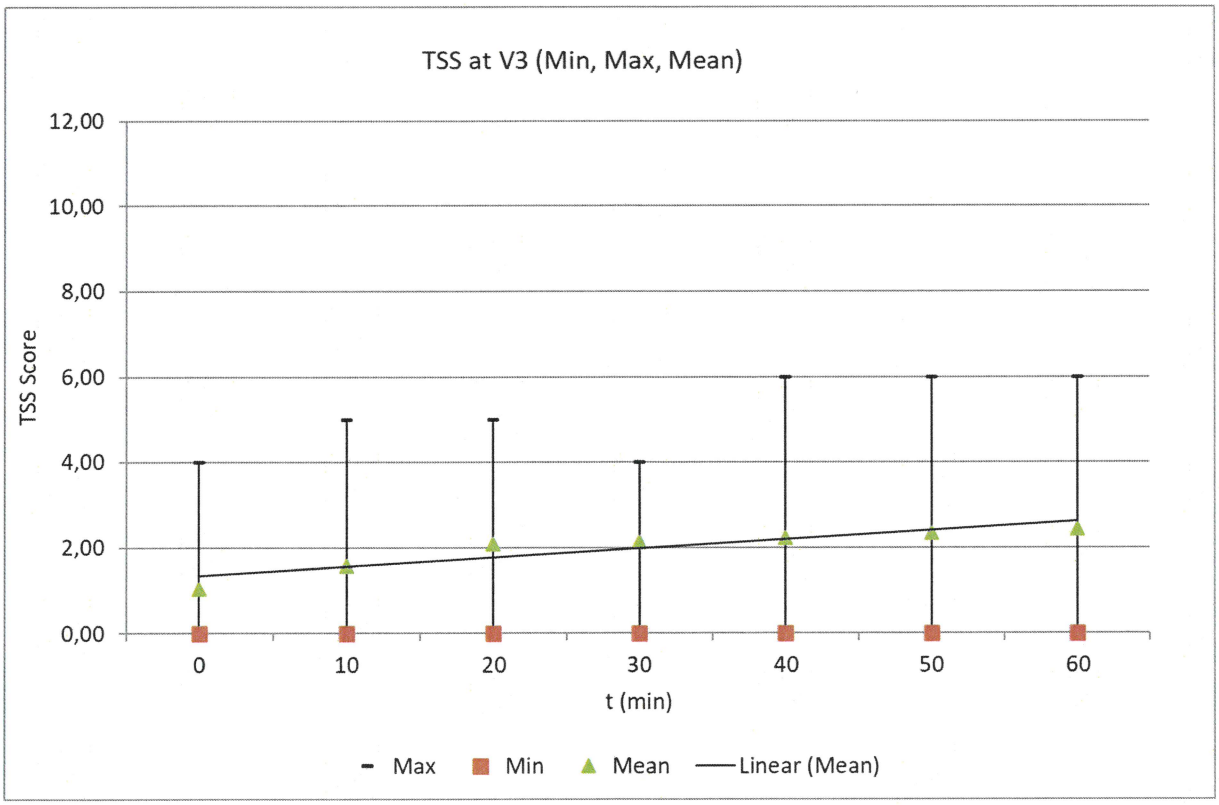

Figure 6: Maximum, minimum, and mean values oft final TSS-Scores

3.2 Total Eye Symptom Score (TESS) and Total Nasal Symptom Score (TNSS)

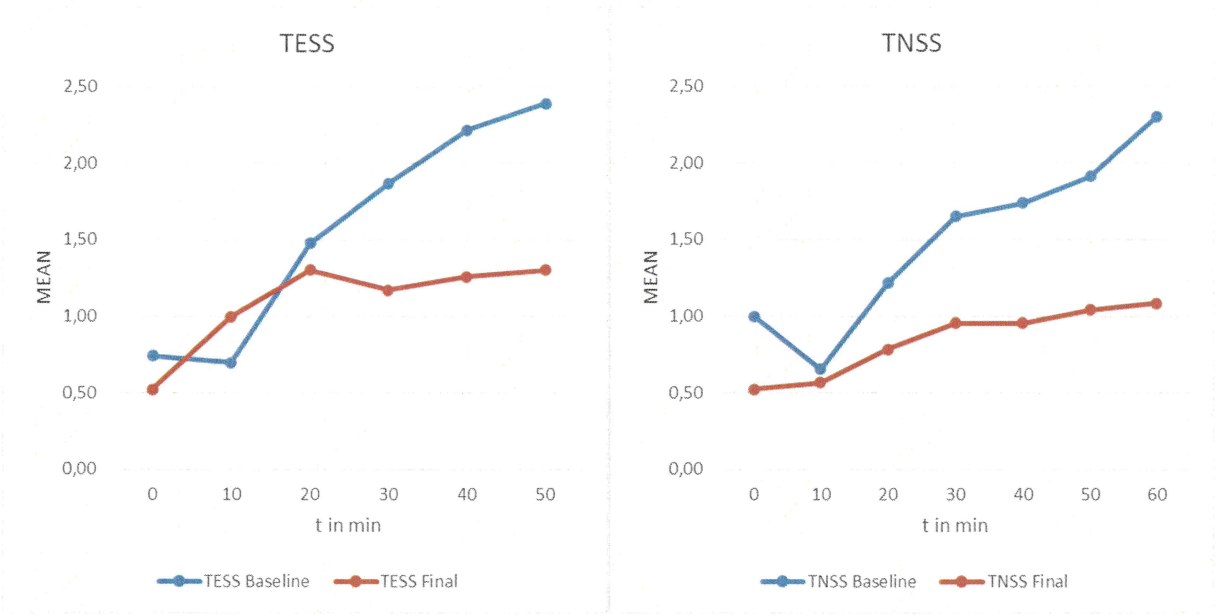

Figure 7 and 8: Mean values of the sums of all symptom scores for eyes (TESS) and nose (TNSS) for baseline and final exposure.

3.3 Nasal Flow at V1 and V3

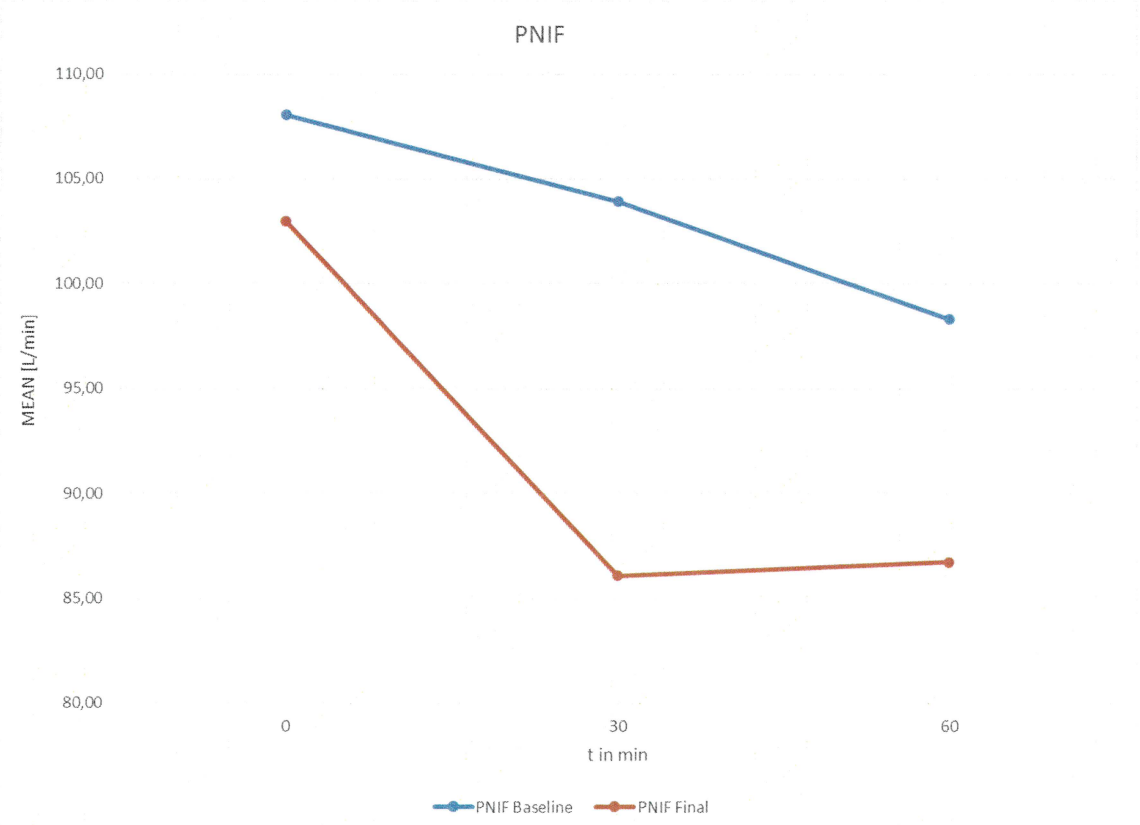

Figure 9: Mean values of the Peak Nasal Inspiratory Flow (PNIF, l/min) at baseline und final exposure.

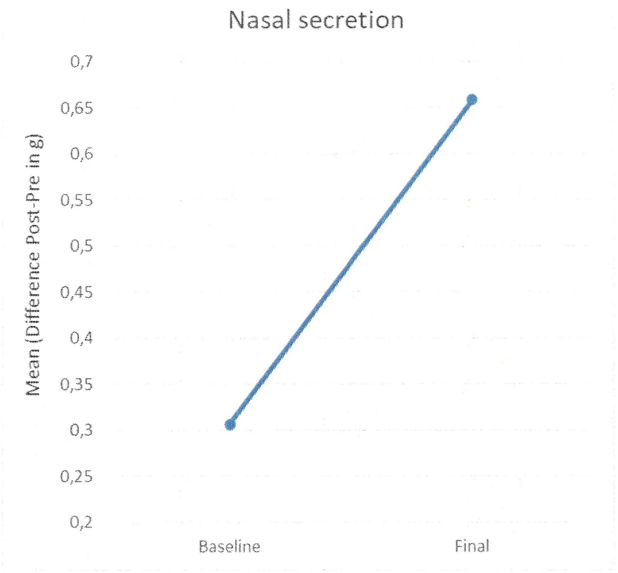

Figure 10: Mean values of differences of nasal secretion (in g) at baseline and final exposure.

3.4 VAS Well-being

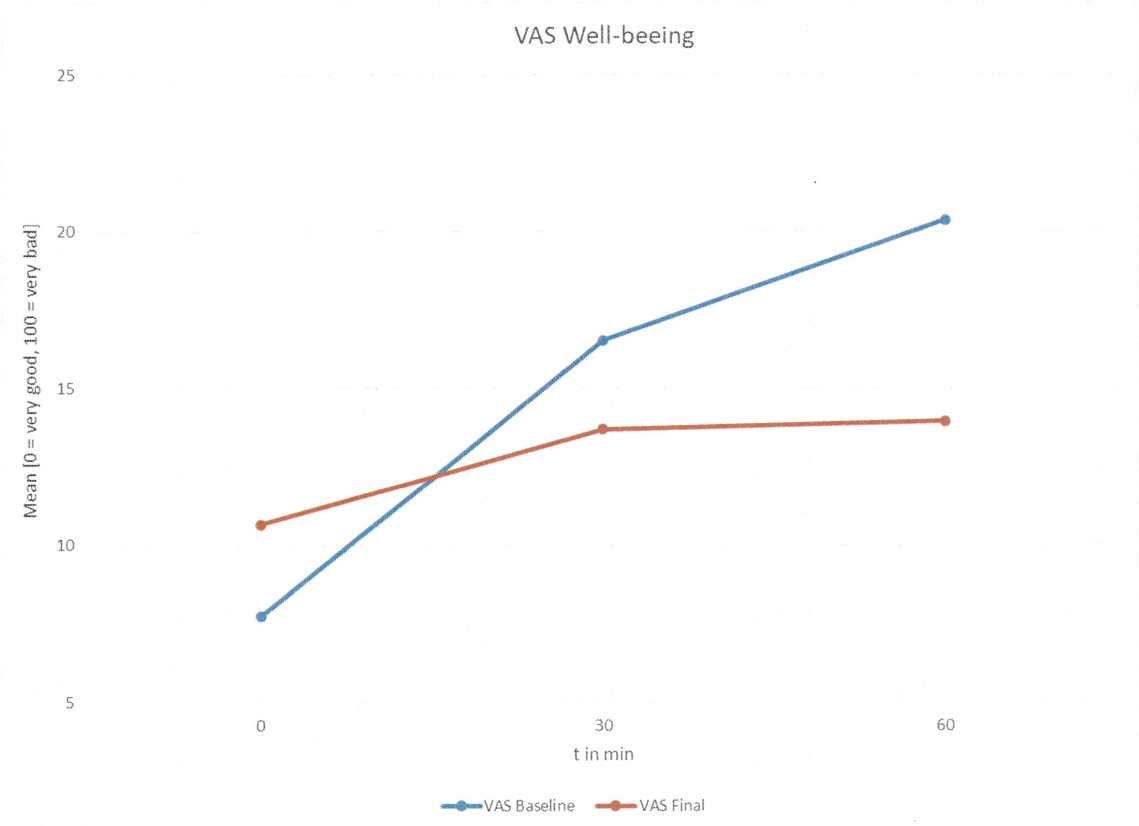

Figure 11: Mean values of the VAS-scores at minutes 0, 30 and 60 at baseline and final exposure.

3.5 Pulmonary function parameters.

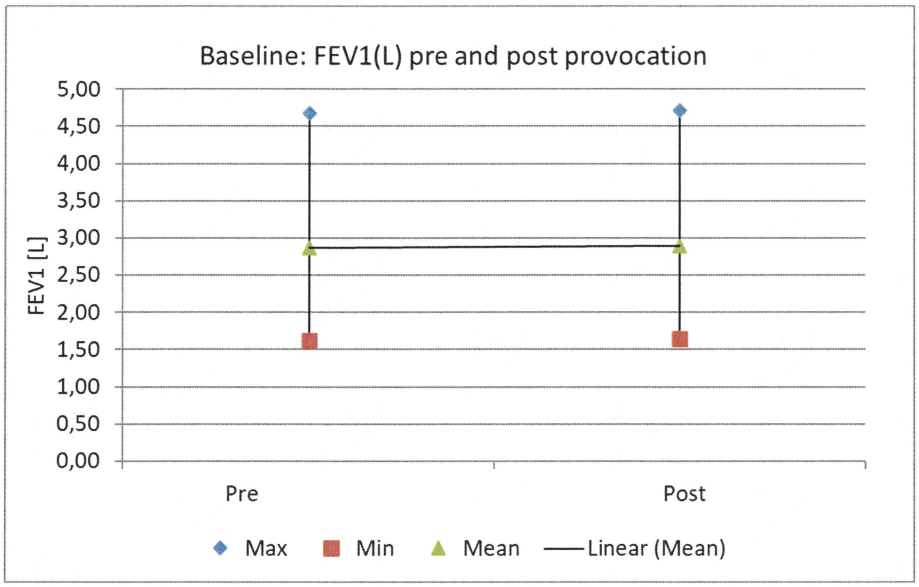

Figure 11: Mean, min and max values of FEV1 (L) at baseline exposure.

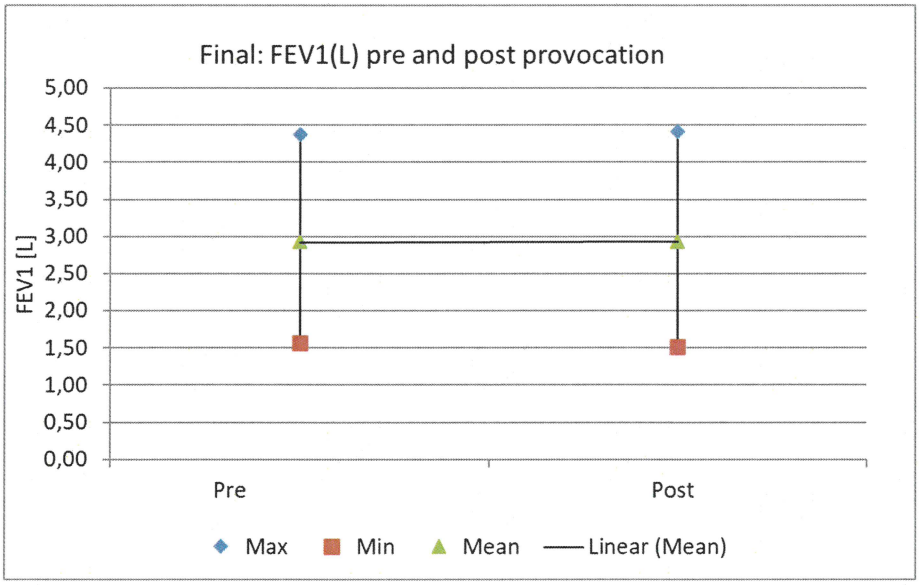

Figure 12: Mean, min and max values of FEV1 (L) at final exposure.

3.6 Safety Call V2/V4

As a safety measure, subjects were called approximately 24 hours after allergen exposure (V1 baseline and V3 final). In this follow-up phone call (V2 and V4), subjects were asked about their well-being and late reactions.

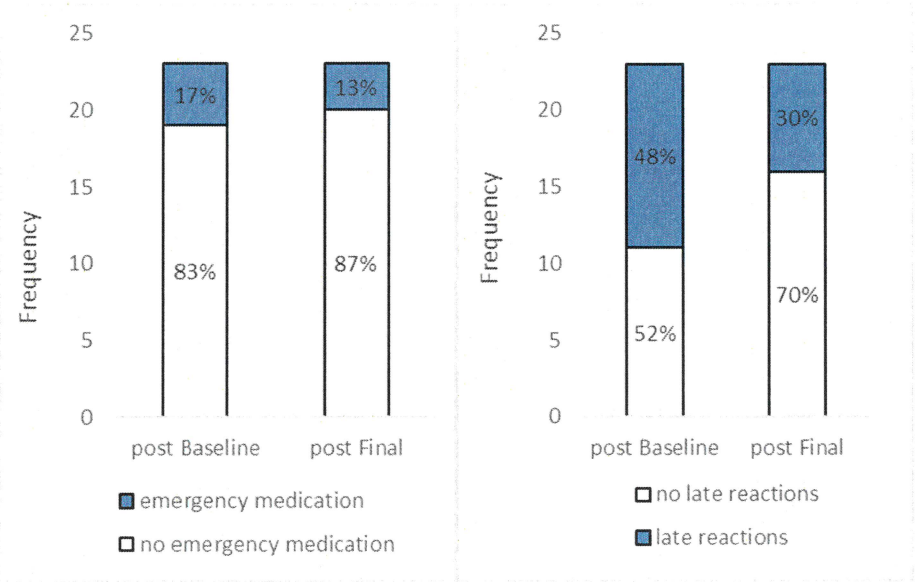

Figure 13: Late reactions and use of emergency medication reported by subjects in a telephone call 24 h after being in the AEC.

Assessment: During the safety call, 24 hours after baseline provocation (V1), late reactions were described by a total of 12 of the 23 subjects (48%). During the follow-up telephone call after the final exposure (V3), late reactions were described by 7 subjects (30%).

At this point, it should be noted that the complaints described under late reactions up to 24 hours after provocation are "symptoms after provocation" (and therefore late reaction), but not confirmed allergic late reactions in the sense of allergen-induced complaints.

The emergency medication (usually cetirizine) for the treatment of late reactions was taken by 4 subjects (17%) after the baseline provocation and by 3 subjects (13%) after the final exposure.

4. Results and Clinical Implications

For people suffering from pollen allergy, it is interesting to know whether wearing a wearable air purifier also protects against pollen and thus avoids medical complaints even without medication. A majority of hay-fever sufferers always ask their physician "what can I do beside taking drugs?". Two recent international publications summarize the few evaluated options to do so and it becomes clear from the publications that there are only a few non-drug methods of protection against pollen that have been scientifically proven and were successful. Among these the Respiray Wear A+ is now one of the best methods.

To evaluate such an "anti-pollen effect", 23 adults with confirmed allergic rhinoconjunctivitis were exposed to birch pollen outside the birch pollen season in an exposure chamber for 60 minutes in a standardized manner with and without the device.

Wearing the Respiray Wear A+ leads to a significant reduction in Total Symptom Score (>50%), including nasal and conjunctival symptoms in subjects with an allergic rhinoconjunctivitis due to (birch) pollen. The 60% reduction in nasal symptoms is particularly remarkable because nasal symptoms are the most debilitating symptoms. About 80% of patients report eye problems; these symptoms are also reduced by approx. 40%. Therefore, the Well-being is supported during pollen exposure.

Very interesting is the lower incidence of delayed reactions after using Respiray Wear A+ compared to pollen exposure without the Respiray device. The occurrence of allergic asthma caused by pollen is promoted by the onset of delayed reactions and these should therefore be avoided as far as possible.

The study makes it clear that people with a pollen allergy, experience a significant benefit from using the Respiray Wear A+ even without any drug therapy; this is also the case on days with a heavy pollen load. During the provocations, the subjects were exposed to high doses of birch pollen.

Wearing the Respiray Wear A+ during the pollen season can be recommended from a medical point of view as an effective non-drug option for those allergic to pollen.

5. References

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6. Abbreviations

AE	Adverse Event
AEC	Allergen Exposure Chamber
FEV1	Forced Expiratory Volume in 1 second
FVC	Forced Vital Capacity
NPT	Nasal Provocation Test
OAS	Oral Allergy Syndrome
PEF	Peak Expiratory Flow
PNIF	Peak Nasal Inspiratory Flow
SAE	Serious Adverse Event
SCIT	Subcutaneous Immunotherapy
SLIT	Sublingual Immunotherapy
SPT	Skin Prick Test
TBSS	Total Bronchial Symptom Score
TESS	Total Eye Symptom Score
TNSS	Total Nasal Symptom Score
TOSS	Total Other Symptom Score
TSS	Total Symptom Score
VAS	Visual Analogue Scale