## Online Supplements

Rhinitis phenotypes and multimorbidities in the general population Constances cohort Marine Savouré et al.

## Supplement on the method - CONSTANCES

## Assets

Constances is a "general purpose" population-based epidemiological cohort. It is a nationally representative sample of 220,000 adults aged between 18 and 69 years at inclusion.

Due to its population size, the quality and diversity of data, and its monitoring methods, Constances is a unique epidemiological research tool. Constances, is a research platform broadly accessible to the scientific community that can be compared to the largest international cohorts.

Constances is also a public health tool, designed to support the public health objectives of the French National Health Insurance Fund for Employees (CNAMTS) and of the national government, owing to the collection of highly diverse data from multiple sources on a representative sample.

Constances is an epidemiological surveillance tool, implemented through a partnership with the French institute for public health surveillance. Its data covers multiple domains, such as the epidemiological surveillance of occupational hazards.

The Constances project, managed through the participation of French local health insurance funds and health clinics, is a partnership between INSERM, Versailles Saint Quentin University (UVSQ), the French national health insurance fund (CNAMTS), the French national retirement pension fund (Cnav) and the support of the French Ministry of health (Directorate general for health). Constances has received French government funding for an 8-year period (Investment for the Future Program).

## Protocol

The goal of the Constances project is to implement a large epidemiological cohort aimed at contributing to the development of epidemiological research and to provide public health information. The purpose of this cohort, created in the context of a partnership between the French national health insurance fund (CNAM) and the French national Old-Age insurance fund (Cnav), is to constitute an infrastructure open to the research community. Constances is labelled National Biology and Health Research Infrastructure by the French government's Commissariat-General for Investment.

Constances is a "general purpose" research infrastructure designed to help analysing a broad range of scientific problems. Constances was also designed as a public health and surveillance tool, thanks to the particularly exhaustive nature of the system for collecting and monitoring a great variety of data from a large representative sample of the adult population covered by the General Social Security scheme.

Random sampling: subjects considered as eligible due to their age and place of residence are drawn randomly by stratified sampling with unequal probabilities, over-representing individuals with a higher probability of non-volunteering according to age, gender and SES. Random sampling is performed by the Cnav from the French national inter-scheme registry of
health insurance beneficiaries (RNIAM), linked to the National careers management system (SNGC).

Data flow: the Constances cohort constitutes a complex database with characteristics rendering it highly sensitive under the terms of the French data protection act, in particular due to the collection of personal data. Moreover, some data collected at the individual level come from linkage to national databases: National inter-scheme health insurance information system (SNIIRAM), causes of death information system (CépiDc-INSERM) and the Cnav (Annual Social Security declarations, Named quarterly data, absenteeism due to illness, Active solidarity income, maternity). Very strict data collection, organisation, and management constraints are required. The procedures in place conform to legislative and regulatory texts intended to preserve high-level personal data confidentiality and security.

## Confidentiality, safety and security approvals

All confidentiality, safety and security procedures were approved by the French legal authorities (online supplement 1). Approvals were obtained from the National Data Protection Authority on March 3, 2011 (Commission Nationale de l'Informatique et des Libertés-CNIL, French National Data Protection Authority (authorisation no. 910486)), the National Council for Statistical Information (Conseil National de l'Information Statistique-CNIS), the National Medical Council (Conseil National de l'Ordre des Médecins-CNOM), and the Institutional Review Board of the National Institute for Medical Research-INSERM (authorisation no. 01011). All participants signed a written informed consent.

## Health check and questionnaires

The invitation to participate to Constances implies to undergo a health examination in a health clinic. The randomly drawn individuals first receive at home an invitation letter presenting the project, along with a mail-back coupon enabling them to give their consent.

The persons having consented to participate in Constances are invited by letter to come to a health screening center (HSC), specifying the date and location of the examination. They also receive two self-questionnaires to be filled in at home: a health and lifestyle questionnaire, and a professional calendar tracing their full job history.

In addition to the self-questionnaire completed at home, subjects undergo a health examination used to collect health-related data: clinical examination, blood analysis, blood pressure, weight, height and waist-to-hip ratio, electrocardiogram and spirometry, sight and hearing examination. This examination is standardised by means of Standard Operating Procedures (SOPs) and permanent quality control is ensured in collaboration with the ClinSearch company and the Asqualab and Eurocell associations.

Additional questionnaires, to be completed on-site (whole-life occupational exposures, women's health), are collected at the health clinic. The informed consent signature validates the collection of these data and authorises their use for research purposes.

Participants aged 45 years and over are invited to undergo a cognitive and functional check-up. This examination is performed by a neuropsychologist and includes a series of tests. The documents pertaining to this check-up (protocol, data collection form), along with related videos, are available on request.

A yearly postal or Web-based self-questionnaire is used for active follow-up at the subjects' homes, and an invitation to come to an HSC once every 4 years is scheduled for all cohort participants.

Moreover, health and socio-professional data, along with causes of death, are regularly retrieved from the national health insurance, retirement pension fund and mortality databases.

More information on the full Constances' protocol is available here:
https://www.constances.fr/_assets/_pdf/Scientific-protocol-01-2015.pdf

For further information see the Constances website: https://www.constances.fr/index EN.php

## Rhinitis questionnaire

English translation of the rhinitis part of the 2014 annual follow-up questionnaire (available in French at: https://www.constances.fr/S2014)
Q.22: "During your lifetime, have you ever had any nasal allergies including hay fever?" Yes/No
Q.23: "During your lifetime, have you ever had a problem with sneezing, or a runny, or a blocked nose when you did not have a cold or the flu? " Yes/No

If yes:

- Q23.A: "Did your eyes itch or cry when you had these nose problems?" Yes/No
- Q23.B: "How old were you the first time?" .... Years
- Q23.C: "Have you had these nose problems in the last 12 months?" Yes/No

Questions 24 to 29 ask about nose problems you have had in the last 12 months.
Q.24: "In which month did you have these nose problems? (several answers possible)" January, February, March, April, May, June, July, August, September, October, November, December
Q.25: "What factor triggered or increased these nose problems? (several answers possible)" Dust mites or house dust, Animals, Air pollution, Change in weather, Tobacco, Pollens, Cold air, Other, Unknown
Q.26: "Have you had these nose problems for more than 4 days in a week?" Yes/No

If yes

- Q.26.A: "Did these problems last more than 4 consecutive weeks?" Yes/No

Q27: "For each of the following problems, indicate whether you have had it in the last 12 months and whether it has been bothersome. If you have not been affected by any of them, indicate this in the first column of the table."

|  |  | I had this problem but: |  |
| :--- | :--- | :--- | :--- |
|  | $\begin{array}{c}\text { I didn't have } \\ \text { this problem }\end{array}$ | $\begin{array}{c}\text { It didn't } \\ \text { bother me }\end{array}$ | $\begin{array}{c}\text { Ithered me } \\ \text { without affecting my } \\ \text { daily activities or my } \\ \text { sleep }\end{array}$ | \(\left.\begin{array}{c}It has bothered me <br>

and affected my <br>
daily activities or <br>
sleep\end{array}\right]\)
Q.28: "Have you used nasal corticosteroid sprays to treat these nose problems? (Nasacort, Nasonex, Avamys, Rhinocort, Beconase, Beclometasone...)" Yes/No
Q.29: "Have you used any oral antihistamines/anti-allergic treatments to treat these nose problems? (Aerius, Xyzall, Clarityne, Kestin, Virlix, Zyrtec, Cetirizine, Loratadine, Desloratadine...)" Yes/No

## Definitions of nasal allergies, rhinitis duration, rhinitis severity and reported symptoms

Nasal allergies: based on the answer to the Q. 22 "During your lifetime, have you ever had any nasal allergies including hay fever?".

Rhinitis duration and severity were defined according to the Allergic Rhinitis and its Impact on Asthma (ARIA) recommendations.(1) Rhinitis was considered to be persistent if symptoms occur more than four days per week and more than four consecutive weeks (Q.26). Otherwise, the symptoms were considered intermittent. Rhinitis was considered to be moderate/severe if at least one of the symptoms of rhinitis (rhinorrhea, nasal congestion, nasal pruritus, sneezing) has been reported as a disturbing problem affecting daily activities and sleep (Q.27). Otherwise, rhinitis was considered to be mild if none of the symptoms have been reported as a disturbing problem affecting daily activities and sleep.

Reported symptoms (rhinorrhea, nasal congestion, nasal pruritus, sneezing, associated-eye symptoms): if in Q. 27 participants reported having this problem.

## Alternate definitions of rhinitis

Alternate definition of ever-rhinitis: yes to: "During your lifetime, have you ever had a problem with sneezing, or a runny, or a blocked nose when you did not have a cold or the flu?" or yes to: "During your lifetime, have you ever had any nasal allergies including hay fever?".

Alternate definition of ever AR = definition based on adaptation of the ECRHS question on nasal allergies (2): yes to: "During your lifetime, have you ever had any nasal allergies including hay fever?".

Alternate definition 1 of current AR and NAR = Triggers-based:

- Current AR: Yes to: "Have you had these nose problems in the last 12 months?" and answer pollens or dust mites or house dust, or animal to: "what factor triggered or increased these nose problems? (several answers possible)".
- Current NAR: Yes to: "Have you had these nose problems in the last 12 months?" and no answer pollens or dust mites or house dust, or animal to: "What factor triggered or increased these nose problems? (several answers possible)".

Alternate definition 2 of current $\mathrm{AR}=$ Classification tree-based: this definition was adapted from the classification tree obtained by Burte et al. with an unsupervised approach to identify rhinitis.(3)

- Current AR: Yes to: "Have you had these nose problems in the last 12 months?" and yes to: "During your lifetime, have you ever had any nasal allergies including hay fever?" or answer pollens to: "What factor triggered or increased these nose problems? (several answers possible)" and Yes to: "Did your eyes itch or cry when you had these nose problems?".
- Current NAR: Yes to: "Have you had these nose problems in the last 12 months?" and no to: "During your lifetime, have you ever had any nasal allergies including hay fever?" and no answer pollens to: "What factor triggered or increased these nose problems? (several answers possible)" or no to: "During your lifetime, have
you ever had any nasal allergies including hay fever?" and answer pollens to: "What factor triggered or increased these nose problems? (several answers possible)" and no to: "Did your eyes itch or cry when you had these nose problems?".


## References:

1. Bousquet J, Khaltaev N, Cruz AA, et al. Allergic Rhinitis and its Impact on Asthma (ARIA) 2008*. Allergy 2008; 63: 8-160.
2. ECRHS. Variations in the prevalence of respiratory symptoms, self-reported asthma attacks, and use of asthma medication in the European Community Respiratory Health Survey (ECRHS). European Respiratory Journal 1996; 9: 687-95.
3. Burte E, Bousquet J, Varraso R, et al. Characterization of Rhinitis According to the Asthma Status in Adults Using an Unsupervised Approach in the EGEA Study. PLoS ONE 2015; 10: e0136191.

## Supplement on the method - EGEA

EGEA is a cohort study based on an initial group of asthma cases recruited in chest clinics from five French cities (1991-1995) along with their first-degree relatives, and a group of controls. Briefly, 2047 children ( $<16$ years) and adult participants were enrolled at baseline, including 348 participants with current asthma from chest clinics, their 1244 first-degree relatives, and 415 population-based controls. The protocol and descriptive characteristics of the EGEA study have been previously published. $(1,2)$

A 12-year follow-up of the initial cohort was conducted between 2003 and 2007 (EGEA2). Among the alive cohort ( $\mathrm{n}=2002$ ), $92 \% \quad(\mathrm{n}=1845)$ completed a short self-administered questionnaire, and among them 1602 ( $\mathrm{n}=1571$ adults aged $\geq 16$ years) had a complete examination. As a follow-up study of EGEA2, the third survey (EGEA3, 2011-2013, $\mathrm{n}=1558$ ) was conducted using self-completed questionnaire only.

The EGEA collection was certified ISO 9001 from 2006 to 2018.(3) Ethical approval was obtained from the relevant institutional review board committees (Cochin Port-Royal Hospital and Necker-Enfants Malades Hospital, Paris). All participants signed a written informed consent.

## Analysis population of the present paper

The analyses of the present paper were performed at EGEA2. Among the 1571 adults, those with missing data regarding the definitions of rhinitis ( $n=13$ ), or the presence of nasal allergies ( $\mathrm{n}=29$ ) were excluded from the analyses.

A total of 842 participants reported current rhinitis and were included in the analyses.

## Variables of interest

Current rhinitis was defined by a positive response to: "Have you had problems with sneezing, runny nose or stuffy nose when you didn't have a cold or flu in the last 12 months?". Among the participants with current rhinitis, participants who responded positively to "Have you ever had allergic rhinitis?" or "Have you ever had hay fever?" were classified as AR otherwise as NAR.

Participants with ever-asthma were defined by a positive answer to: "Have you ever had attacks of breathlessness at rest with wheezing?" or "Have you ever had asthma attacks?" or if they were recruited as asthmatic cases at the first survey. ${ }^{2}$

Ever-conjunctivitis: positive answer to "Have you ever had allergic conjunctivitis?". Age of onset: answer to "At what age did you first experience these nose problems?".

Reported triggers of the symptoms of rhinitis: answer to "In the last 12 months, what factors have triggered or increased these nose problems? a. dust mites or house dust b. pollens $c$. animals d. other". Several responses were possible, participants who did not provide any of the possible answers were categorized as "no trigger reported".

SPTs to 12 aeroallergens ((indoor: cat, Dermatophagoides pteronyssinus, Blattela germanica; outdoor: olive, birch, Parieteria judaica, timothy grass, ragweed pollen and Cupressus; moulds: Aspergillus, Cladosporium herbarum, Alternaria tenuis) were performed.

## Alternate definition of AR and NAR

We performed the description of allergic and non-allergic rhinitis defined by SPT in EGEA2. Current rhinitis was defined by a positive response to: "Have you had problems with sneezing, runny nose or stuffy nose when you didn't have a cold or flu in the last 12 months?". Among the participants with current rhinitis, those who had at least one positive SPT were classified as SPT-based AR (AR-SPT), otherwise as SPT-based NAR (NAR-SPT).

## EGEA cooperative group:

Coordination: V Siroux (epidemiology, PI since 2013); F Demenais (genetics); I Pin (clinical aspects); R Nadif (biology); F Kauffmann (PI 1992-2012). Respiratory epidemiology: Inserm ex-U 700, Paris: M Korobaeff (Egea1), F Neukirch (Egea1); Inserm ex-U 707, Paris: I Annesi-Maesano (Egea1-2); Inserm U 1018, Villejuif: O Dumas, F Kauffmann, N Le Moual, R Nadif, MP Oryszczyn (Egea1-2), R Varraso; Inserm U 1209 Grenoble: J Lepeule, V Siroux. Genetics: Inserm ex-U 393, Paris: J Feingold; Inserm UMR 1124, Paris: E Bouzigon, MH Dizier, F Demenais; CNG, Evry: I Gut (now CNAG, Barcelona, Spain), M Lathrop (now Univ McGill, Montreal, Canada). Clinical centres: Grenoble: I Pin, C Pison; Lyon: D Ecochard (Egea1), F Gormand, Y Pacheco;Marseille: D Charpin (Egea1), D Vervloet (Egea12); Montpellier: J Bousquet; Paris Cochin: A Lockhart (Egea1), R Matran (now in Lille); Paris Necker: E Paty (Egea1-2), P Scheinmann (Egea1-2); Paris-Trousseau: A Grimfeld (Egea1-2), J Just. Data management and quality: Inserm ex-U155, Paris: J Hochez (Egea1); Inserm U 1018, Villejuif: N Le Moual, L Orsi; Inserm ex-U780, Villejuif: C Ravault (Egea1-2); Inserm ex-U794, Evry: N Chateigner (Egea1-2); Inserm UMR 1124, Paris: H Mohamdi; Inserm U1209, Grenoble: A Boudier, J Quentin (Egea1-2).

The authors thank all those who participated in the setting of the study and in the various aspects of the examinations involved: interviewers, technicians for lung function testing and skin prick tests, blood sampling, IgE determinations, coders, those involved in quality control, data and sample management and all those who supervised the study in all centres. The authors are grateful to the three CIC-Inserm (Necker, Grenoble and Marseille) that supported the study and in which participants were examined. They are also grateful to the biobanks in Lille (CIC Inserm), and in Annemasse (Etablissement Français du Sang) where biological samples were stored.

## References

1. Kauffmann F, Dizier MH. EGEA (Epidemiological study on the Genetics and Environment of Asthma, bronchial hyperresponsiveness and atopy)-design issues. EGEA Co-operative Group. Clin Exp Allergy. 1995 Nov;25 Suppl 2:19-22.
2. Kauffmann F, Dizier MH, Annesi-Maesano I, Bousquet J, Charpin D, Demenais F, et al. EGEA (Epidemiological study on the Genetics and Environment of Asthma, bronchial
hyperresponsiveness and atopy) - descriptive characteristics. Clin Exp Allergy. 1999 Dec;29 Suppl 4:17-21.
3. Nadif R, Bouzigon E, Le Moual N, Siroux V. EGEA Collection: A Biobank Devoted to Asthma and Asthma-related Phenotypes. Open Journal of Bioresources. 2017;4(1):5. DOI: http://doi.org/10.5334/ojb. 24

Table S1: Comparison between participants included and non-included in the analysis

|  | Non-included ( $\mathrm{n}=5965$ ) | Included ( $\mathrm{n}=20772$ ) | $p$ value |
| :---: | :---: | :---: | :---: |
| Sex |  |  | 0.0001 |
| Men | 2836 (47.5\%) | 9297 (44.8\%) |  |
| Women | 3129 (52.5\%) | 11475 (55.2\%) |  |
| Age at inclusion, years | 48.4 (13.6) | 51.0 (12.6) | <0.0001 |
| Tobacco status at inclusion |  |  | <0.0001 |
| Never-smoker | 2326 (41.7\%) | 9395 (47.2\%) |  |
| Ex-smoker | 1736 (31.1\%) | 7366 (37.0\%) |  |
| Current smoker | 1521 (27.2\%) | 3126 (15.7\%) |  |
| Educational level at inclusion |  |  | <0.0001 |
| Less than high school | 974 (16.7\%) | 1938 (9.4\%) |  |
| High school | 2283 (39.2\%) | 6755 (32.9\%) |  |
| University | 2566 (44.1\%) | 11825 (57.6\%) |  |
| Body-mass index at inclusion, $\mathrm{kg} / \mathrm{m}^{2}$ |  |  | <0.0001 |
| <18.5 | 162 (2.8\%) | 449 (2.2\%) |  |
| [18.5-25[ | 2879 (49.5\%) | 11164 (54.7\%) |  |
| [25-30[ | 1855 (31.9\%) | 6492 (31.8\%) |  |
| $\geq 30$ | 918 (15.8\%) | 2308 (11.3\%) |  |
| Asthma at inclusion |  |  | <0.0001 |
| Never asthma | 4955 (86.0\%) | 17911 (88.0\%) |  |
| Ever asthma | 805 (14.0\%) | 2440 (12.0\%) |  |
| Ever rhinitis at inclusion |  |  | <0.0001 |
| Never rhinitis | 2982 (52.0\%) | 11202 (55.1\%) |  |
| Ever rhinitis | 2748 (48.0\%) | 9130 (44.9\%) |  |

Data are mean (SD) or n (\%)

Table S2: Prevalence of rhinitis according to different definitions

|  | Definition | n/N | Crude Prevalence [CI 95\%] |
| :---: | :---: | :---: | :---: |
| Ever-rhinitis |  |  |  |
| Main definition | Yes to: "During your lifetime, have you ever had a problem with sneezing, or a runny, or a blocked nose when you did not have a cold or the flu?" | 11098/20772 | $\begin{array}{r} 53.4 \% \\ {[52.8 \%-54.1 \%]} \end{array}$ |
| Alternate definition | - Yes to: "During your lifetime, have you ever had a problem with sneezing, or a runny, or a blocked nose when you did not have a cold or the flu?" or <br> - Yes to: "During your lifetime, have you ever had any nasal allergies including hay fever?" | 12207/20772 | $\begin{array}{r} 58.8 \% \\ {[58.1 \%-59.4 \%]} \end{array}$ |
| Ever AR |  |  |  |
| Main definition | - Yes to: "During your lifetime, have you ever had a problem with sneezing, or a runny, or a blocked nose when you did not have a cold or the flu?" <br> and <br> - Yes to: "During your lifetime, have you ever had any nasal allergies including hay fever?" | 7589/20772 | $\begin{array}{r} 36.5 \% \\ {[35.9 \%-37.2 \%]} \end{array}$ |
| Alternate definition | Yes to: "During your lifetime, have you ever had any nasal allergies including hay fever?" | 8698/20772 | $\begin{array}{r} 41.9 \% \\ {[41.2 \%-42.5 \%]} \end{array}$ |
| Ever NAR |  |  |  |
| Main definition | - Yes to: "During your lifetime, have you ever had a problem with sneezing, or a runny, or a blocked nose when you did not have a cold or the flu?" and - No to: "During your lifetime, have you ever had any nasal allergies including hay fever?" | 3509/20772 | $\begin{array}{r} 16.9 \% \\ {[16.4 \%-17.4 \%]} \end{array}$ |
| Current rhinitis |  |  |  |
| Main definition | Yes to: "Have you had these nose problems in the last 12 months?" | 8069/20772 | $\begin{array}{r} 38.9 \% \\ {[38.2 \%-39.5 \%]} \end{array}$ |
| Current AR |  |  |  |
| Main definition | - Yes to: "Have you had these nose problems in the last 12 months?" and - Yes to: "During your lifetime, have you ever had any nasal allergies including hay fever?" | 5806/20772 | $\begin{array}{r} 28.0 \% \\ {[27.3 \%-28.6 \%]} \end{array}$ |
| Alternate definition 1 | - Yes to: "Have you had these nose problems in the last 12 months?" and - Answer pollens or dust mites or house dust or animal to: "What factor triggered or increased these nose problems? (several answers possible)" | 4208/20772 | $20.3 \%$ $[19.7 \%-20.8 \%]$ |
| Alternate definition 2 | - Yes to: "Have you had these nose problems in the last 12 months?" <br> and <br> - Yes to: "During your lifetime, have you ever had any nasal allergies including hay fever?" <br> or <br> - Answer pollens to: "What factor triggered or increased these nose problems? (several answers possible)" and Yes to: "Did your eyes itch or cry when you had these nose problems?" | 5858/20627 | $\begin{array}{r} 28.4 \% \\ {[27.8 \%-29.0 \%]} \end{array}$ |
| Current NAR |  |  |  |
| Main definition | - Yes to: "Have you had these nose problems in the last 12 months?" and - No to: "During your lifetime, have you ever had any nasal allergies including hay fever?" | 2263/20772 | $\begin{array}{r} 10.9 \% \\ {[10.5 \%-11.3 \%]} \end{array}$ |
| Alternate definition 1 <br> = Triggers-based | - Yes to: "Have you had these nose problems in the last 12 months?" and - No answer pollens or dust mites or house dust or animal to: "What factor triggered or increased these nose problems? (several answers possible)" | 3861/20772 | $\begin{array}{r} 18.6 \% \\ {[18.1 \%-19.1 \%]} \end{array}$ |
| Alternate definition 2 <br> = Classification treebased | - Yes to: "Have you had these nose problems in the last 12 months?" and <br> - No to: "During your lifetime, have you ever had any nasal allergies including hay fever?" and no answer pollens to: "What factor triggered or increased these nose problems? (several answers possible)" <br> or <br> - No to: "During your lifetime, have you ever had any nasal allergies including hay fever?" and answer pollens to: "What factor triggered or increased these nose problems? (several answers possible)" and no to: "Did your eyes itch or cry when you had these nose problems?" | 2066/20627 | $\begin{array}{r} 10.0 \% \\ {[9.6 \%-10.4 \%]} \end{array}$ |
| $\mathrm{n} / \mathrm{N}$ : number | of cases/Total number of participants, CI 95\%: | Confidence | Interval 95\% |

Table S3: Comparison of participants with current Allergic Rhinitis (AR) and current Non-Allergic Rhinitis (NAR) according to alternate definitions

|  | Main definition |  |  | Alternate definition 1: Triggers-based |  |  | Alternate definition 2: Classification tree-based |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | $\begin{gathered} \mathrm{AR} \\ (\mathrm{n}=5806) \end{gathered}$ | $\begin{gathered} \text { NAR } \\ (\mathrm{n}=2263) \end{gathered}$ | p value | $\begin{gathered} \mathrm{AR} \\ (\mathrm{n}=4208) \end{gathered}$ | $\begin{gathered} \text { NAR } \\ (\mathrm{n}=3861) \end{gathered}$ | p value | $\begin{gathered} \mathrm{AR} \\ (\mathrm{n}=5858) \end{gathered}$ | $\begin{gathered} \text { NAR } \\ (\mathrm{n}=2066) \end{gathered}$ | p value |
| Sex |  |  | 0.072 |  |  | 0.14 |  |  | 0.0056 |
| Men | 2468 (42.5\%) | 1012 (44.7\%) |  | 1782 (42.3\%) | 1698 (44.0\%) |  | 2471 (42.2\%) | 944 (45.7\%) |  |
| Women | 3338 (57.5\%) | 1251 (55.3\%) |  | 2426 (57.7\%) | 2163 (56.0\%) |  | 3387 (57.8\%) | 1122 (54.3\%) |  |
| Age, years | 51.7 (12.8) | 52.4 (13.3) | 0.032 | 49.5 (12.9) | 54.5 (12.5) | <0.0001 | 51.5 (12.8) | 52.5 (13.3) | 0.0029 |
| Tobacco status |  |  | 0.0044 |  |  | <0.0001 |  |  | 0.0059 |
| Never-smoker | 2534 (46.0\%) | 954 (44.3\%) |  | 1942 (48.5\%) | 1546 (42.2\%) |  | 2568 (46.2\%) | 870 (44.3\%) |  |
| Ex-smoker | 2289 (41.5\%) | 870 (40.4\%) |  | 1580 (39.5\%) | 1579 (43.1\%) |  | 2299 (41.3\%) | 794 (40.4\%) |  |
| Current smoker | 688 (12.5\%) | 330 (15.3\%) |  | 483 (12.1\%) | 535 (14.6\%) |  | 697 (12.5\%) | 302 (15.4\%) |  |
| Educational level |  |  | 0.77 |  |  | $<0.0001$ |  |  | 0.53 |
| Less than high school | 495 (8.6\%) | 200 (8.9\%) |  | 321 (7.7\%) | 374 (9.8\%) |  | 502 (8.7\%) | 183 (9.0\%) |  |
| High school | 1717 (29.9\%) | 681 (30.4\%) |  | 1164 (28.0\%) | 1234 (32.3\%) |  | 1721 (29.7\%) | 630 (30.8\%) |  |
| University | 3528 (61.5\%) | 1356 (60.6\%) |  | 2675 (64.3\%) | 2209 (57.9\%) |  | 3570 (61.6\%) | 1231 (60.2\%) |  |
| Body-mass index, $\mathrm{kg} / \mathrm{m}^{2}$ |  |  | 0.34 |  |  | 0.094 |  |  | 0.089 |
| <18.5 | 124 (2.2\%) | 48 (2.2\%) |  | 99 (2.4\%) | 73 (1.9\%) |  | 122 (2.1\%) | 43 (2.1\%) |  |
| [18.5-25[ | 3264 (57.5\%) | 1309 (59.0\%) |  | 2429 (58.9\%) | 2144 (56.9\%) |  | 3284 (57.3\%) | 1214 (60.0\%) |  |
| [25-30[ | 1690 (29.8\%) | 657 (29.6\%) |  | 1194 (28.9\%) | 1153 (30.6\%) |  | 1713 (29.9\%) | 585 (28.9\%) |  |
| $\geq 30$ | 599 (10.6\%) | 205 (9.2\%) |  | 404 (9.8\%) | 400 (10.6\%) |  | 612 (10.7\%) | 182 (9.0\%) |  |
| Asthma |  |  | $<0.0001$ |  |  | <0.0001 |  |  | $<0.0001$ |
| Never asthma | 4304 (75.7\%) | 2056 (92.5\%) |  | 2959 (71.8\%) | 3401 (89.9\%) |  | 4347 (75.8\%) | 1889 (93.1\%) |  |
| Ever asthma | 1383 (24.3\%) | 166 (7.5\%) |  | 1165 (28.2\%) | 384 (10.1\%) |  | 1388 (24.2\%) |  |  |
| Conjunctivitis |  |  | $<0.0001$ |  |  | $<0.0001$ |  |  | $<0.0001$ |
| Never conjunctivitis | 2317 (44.7\%) | 1652 (80.4\%) |  | 1628 (42.1\%) | 2341 (69.4\%) |  | 2369 (45.1\%) | 1532 (81.8\%) |  |
| Ever conjunctivitis | 2868 (55.3\%) | 402 (19.6\%) |  | 2236 (57.9\%) | 1034 (30.6\%) |  | 2885 (54.9\%) | 342 (18.2\%) |  |
| Eczema |  |  | $<0.0001$ |  |  | <0.0001 |  |  | $<0.0001$ |
| Never eczema | 3021 (59.2\%) | 1561 (74.5\%) |  | 2202 (58.4\%) | 2380 (69.5\%) |  | 3078 (59.6\%) | 1436 (74.9\%) |  |
| Ever eczema | 2081 (40.8\%) | 535 (25.5\%) |  | 1571 (41.6\%) | 1045 (30.5\%) |  | 2088 (40.4\%) | 481 (25.1\%) |  |
| Nasal allergies |  |  | $<0.0001$ |  |  | <0.0001 |  |  | <0.0001 |
| Never nasal allergies | 0 (0.0\%) | 2263 (100.0\%) |  | 439 (10.4\%) | 1824 (47.2\%) |  | 139 (2.4\%) | 2066 (100.0\%) |  |
| Ever nasal allergies | 5806 (100.0\%) | 0 (0.0\%) |  | 3769 (89.6\%) | 2037 (52.8\%) |  | 5719 (97.6\%) | 0 (0.0\%) |  |
| Eosinophils count, cell $/ \mathrm{mm}^{3}$ | 208.6 (146.4) | 177.3 (117.9) | $<0.0001$ | 212.1 (147.6) | 186.3 (129.0) | <0.0001 | 207.9 (146.1) | 176.2 (116.4) | $<0.0001$ |
| Age of onset of rhinitis, year | 24.3 (15.3) | 34.6 (17.5) | $<0.0001$ | 23.1 (14.7) | 31.9 (17.5) | <0.0001 | 24.5 (15.4) | 34.5 (17.7) | $<0.0001$ |
| Reported triggers of rhinitis symptoms $\dagger$ |  |  |  |  |  |  |  |  |  |
| Dust mites or house dust | 1937 (33.4\%) | 235 (10.4\%) | $<0.0001$ | 2172 (51.6\%) | 0 (0.0\%) | <0.0001 | 1946 (33.2\%) | 198 (9.6\%) | $<0.0001$ |
| Animals | 677 (11.7\%) | 55 (2.4\%) | <0.0001 | 732 (17.4\%) | 0 (0.0\%) | <0.0001 | 675 (11.5\%) | 48 (2.3\%) | <0.0001 |


|  | Main definition |  |  | Alternate definition 1: Triggers-based |  |  | Alternate definition 2: Classification tree-based |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | $\begin{gathered} \mathrm{AR} \\ (\mathrm{n}=5806) \end{gathered}$ | $\begin{gathered} \text { NAR } \\ (\mathrm{n}=2263) \end{gathered}$ | p value | $\begin{gathered} \mathrm{AR} \\ (\mathrm{n}=4208) \end{gathered}$ | $\begin{gathered} \text { NAR } \\ (\mathrm{n}=3861) \end{gathered}$ | p value | $\begin{gathered} \mathrm{AR} \\ (\mathrm{n}=5858) \\ \hline \end{gathered}$ | $\begin{gathered} \text { NAR } \\ (\mathrm{n}=2066) \end{gathered}$ | p value |
| Air pollution | 1560 (26.9\%) | 287 (12.7\%) | $<0.0001$ | 1361 (32.3\%) | 486 (12.6\%) | <0.0001 | 1590 (27.1\%) | 235 (11.4\%) | $<0.0001$ |
| Change in weather | 1677 (28.9\%) | 601 (26.6\%) | 0.037 | 1240 (29.5\%) | 1038 (26.9\%) | 0.010 | 1689 (28.8\%) | 546 (26.4\%) | 0.037 |
| Tobacco | 359 (6.2\%) | 93 (4.1\%) | 0.0003 | 315 (7.5\%) | 137 (3.5\%) | <0.0001 | 356 (6.1\%) | 86 (4.2\%) | 0.0011 |
| Pollens | 3035 (52.3\%) | 231 (10.2\%) | <0.0001 | 3266 (77.6\%) | 0 (0.0\%) | <0.0001 | 3144 (53.7\%) | 88 (4.3\%) | <0.0001 |
| Cold air | 1423 (24.5\%) | 627 (27.7\%) | 0.0030 | 1055 (25.1\%) | 995 (25.8\%) | 0.47 | 1433 (24.5\%) | 585 (28.3\%) | 0.0005 |
| Other | 735 (12.7\%) | 282 (12.5\%) | 0.81 | 478 (11.4\%) | 539 (14.0\%) | 0.0004 | 733 (12.5\%) | 267 (12.9\%) | 0.63 |
| Unknown | 1573 (27.1\%) | 1100 (48.6\%) | <0.0001 | 410 (9.7\%) | 2263 (58.6\%) | <0.0001 | 1562 (26.7\%) | 1051 (50.9\%) | <0.0001 |
| Reported symptoms $\dagger$ |  |  |  |  |  |  |  |  |  |
| Rhinorrhoea | 4051 (75.1\%) | 1215 (59.0\%) | <0.0001 | 2969 (74.9\%) | 2297 (65.9\%) | <0.0001 | 4084 (74.9\%) | 1111 (59.0\%) | <0.0001 |
| Nasal congestion/obstruction | 4000 (76.3\%) | 1257 (62.1\%) | $<0.0001$ | 2886 (75.0\%) | 2371 (69.3\%) | <0.0001 | 4019 (75.9\%) | 1148 (61.9\%) | <0.0001 |
| Nasal itching | 3445 (67.0\%) | 767 (39.7\%) | $<0.0001$ | 2696 (70.4\%) | 1516 (46.7\%) | <0.0001 | 3476 (66.9\%) | 670 (37.9\%) | <0.0001 |
| Sneezing | 4073 (75.9\%) | 1055 (52.2\%) | $<0.0001$ | 3098 (78.1\%) | 2030 (59.3\%) | <0.0001 | 4104 (75.6\%) | 958 (51.7\%) | <0.0001 |
| Associated-eye symptoms | 3693 (68.8\%) | 698 (35.3\%) | <0.0001 | 2943 (73.9\%) | 1448 (43.0\%) | <0.0001 | 3768 (69.4\%) | 574 (31.7\%) | <0.0001 |
| Number of reported symptoms | 3.6 (1.3) | 2.3 (1.3) | $<0.0001$ | 3.7 (1.2) | 2.7 (1.4) | <0.0001 | 3.5 (1.3) | 2.3 (1.3) | <0.0001 |
| Rhinitis severity |  |  | <0.0001 |  |  | <0.0001 |  |  | <0.0001 |
| Mild | 2862 (59.9\%) | 1391 (75.8\%) |  | 2132 (59.7\%) | 2121 (69.8\%) |  | 2902 (60.0\%) | 1286 (76.3\%) |  |
| Moderate/severe | 1913 (40.1\%) | 445 (24.2\%) |  | 1441 (40.3\%) | 917 (30.2\%) |  | 1938 (40.0\%) | 399 (23.7\%) |  |
| Rhinitis duration |  |  | $<0.0001$ |  |  | 0.11 |  |  | $<0.0001$ |
| Intermittent | 3798 (68.4\%) | 1624 (74.9\%) |  | 2884 (71.0\%) | 2538 (69.3\%) |  | 3863 (68.8\%) | 1465 (73.9\%) |  |
| Persistent | 1758 (31.6\%) | 544 (25.1\%) |  | 1179 (29.0\%) | 1123 (30.7\%) |  | 1750 (31.2\%) | 518 (26.1\%) |  |
| Rhinitis treatment |  |  | $<0.0001$ |  |  | <0.0001 |  |  | $<0.0001$ |
| Neither oral antihistamines nor intranasal corticoids | 1911 (34.1\%) | 1596 (73.5\%) |  | 1255 (30.7\%) | 2252 (61.1\%) |  | 1954 (34.5\%) | 1484 (74.7\%) |  |
| Oral antihistamines only | 1204 (21.5\%) | 118 (5.4\%) |  | 1022 (25.0\%) | 300 (8.1\%) |  | 1204 (21.3\%) | 95 (4.8\%) |  |
| Intranasal corticoids only | 700 (12.5\%) | 325 (15.0\%) |  | 376 (9.2\%) | 649 (17.6\%) |  | 705 (12.4\%) | 304 (15.3\%) |  |
| Oral antihistamines and intranasal corticoids | 1794 (32.0\%) | 131 (6.0\%) |  | 1439 (35.2\%) | 486 (13.2\%) |  | 1802 (31.8\%) | 104 (5.2\%) |  |

Data are mean (SD) or $\mathrm{n}(\%), \dagger$ : several possible answers
Current rhinitis: Yes to Q. 23 "During your lifetime, have you ever had a problem with sneezing, or a runny, or a blocked nose when you did not have a cold or the flu?"
AR Main definition: current rhinitis and Yes to Q.22: "During your lifetime, have you ever had any nasal allergies including hay fever?"
NAR Main definition: current rhinitis and No to Q.22: "During your lifetime, have you ever had any nasal allergies including hay fever?"
AR Alternate Definition 1: current rhinitis and answer pollens or dust mites or house dust or animal to Q.25: "What factor triggered or increased these nose problems? (several answers possible)"
NAR Alternate Definition 1: current rhinitis and no answer pollens and dust mites and house dust and animal to Q.25: "What factor triggered or increased these nose problems? (several answers possible)"
AR Alternate Definition 2: current rhinitis and Yes to Q.22: "During your lifetime, have you ever had any nasal allergies including hay fever?" or Answer pollens to Q.25: "What factor triggered or increased these nose problems? (several answers possible)" and Yes to Q.23.A "Did your eyes itch or cry when you had these nose problems?"
NAR Alternate Definition 2: current rhinitis and No to Q.22: "During your lifetime, have you ever had any nasal allergies including hay fever?" and no answer pollens to Q.25: "What factor triggered or increased these nose problems? (several answers possible)" or no to Q.23.A "Did your eyes itch or cry when you had these nose problems?"
Kappa concordance coefficient between the main definition and the alternate definition $1=0.37$

Kappa concordance coefficient between the main definition and the alternate definition $2=0.96$

Table S4: Characteristics of participants with current Allergic Rhinitis (AR) or current Non-Allergic Rhinitis (NAR) including ever-asthma status in EGEA

|  | AR |  |  | NAR |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | Never asthma ( $\mathrm{n}=174$ ) | Ever asthma $(\mathrm{n}=380)$ | p-value | Never asthma ( $\mathrm{n}=176$ ) | Ever asthma ( $\mathrm{n}=83$ ) | p-value |
| Sex |  |  | 0.49 |  |  | 0.01 |
| Men | 81 (46.6\%) | 189 (49.7\%) |  | 68 (38.6\%) | 46 (55.4\%) |  |
| Women | 93 (53.5\%) | 191 (50.3\%) |  | 108 (61.4\%) | 37 (44.6\%) |  |
| Age, years | 44.7 (15.4) | 38.4 (15.8) | <0.0001 | 48.3 (15.2) | 37.2 (17.3) | $<0.0001$ |
| Tobacco status |  |  | 0.23 |  |  | 0.01 |
| Never-smoker | 85 (48.9\%) | 189 (49.9\%) |  | 90 (51.1\%) | 51 (61.5\%) |  |
| Ex-smoker | 50 (28.7\%) | 86 (22.7\%) |  | 51 (29.0\%) | 10 (12.1\%) |  |
| Current smoker | 39 (22.4\%) | 104 (27.4\%) |  | 35 (19.9\%) | 22 (26.5\%) |  |
| Educational level |  |  | 0.12 |  |  | 0.25 |
| Less than high school | 35 (21.0\%) | 62 (17.3\%) |  | 51 (30.2\%) | 19 (23.2\%) |  |
| High school | 43 (25.8\%) | 124 (34.5\%) |  | 44 (26.0\%) | 18 (22.0\%) |  |
| University | 89 (53.3\%) | 173 (48.2\%) |  | 74 (43.8\%) | 45 (54.9\%) |  |
| Conjunctivitis |  |  | 0.04 |  |  | 0.80 |
| Never conjunctivitis | 92 (53.8\%) | 166 (44.2\%) |  | 134 (77.0\%) | 62 (78.5\%) |  |
| Ever conjunctivitis | 79 (46.2\%) | 210 (55.9\%) |  | 40 (23.0\%) | 17 (21.5\%) |  |
| Eczema |  |  | 0.0003 |  |  | 0.02 |
| Never eczema | 110 (64.0\%) | 178 (47.2\%) |  | 130 (74.3\%) | 49 (59.8\%) |  |
| Ever eczema | 62 (36.1\%) | 199 (52.8\%) |  | 45 (25.7\%) | 33 (40.2\%) |  |
| All SPTs |  |  | 0.0006 |  |  | <. 0001 |
| No positive SPT | 45 (29.2\%) | 53 (15.8\%) |  | 110 (77.5\%) | 27 (41.5\%) |  |
| At least one positive SPT | 109 (70.8\%) | 282 (84.2\%) |  | 32 (22.5\%) | 38 (58.5\%) |  |
| Indoor SPTs |  |  | <. 0001 |  |  | <. 0001 |
| No positive SPT | 80 (52.0\%) | 108 (32.2\%) |  | 119 (83.8\%) | 31 (47.7\%) |  |
| At least one positive SPT | 74 (48.1\%) | 227 (67.8\%) |  | 23 (16.2\%) | 34 (52.3\%) |  |
| Mould SPTs |  |  | 0.19 |  |  | 0.01 |
| No positive SPT | 130 (84.4\%) | 266 (79.4\%) |  | 136 (95.8\%) | 56 (86.2\%) |  |
| At least one positive SPT | 24 (15.6\%) | 69 (20.6\%) |  | 6 (4.2\%) | 9 (13.9\%) |  |
| Outdoor SPTs |  |  | 0.03 |  |  | <. 0001 |
| No positive SPT | 69 (44.8\%) | 115 (34.3\%) |  | 125 (88.0\%) | 36 (55.4\%) |  |
| At least one positive SPT | 85 (55.2\%) | 220 (65.7\%) |  | 17 (12.0\%) | 29 (44.6\%) |  |
| Number of positive SPTs | 1.9 (1.8) | 2.6 (1.9) | <0.0001 | 0.4 (0.9) | 1.6 (1.6) | <0.0001 |
| Immunoglobulin E, IU/ml | 82.3 (34.5-201.0) | 60.2 (68.7-385.0) | <0.0001 | 3.4 (15.4-105.0) | 19.4 (32.1-350.0) | <. 0001 |
| Blood eosinophils count, cell $/ \mathrm{mm}^{3}$ | 191.6 (125.5) | 260.1 (200.6) | <0.0001 | 170.7 (143.9) | 262.0 (208.6) | 0.001 |
| Age of onset of rhinitis, year | 24.9 (15.8) | 14.3 (12.3) | <0.0001 | 34.4 (17.9) | 20.9 (18.4) | <. 0001 |
| Reported triggers of rhinitis symptoms $\dagger$ |  |  |  |  |  |  |
| Dust mites or house dust | 57 (32.8\%) | 206 (54.2\%) | <. 0001 | 40 (22.7\%) | 29 (34.9\%) | 0.04 |
| Animals | 29 (16.7\%) | 133 (35.0\%) | <. 0001 | 5 (2.8\%) | 12 (14.5\%) | 0.0004 |
| Pollens | 121 (69.5\%) | 250 (65.8\%) | 0.38 | 37 (21.0\%) | 13 (15.7\%) | 0.31 |
| Other | 20 (11.5\%) | 33 (8.7\%) | 0.30 | 55 (31.3\%) | 19 (22.9\%) | 0.16 |
| No trigger reported | 12 (6.9\%) | 25 (6.6\%) | 0.89 | 54 (30.7\%) | 23 (27.7\%) | 0.63 |
| Reported symptoms $\dagger$ |  |  |  | 0 (0.0\%) |  |  |
| Rhinorrhoea | 114 (72.2\%) | 288 (81.4\%) | 0.02 | 67 (46.5\%) | 39 (52.0\%) | 0.44 |
| Sneezing | 141 (87.0\%) | 315 (88.0\%) | 0.76 | 104 (68.4\%) | 48 (63.2\%) | 0.43 |
| Associated-eye symptoms | 135 (86.0\%) | 289 (80.5\%) | 0.13 | 92 (60.1\%) | 47 (59.5\%) | 0.93 |
| Impairment in daily activities |  |  | 0.01 |  |  | 0.002 |
| None | 86 (49.4\%) | 155 (40.8\%) |  | 139 (79.0\%) | 48 (57.8\%) |  |
| A little | 61 (35.1\%) | 123 (32.4\%) |  | 27 (15.3\%) | 21 (25.3\%) |  |
| Moderate | 22 (12.6\%) | 68 (17.9\%) |  | 8 (4.6\%) | 9 (10.8\%) |  |
| A lot | 5 (2.9\%) | 34 (9.0\%) |  | 2 (1.1\%) | 5 (6.0\%) |  |
| Duration |  |  | 0.10 |  |  | 0.45 |
| <1 month/year | 70 (40.5\%) | 116 (30.6\%) |  | 87 (49.7\%) | 38 (45.8\%) |  |
| $>1$ month/year and <4 days/week | 47 (27.2\%) | 117 (30.9\%) |  | 30 (17.1\%) | 17 (20.5\%) |  |
| $>1$ month/year and $>4$ days/week | 56 (32.4\%) | 143 (37.7\%) |  | 58 (33.1\%) | 27 (32.5\%) |  |

Data are mean (SD) or geometric mean (quartile 1 - quartile 3) or n (\%), $\dagger$ : several possible answers, all SPTs: skin prick tests to 12 aeroallergens: indoor: cat, Dermatophagoides pteronyssinus, Blattela germanica; outdoor: olive, birch, Parieteria judaica, timothy grass, ragweed pollen and Cupressus; moulds: Aspergillus, Cladosporium herbarum, Alternaria tenuis

Table S5: Characteristics of participants with current allergic rhinitis (AR) or current non-allergic rhinitis (NAR) defined by SPTs and including ever-asthma status in EGEA

|  | AR-SPT |  |  | NAR-SPT |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | Never asthma ( $\mathrm{n}=141$ ) | Ever asthma ( $\mathrm{n}=320$ ) | p-value | Never asthma ( $\mathrm{n}=155$ ) | Ever asthma $(\mathrm{n}=80)$ | p-value |
| Sex |  |  | 0.02 |  |  | 0.56 |
| Men | 60 (42.6\%) | 175 (54.7\%) |  | 56 (36.1\%) | 32 (40.0\%) |  |
| Women | 81 (57.5\%) | 145 (45.3\%) |  | 99 (63.9\%) | 48 (60.0\%) |  |
| Age, years | 40.6 (14.3) | 35.9 (15.1) | 0.002 | 51.3 (14.8) | 47.9 (16.7) | 0.11 |
| Tobacco status |  |  | 0.45 |  |  | 0.46 |
| Never-smoker | 72 (51.1\%) | 171 (53.4\%) |  | 78 (50.3\%) | 37 (46.3\%) |  |
| Ex-smoker | 34 (24.1\%) | 61 (19.1\%) |  | 49 (31.6\%) | 23 (28.8\%) |  |
| Current smoker | 35 (24.8\%) | 88 (27.5\%) |  | 28 (18.1\%) | 20 (25.0\%) |  |
| Educational level |  |  | 0.11 |  |  | 0.98 |
| Less than high school | 21 (14.9\%) | 46 (14.5\%) |  | 50 (32.3\%) | 25 (31.3\%) |  |
| High school | 34 (24.1\%) | 107 (33.8\%) |  | 41 (26.5\%) | 21 (26.3\%) |  |
| University | 86 (61.0\%) | 164 (51.7\%) |  | 64 (41.3\%) | 34 (42.5\%) |  |
| Conjunctivitis |  |  | 0.05 |  |  | 0.06 |
| Never conjunctivitis | 76 (55.1\%) | 143 (45.3\%) |  | 110 (71.9\%) | 46 (59.7\%) |  |
| Ever conjunctivitis | 62 (44.9\%) | 173 (54.8\%) |  | 43 (28.1\%) | 31 (40.3\%) |  |
| Eczema |  |  | <. 0001 |  |  | 0.99 |
| Never eczema | 98 (70.0\%) | 143 (45.0\%) |  | 100 (64.9\%) | 52 (65.0\%) |  |
| Ever eczema | 42 (30.0\%) | 175 (55.0\%) |  | 54 (35.1\%) | 28 (35.0\%) |  |
| Indoor SPTs |  |  | 0.002 |  |  | - |
| No positive SPT | 44 (31.2\%) | 59 (18.4\%) |  | - | - |  |
| At least one positive SPT | 97 (68.8\%) | 261 (81.6\%) |  | - | - |  |
| Mould SPTs |  |  | 0.47 |  |  | - |
| No positive SPT | 111 (78.7\%) | 242 (75.6\%) |  | - | - |  |
| At least one positive SPT | 30 (21.3\%) | 78 (24.4\%) |  | - | - |  |
| Outdoor SPTs |  |  | 0.20 |  |  | - |
| No positive SPT | 39 (27.7\%) | 71 (22.2\%) |  | - | - |  |
| At least one positive SPT | 102 (72.3\%) | 249 (77.8\%) |  | - | - |  |
| Number of positive SPTs | 2.4 (1.6) | 3.0 (1.6) | 0.0004 | - | - - | - |
| Immunoglobulin E, IU/ml | 95.8 (46.7-209.0) | 197.1 (86.1-451.0) | <. 0001 | 40.5 (15.4-91.3) | 49.8 (16.7-138.0) | 0.32 |
| Blood eosinophils count, cell $/ \mathrm{mm}^{3}$ | 198.0 (130.5) | 259.6 (191.9) | 0.0006 | 170.1 (140.1) | 229.9 (212.3) | 0.03 |
| Age of onset of rhinitis, year | 21.7 (13.1) | 13.3 (11.9) | <. 00001 | 36.1 (18.3) | 24.3 (16.6) | <. 0001 |
| Reported triggers of rhinitis symptoms $\dagger$ |  |  |  |  |  |  |
| Dust mites or house dust | 53 (37.6\%) | 182 (56.9\%) | 0.0001 | 32 (20.7\%) | 24 (30.0\%) | 0.11 |
| Animals | 26 (18.4\%) | 124 (38.8\%) | <. 0001 | 4 (2.6\%) | 3 (3.8\%) | 0.62 |
| Pollens | 96 (68.1\%) | 208 (65.0\%) | 0.52 | 42 (27.1\%) | 25 (31.3\%) | 0.50 |
| Other | 13 (9.2\%) | 25 (7.8\%) | 0.61 | 49 (31.6\%) | 17 (21.3\%) | 0.09 |
| No trigger reported | 7 (5.0\%) | 17 (5.3\%) | 0.88 | 45 (29.0\%) | 22 (27.5\%) | 0.81 |
| Reported symptoms $\dagger$ |  |  |  |  |  |  |
| Rhinorrhoea | 95 (70.4\%) | 241 (78.8\%) | 0.06 | 66 (50.4\%) | 47 (67.1\%) | 0.02 |
| Sneezing | 123 (88.5\%) | 264 (85.4\%) | 0.38 | 98 (70.0\%) | 50 (71.4\%) | 0.83 |
| Associated-eye symptoms | 112 (83.6\%) | 248 (80.5\%) | 0.45 | 88 (63.3\%) | 49 (65.3\%) | 0.77 |
| Impairment in daily activities |  |  | 0.009 |  |  | 0.001 |
| None | 75 (53.2\%) | 141 (44.1\%) |  | 113 (72.9\%) | 38 (47.5\%) |  |
| A little | 47 (33.3\%) | 98 (30.6\%) |  | 27 (17.4\%) | 23 (28.8\%) |  |
| Moderate | 17 (12.1\%) | 52 (16.3\%) |  | 11 (7.1\%) | 13 (16.3\%) |  |
| A lot | 2 (1.4\%) | 29 (9.1\%) |  | 4 (2.6\%) | 6 (7.5\%) |  |
| Duration |  |  | 0.05 |  |  | 0.25 |
| <1 month/year | 64 (45.7\%) | 108 (33.8\%) |  | 72 (46.8\%) | 28 (35.4\%) |  |
| $>1$ month/year and <4 days/week | 32 (22.9\%) | 91 (28.4\%) |  | 35 (22.7\%) | 23 (29.1\%) |  |
| $>1$ month/year and >4 days/week | 44 (31.4\%) | 121 (37.8\%) |  | 47 (30.5\%) | 28 (35.4\%) |  |

Data are mean (SD) or geometric mean (quartile 1 - quartile 3) or $\mathrm{n}(\%), \dagger$ : several possible answers, all SPTs : skin prick tests to 12 aeroallergens : indoor: cat, Dermatophagoides pteronyssinus, Blattela germanica; outdoor : olive, birch, Parieteria judaica, timothy grass, ragweed pollen and Cupressus; moulds : Aspergillus, Cladosporium herbarum, Alternaria tenuis

Table S6: Characteristics of participants with current Allergic Rhinitis (AR) including ever-asthma (A) and ever-conjunctivitis (C) status in EGEA

|  | AR alone $(\mathrm{n}=92)$ | $\underset{(n=79)}{A R}$ | AR and A ( $\mathrm{n}=166$ ) | $A R$ and $C$ and A ( $\mathrm{n}=\mathbf{2 1 0}$ ) | $\begin{gathered} \mathbf{p -} \\ \text { value } \end{gathered}$ |
| :---: | :---: | :---: | :---: | :---: | :---: |
| Sex |  |  |  |  | 0.39 |
| Men | 48 (52.2\%) | 32 (40.5\%) | 85 (51.2\%) | 102 (48.6\%) |  |
| Women | 44 (47.8\%) | 47 (59.5\%) | 81 (48.8\%) | 108 (51.4\%) |  |
| Age, years | 43.9 (16.2) | 45.5 (14.8) | 36.4 (15.4) | 40.1 (16.0) | $<0.000$ 1 |
| Tobacco status |  |  |  |  | 0.37 |
| Never-smoker | 40 (43.5\%) | 44 (55.7\%) | 78 (47.0\%) | 111 (53.1\%) |  |
| Ex-smoker | 29 (31.5\%) | 19 (24.1\%) | 40 (24.1\%) | 44 (21.1\%) |  |
| Current smoker | 23 (25.0\%) | 16 (20.3\%) | 48 (28.9\%) | 54 (25.8\%) |  |
| Educational level |  |  |  |  | 0.07 |
| Less than high school | 20 (23.0\%) | 15 (19.5\%) | 33 (21.4\%) | 28 (13.9\%) |  |
| High school | 24 (27.6\%) | 18 (23.4\%) | 58 (37.7\%) | 66 (32.8\%) |  |
| University | 43 (49.4\%) | 44 (57.1\%) | 63 (40.9\%) | 107 (53.2\%) |  |
| Eczema |  |  |  |  | 0.001 |
| Never eczema | 58 (64.4\%) | 49 (62.0\%) | 87 (53.4\%) | 90 (42.9\%) |  |
| Ever eczema | 32 (35.6\%) | 30 (38.0\%) | 76 (46.6\%) | 120 (57.1\%) |  |
| All SPTs |  |  |  |  | 0.003 |
| No positive SPT | 25 (30.9\%) | 20 (28.6\%) | 26 (18.2\%) | 26 (13.8\%) |  |
| At least one positive SPT | 56 (69.1\%) | 50 (71.4\%) | 117 (81.8\%) | 162 (86.2\%) |  |
| Indoor SPTs |  |  |  |  | <. 0001 |
| No positive SPT | 46 (56.8\%) | 34 (48.6\%) | 41 (28.7\%) | 65 (34.6\%) |  |
| At least one positive SPT | 35 (43.2\%) | 36 (51.4\%) | 102 (71.3\%) | 123 (65.4\%) |  |
| Mould SPTs |  |  |  |  | 0.63 |
| No positive SPT | 69 (85.2\%) | 59 (84.3\%) | 114 (79.7\%) | 150 (79.8\%) |  |
| At least one positive SPT | 12 (14.8\%) | 11 (15.7\%) | 29 (20.3\%) | 38 (20.2\%) |  |
| Outdoor SPTs |  |  |  |  | 0.01 |
| No positive SPT | 35 (43.2\%) | 32 (45.7\%) | 60 (42.0\%) | 52 (27.7\%) |  |
| At least one positive SPT | 46 (56.8\%) | 38 (54.3\%) | 83 (58.0\%) | 136 (72.3\%) |  |
| Number of positive SPTs | 1.6 (1.6) | 2.1 (2.1) | 2.4 (1.9) | 2.7 (1.8) | 0.0002 |
| Immunoglobulin $\mathrm{E}, \mathrm{IU} / \mathrm{ml}$ | $\begin{array}{r} 79.2 \text { (30.9- } \\ 196.0) \end{array}$ | $\begin{array}{r} 86.9 \text { (36.3- } \\ 209.0) \end{array}$ | $\begin{array}{r} 162.9 \text { (67.8- } \\ 394.0) \end{array}$ | $\begin{array}{r} 157.5 \text { (68.9- } \\ 351.3) \end{array}$ | <. 0001 |
| Blood eosinophils count, cell $/ \mathrm{mm}^{3}$ | 179.6 (128.3) | 206.7 (122.0) | 260.2 (184.4) | 259.9 (213.7) | 0.001 |
| Age of onset of rhinitis, year | 23.1 (15.5) | 27.2 (15.9) | 14.9 (12.8) | 13.6 (11.9) | <. 0001 |
| Reported triggers of rhinitis symptoms $\dagger$ | Reported triggers of rhinitis |  |  |  |  |
| Dust mites or house dust | 28 (30.4\%) | 27 (34.2\%) | 95 (57.2\%) | 111 (52.9\%) | <. 0001 |
| Animals | 14 (15.2\%) | 15 (19.0\%) | 48 (28.9\%) | 84 (40.0\%) | <. 0001 |
| Pollens | 67 (72.8\%) | 53 (67.1\%) | 93 (56.0\%) | 155 (73.8\%) | 0.002 |
| Other | 8 (8.7\%) | 11 (13.9\%) | 18 (10.8\%) | 15 (7.1\%) | 0.31 |
| No trigger reported | 6 (6.5\%) | 6 (7.6\%) | 12 (7.2\%) | 12 (5.7\%) | 0.92 |
| Reported symptoms $\dagger$ |  |  |  |  |  |
| Rhinorrhoea | 62 (73.8\%) | 50 (70.4\%) | 121 (77.1\%) | 163 (84.5\%) | 0.04 |
| Sneezing | 76 (88.4\%) | 63 (86.3\%) | 138 (87.3\%) | 173 (88.3\%) | 0.97 |
| Associated-eye symptoms | 69 (83.1\%) | 63 (88.7\%) | 112 (71.8\%) | 173 (86.9\%) | 0.001 |
| Impairment in daily activities |  |  |  |  | 0.005 |
| None | 53 (57.6\%) | 32 (40.5\%) | 80 (48.2\%) | 75 (35.7\%) |  |
| A little | 25 (27.2\%) | 35 (44.3\%) | 47 (28.3\%) | 73 (34.8\%) |  |
| Moderate | 12 (13.0\%) | 9 (11.4\%) | 27 (16.3\%) | 40 (19.1\%) |  |
| A lot | 2 (2.2\%) | 3 (3.8\%) | 12 (7.2\%) | 22 (10.5\%) |  |
| Duration |  |  |  |  | 0.01 |
| <1 month/year | 43 (47.3\%) | 27 (34.2\%) | 61 (37.0\%) | 55 (26.2\%) |  |
| $>1$ month/year and <4 days/week | 26 (28.6\%) | 19 (24.1\%) | 49 (29.7\%) | 67 (31.9\%) |  |
| $>1$ month/year and >4 days/week | 22 (24.2\%) | 33 (41.8\%) | 55 (33.3\%) | 85 (40.5\%) |  |

Data are mean (SD) or $\mathrm{n}(\%)$, $\dagger$ : several possible answers, all SPTs: skin prick tests to 12 aeroallergens: indoor: cat, Dermatophagoides pteronyssinus, Blattela germanica; outdoor: olive, birch, Parieteria judaica, timothy grass, ragweed pollen and Cupressus; moulds: Aspergillus, Cladosporium herbarum, Alternaria tenuis

Table S7: Characteristics of participants with current Allergic Rhinitis (AR) defined by SPTs including ever-asthma (A) and ever-conjunctivitis (C) status in EGEA

| Sex | AR-SPT alone $(\mathrm{n}=76)$ | AR-SPT and C ( $\mathrm{n}=62$ ) | AR-SPT and A ( $\mathrm{n}=143$ ) | AR-SPT and C and A $(\mathrm{n}=173)$ | p-value |
| :---: | :---: | :---: | :---: | :---: | :---: |
| Sex |  |  |  |  | 0.06 |
| Men | 35 (46.1\%) | 24 (38.7\%) | 83 (58.0\%) | 89 (51.5\%) |  |
| Women | 41 (54.0\%) | 38 (61.3\%) | 60 (42.0\%) | 84 (48.6\%) |  |
| Age, years | 38.6 (14.1) | 42.8 (14.6) | 33.9 (14.9) | 37.8 (15.2) | 0.001 |
| Tobacco status |  |  |  |  | 0.86 |
| Never-smoker | 36 (47.4\%) | 35 (56.5\%) | 77 (53.9\%) | 93 (53.8\%) |  |
| Ex-smoker | 20 (26.3\%) | 12 (19.4\%) | 28 (19.6\%) | 32 (18.5\%) |  |
| Current smoker | 20 (26.3\%) | 15 (24.2\%) | 38 (26.6\%) | 48 (27.8\%) |  |
| Educational level |  |  |  |  | 0.15 |
| Less than high school | 14 (18.4\%) | 7 (11.3\%) | 26 (18.4\%) | 20 (11.6\%) |  |
| High school | 18 (23.7\%) | 15 (24.2\%) | 48 (34.0\%) | 59 (34.3\%) |  |
| University | 44 (57.9\%) | 40 (64.5\%) | 67 (47.5\%) | 93 (54.1\%) |  |
| Eczema |  |  |  |  | <. 0001 |
| Never eczema | 53 (70.7\%) | 42 (67.7\%) | 71 (50.4\%) | 70 (40.5\%) |  |
| Ever eczema | 22 (29.3\%) | 20 (32.3\%) | 70 (49.7\%) | 103 (59.5\%) |  |
| Indoor SPTs |  |  |  |  | 0.001 |
| No positive SPT | 26 (34.2\%) | 18 (29.0\%) | 18 (12.6\%) | 40 (23.1\%) |  |
| At least one positive SPT | 50 (65.8\%) | 44 (71.0\%) | 125 (87.4\%) | 133 (76.9\%) |  |
| Mould SPTs |  |  |  |  | 0.89 |
| No positive SPT | 61 (80.3\%) | 48 (77.4\%) | 108 (75.5\%) | 133 (76.9\%) |  |
| At least one positive SPT | 15 (19.7\%) | 14 (22.6\%) | 35 (24.5\%) | 40 (23.1\%) |  |
| Outdoor SPTs |  |  |  |  | 0.11 |
| No positive SPT | 22 (29.0\%) | 15 (24.2\%) | 39 (27.3\%) | 30 (17.3\%) |  |
| At least one positive SPT | 54 (71.1\%) | 47 (75.8\%) | 104 (72.7\%) | 143 (82.7\%) |  |
| Number of positive SPTs | 2.2 (1.3) | 2.8 (1.9) | 2.9 (1.7) | 3.1 (1.6) | 0.0006 |
| Immunoglobulin E, IU/ml | 92.4 (46.4-197.0) | 102.3 (48.0-209.0) | 212.2 (90.0-495.0) | 184.4 (84.1-385.0) | <. 0001 |
| Blood eosinophils count, cell/ $/ \mathrm{mm}^{3}$ | 182.3 (136.6) | 219.3 (121.5) | 271.3 (198.4) | 249.4 (187.5) | 0.004 |
| Age of onset of rhinitis, year | 20.7 (12.9) | 23.0 (13.3) | 14.3 (13.1) | 12.5 (10.9) | <. 0001 |
| Reported triggers of rhinitis symptoms $\dagger$ |  |  |  |  |  |
| Dust mites or house dust | 26 (34.2\%) | 25 (40.3\%) | 83 (58.0\%) | 99 (57.2\%) | 0.0007 |
| Animals | 13 (17.1\%) | 13 (21.0\%) | 44 (30.8\%) | 79 (45.7\%) | <. 0001 |
| Pollens | 50 (65.8\%) | 45 (72.6\%) | 77 (53.9\%) | 130 (75.1\%) | 0.001 |
| Other | 9 (11.8\%) | 3 (4.8\%) | 15 (10.5\%) | 9 (5.2\%) | 0.14 |
| No trigger reported | 4 (5.3\%) | 3 (4.8\%) | 11 (7.7\%) | 5 (2.9\%) | 0.29 |
| Reported symptoms $\dagger$ |  |  |  |  |  |
| Rhinorrhoea | 52 (71.2\%) | 41 (69.5\%) | 102 (74.5\%) | 135 (81.8\%) | 0.14 |
| Sneezing | 66 (88.0\%) | 55 (90.2\%) | 116 (84.7\%) | 144 (85.7\%) | 0.73 |
| Associated-eye symptoms | 56 (77.8\%) | 53 (89.8\%) | 98 (72.1\%) | 146 (86.9\%) | 0.002 |
| Impairment in daily activities |  |  |  |  | 0.004 |
| None | 46 (60.5\%) | 28 (45.2\%) | 76 (53.2\%) | 64 (37.0\%) |  |
| A little | 21 (27.6\%) | 25 (40.3\%) | 34 (23.8\%) | 62 (35.8\%) |  |
| Moderate | 8 (10.5\%) | 8 (12.9\%) | 21 (14.7\%) | 30 (17.3\%) |  |
| A lot | 1 (1.3\%) | 1 (1.6\%) | 12 (8.4\%) | 17 (9.8\%) |  |
| Duration |  |  |  |  | 0.02 |
| <1 month/year | 38 (50.7\%) | 26 (41.9\%) | 57 (39.9\%) | 50 (28.9\%) |  |
| >1 month/year and <4 days/week | 19 (25.3\%) | 11 (17.7\%) | 37 (25.9\%) | 53 (30.6\%) |  |
| $>1$ month/year and >4 days/week | 18 (24.0\%) | 25 (40.3\%) | 49 (34.3\%) | 70 (40.5\%) |  |

Data are mean (SD) or geometric mean (quartile 1 - quartile 3) or $n(\%), \dagger$ : several possible answers, all SPTs: skin prick tests to 12 aeroallergens: indoor: cat, Dermatophagoides pteronyssinus, Blattela germanica; outdoor: olive, birch, Parieteria judaica, timothy grass, ragweed pollen and Cupressus; moulds: Aspergillus, Cladosporium herbarum, Alternaria tenuis

Figure S1: Location of the participating Health Screening Centers in France
Three health screening centers were located in Paris.


Figure S2: Flowchart
AR: Allergic Rhinitis
NAR: Non-Allergic Rhinitis


## Figure S3: Percentage of participants reporting symptoms by months

A: Current Allergic Rhinitis
Current rhinitis: Yes to Q. 23 "During your lifetime, have you ever had a problem with sneezing, or a runny, or a blocked nose when you did not have a cold or the flu?"
.... AR Main definition: current rhinitis and Yes to Q.22: "During your lifetime, have you ever had any nasal allergies including hay fever?"

-     - AR Alternate Definition 1: current rhinitis and answer pollens or dust mites or house dust or animal to Q.25: "What factor triggered or increased these nose problems? (several answers possible)"
- AR Alternate Definition 2: current rhinitis and Yes to Q.22: "During your lifetime, have you ever had any nasal allergies including hay fever?" or Answer pollens to Q.25: "What factor triggered or increased these nose problems? (several answers possible)" and Yes to Q.23.A "Did your eyes itch or cry when you had these nose problems?"


## B: Current Non-Allergic Rhinitis

.... NAR Main definition: current rhinitis and No to Q.22: "During your lifetime, have you ever had any nasal allergies including hay fever?"

-     - NAR Alternate Definition 3: current rhinitis and no answer pollens and dust mites and house dust and animal to Q.25: "What factor triggered or increased these nose problems? (several answers possible)"
- NAR Alternate Definition 4: current rhinitis and No to Q.22: "During your lifetime, have you ever had any nasal allergies including hay fever?" and no answer pollens to Q.25: "What factor triggered or increased these nose problems? (several answers possible)" or no to Q.23.A "Did your eyes itch or cry when you had these nose problems?"
A. ${ }^{70 \%}$

B. ${ }^{70 \%}$



## Figure S4: Triggers of rhinitis symptoms (several possible answers)

A: Current Allergic Rhinitis
Current rhinitis: Yes to Q. 23 "During your lifetime, have you ever had a problem with sneezing, or a runny, or a blocked nose when you did not have a cold or the flu?"
.... AR Main definition: current rhinitis and Yes to Q.22: "During your lifetime, have you ever had any nasal allergies including hay fever?"

-     - AR Alternate Definition 1: current rhinitis and answer pollens or dust mites or house dust or animal to Q.25: "What factor triggered or increased these nose problems? (several answers possible)"
- AR Alternate Definition 2: current rhinitis and Yes to Q.22: "During your lifetime, have you ever had any nasal allergies including hay fever?" or Answer pollens to Q.25: "What factor triggered or increased these nose problems? (several answers possible)" and Yes to Q.23.A "Did your eyes itch or cry when you had these nose problems?"


## B: Current Non-Allergic Rhinitis

.... NAR Main definition: current rhinitis and No to Q.22: "During your lifetime, have you ever had any nasal allergies including hay fever?"
= - NAR Alternate Definition 3: current rhinitis and no answer pollens and dust mites and house dust and animal to Q.25: "What factor triggered or increased these nose problems? (several answers possible)"

- NAR Alternate Definition 4: current rhinitis and No to Q.22: "During your lifetime, have you ever had any nasal allergies including hay fever?" and no answer pollens to Q.25: "What factor triggered or increased these nose problems? (several answers possible)" or no to Q.23.A "Did your eyes itch or cry when you had these nose problems?"


Figure S5: Comparison between Constances and EGEA for prevalence of ever-eczema, mean age of onset, and mean eosinophils count

Blue filling: results from Constances
Hatched orange filling: results from EGEA
AR alone: current Allergic Rhinitis alone
AR +C : current Allergic Rhinitis and ever-conjunctivitis without ever-asthma AR + A: current Allergic Rhinitis and ever-asthma without ever-conjunctivitis $A R+C+A:$ current Allergic Rhinitis and ever-conjunctivitis and ever-asthma




