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Research Article

The Atopy Index Inventory: A Brief and Simple Tool to Identify Atopic Patients

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Abstract
Introduction: Atopy and ear, nose and throat (ENT) diseases are frequently associated; however, no clinical tool has been proposed so far to discriminate which patients could be atopic and therefore deserving of a further immunoallergological evaluation. ***Objective:*** The aim of this study was to assess and validate a set of dichotomous responses suitable for predicting the presence of atopy in adult patients. ***Methods:*** An 11-item questionnaire, i.e., the Atopy Index Inventory (AII), comprised of 4 questions regarding the clinical history for allergic disease and 7 questions evaluating the presence of the most frequent clinical signs affecting allergic patients, was developed and administered to 226 adult subjects (124 atopic subjects and 102 healthy, not atopic subjects). The atopic condition was proven by an immunoallergological evaluation according to the diagnostic criteria of the EAACI guidelines. Internal consistency and clinical validity were tested. ***Results:*** In healthy subjects, the first 4 variables of the AII returned a 100% correct response (all answered "no") and were defined as "decisive" responses. In the logistic regression analysis, when decisive items were negative, the atopic condition was confirmed when answering "yes" to at least 3 "probability" items (cut-off = 2.69). The difference in AII scores between allergic and healthy group was significant using the Mann-Whitney U test ($p < 0.0001$). The sensitivity and specificity of the AII were

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0.97 and 0.91, respectively, with a true predictive value of 0.92 and a false predictive value of 0.97. The ROC curve showed an area of 0.94, with an OR of 0.88 (95% CI 0.87–0.97, $p = 0.0001$). The internal consistency as determined by the Cronbach α coefficient was 0.88. ***Conclusion:*** The AII has been proven to be a brief, simple and sufficiently accurate tool for screening ENT patients in search of atopic individuals and to allow their clinical management.

Introduction

Atopy is a polygenic disorder characterized by the expression of certain allergic hypersensitivity reactions, mediated by immunoglobulin E (IgE), to the exposure to allergens. As a consequence, atopy produces allergy with the typical symptoms of asthma, rhino conjunctivitis, or eczema. Atopy has been associated with several ear, nose, and throat (ENT) disorders, such as otitis media with effusion [1–4], adenoid hypertrophy [5–7], rhinitis and sinusitis [8, 9], Ménière disease [10–12], and Reinke edema [13]. When a patient is referred for one of these common diseases, ENT specialists usually address the existence of an allergic substrate by means of a direct, time-consuming interview or empiric treatments [14]. If an allergic condition is only marginally suspected, the patient is frequently referred for an immunoallergological evaluation.

Various clinical measures of allergy (e.g., skin prick test positivity, elevated total IgE, and specific IgE titer) and questionnaires have been assessed in a number of studies, but none of these tools has been studied to screen for an atopic condition [15, 16]. In particular, the questionnaires on atopy [17–22] are aimed at monitoring clinical symptoms, determining the clinical evolution of allergic sensitization, or quantifying the effects of therapy or changes in quality of life, but none of the questionnaires are targeted for screening purposes. Furthermore, it is widely acknowledged that the diagnosis of atopy is not very straightforward [23, 24] due to its polygenic nature and because an increase in total and specific IgE is not a necessary landmark for identifying atopic individuals [23]. In fact, the correlation between skin tests and in vitro tests for specific IgE is not always very strong since mucosal and skin IgE may be different from blood IgE [24–27]. Moreover, currently available allergenic extracts manufactured by different companies for allergy testing are very heterogeneous [28, 29], and some allergens, such as storage mites (Glycyphagidae and Acaridae), though considered important, are not always included in the testing batteries [30].

The aim of this study was to assess and validate a questionnaire to identify patients requiring further allergological evaluation. For this purpose, we developed and assessed an Atopy Index Inventory (AII) that could be easily and rapidly administered and could expedite the assessment of potentially atopic patients in an ENT clinical setting and define which patients should be referred for further investigation of a possible allergic condition since it may have practical implications for treatment.

Materials and Methods

Validation of the AII

Item generations were founded on: (1) an international literature review through Medline database, (2) the most commonly reported symptoms related to atopy [15–22], and (3) the most commonly routine questions posed in clinical practice. The resulting screening questionnaire denominated the AII included 11 items aimed at identifying the allergic condition (Table 1).

The statistical analysis of this study consisted of 2 separate phases, i.e., scale development followed by a reliability and validity analysis.

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Table 1. The Atopy Index Inventory

Decisive questions			
s1	Do you think you suffer from an allergy or have you received medical treatments for allergies?	Yes	No
s2	Did you have atopic dermatitis (eczema of the skin) in the first years of life?	Yes	No
s3	Do you have allergic reactions when you are in contact with pets?	Yes	No
s4	Do you suffer from frequent colds and/or red and itchy eyes in the spring/summer time?	Yes	No
Probability questions			
r1	Are the upper teeth not coincident with the lower ones (overbite)?	Yes	No
r2	Do you often have a stuffy nose, e.g., do you breathe through your mouth and feel that your nasal passages are not completely clear?	Yes	No
r3	Is your mouth open when you sleep, or do you snore?	Yes	No
r4	Do you need to blow (clean) your nose or sneeze when you wake up in the morning?	Yes	No
r5	Have you used more than one handkerchief/day for more than 1 week in any season?	Yes	No
r6	Do you have family members (grandparents, parents, or siblings) who suffer from allergies?	Yes	No
r7	Are there any foods that give you problems in your mouth (oral allergy syndrome)?	Yes	No

According to STARD guidelines, we tested the AII on 226 consecutive subjects attending our outpatient clinic between 2012 and 2015 at the time of their first referral visit for audiological evaluation. Patients were administered the AII as part of the clinical assessment, and no other questions concerning the possibility of "atopy" were asked. ENT specialists filled out the AII. All 226 subjects were then referred for an immunoallergological evaluation. All underwent skin tests using a standardized method as follows: (1) prick tests for the most common inhalants, cow milk proteins, ovoalbumin, and water extract from wheat flour and (2) prick tests for tomato, potato, apple, and carrots (fresh foods). Histamine was used as a positive control and extract diluent as a negative control. Patients with negative prick tests were further investigated by an intradermal test with a *Dermatophagoides* mixture. Subsequently, the 226 patients were classified by immunologists into 2 subgroups according to the immunoallergological results into an atopic group and a control group according to EAACI guidelines [19].

Atopic Group

This group included 124 individuals, i.e., 76 females (age range 4–79 years, mean 36.8 ± 19.11) and 48 males (age range 6–70 years, mean 32.7 ±18.97). According to EAACI guidelines [19], this group included those patients with a positive skin prick test to at least one of the allergens tested and/or a positive result on an intradermal test (wheal diameter >5 mm) and/or elevated total IgE >260 IU/mL and/or specific IgE >0.70 kU/L, allergic rhinopathy according to the International Consensus Statement on Allergy and Rhinology: Allergic Rhinitis [31], and/or successful treatment with immunotherapy.

Control Group

This group comprised 102 individuals, i.e., 61 females (age range 19–74 years, mean 36.0 ± 14.3) and 41 males (age range 19–74 years, mean 38.8 ± 17.6). The control group was constituted by all (nonatopic) patients who tested negative on all of the previously reported parameters at the immunoallergological evaluation.

Statistical Analysis

Data were collected using an Excel datasheet and imported and analyzed by means of the R Project for Statistical Computing (R Core Team, 2015), using the package MASS to carry out logistic regression and the packages ROCR and AUC to estimate and plot different performance measures, such as optimum cut-off, accuracy, sensitivity and specificity, odds, true and false predictive values (TPV and FPV, respectively), and CI. The internal consistency of the 11 tests was assessed using the Cronbach α coefficient with the package PSY (CRAN, R core team, 2015). The presence of ceiling and floor effects was evaluated on the basis of the percentage of patients with the maximum or minimum AII score and it was considered present if this was the case in 15% or more of the patients [33]. The Kaiser-Meyer-Olkin measure of sampling adequacy and the Bartlett test of sphericity were conducted on the data prior to factor extraction to ensure that the character-

Table 2. Individual items of AII association with atopy

Question	Sensitivity	Specificity	TVP	FVP	Accuracy	Hits-misses	OR	TPV 95% CI
s1	0.73	1	1	0.75	0.85	5.65	Inf	1.00–100
s2	0.16	1	1	0.5	0.54	1.17	Inf	1.00–100
s3	0.31	1	1	0.54	0.62	1.63	Inf	1.00–100
s4	0.60	1	1	0.67	0.78	3.52	Inf	1.00–100
r1	0.85	0.96	0.96	0.84	0.90	8.83	135.39	0.93–1.00
r2	0.77	0.83	0.85	0.75	0.80	3.91	16.38	0.78–1.00
r3	0.72	0.89	0.89	0.72	0.80	3.91	21.04	0.82–0.96
r4	0.62	0.94	0.93	0.67	0.77	3.26	26.21	0.87–0.99
r5	0.83	0.88	0.90	0.81	0.86	5.85	36.79	0.84–0.95
r6	0.56	0.88	0.85	0.63	0.71	2.42	9.72	0.77–0.94
r7	0.31	0.94	0.87	0.53	0.60	1.48	7.34	0.76–0.97

Inf, infinite.

istics of the data set were suitable for the exploratory factor analysis to be done. For the exploratory factor analysis, the number of factors to extract was determined by the screen plot and Kaiser's criterion of unity (i.e., Eigen values >1). Principal component analysis with Varimax rotation was used to maximize the amount of variance explained by the instrument items. Spearman rank correlation was used to evaluate the relationship among the 11 items. The fitted values of the responses obtained from the logistic regression were the starting point to estimate the probabilities of assigning a subject to a group. Since individual items differed in their association with atopy, each item was weighted by its OR in favor of atopy. The fitted values obtained with logistic regression were turned into a binary class decision by choosing a cut-off using the package ROCR. The presence of a normal distribution was assessed using a Shapiro-Wilks normality test; a goodness-of-fit test was used to verify the Poisson distribution. A Wilcoxon Mann-Whitney nonparametric test was used to test significant differences between the 2 groups ($p < 0.05$).

Results

The Cronbach α coefficient was 0.8 (95% CI 0.86–0.90), indicating a high intrinsic reliability of the AII items. The adequacy of the sample was confirmed by Kaiser-Meyer-Olkin sampling adequacy analysis, yielding an index of 0.889. The Bartlett measure of sampling adequacy (anti-image correlation matrix) for the 11 items of the AII was highly significant ($\chi^2 = 1065.3$, d.f. = 55, $p < 0.0001$), indicating that the data satisfied the psychometric criteria for the factor analysis to be performed based on data distribution characteristics. Ceiling and floor effects were absent. Exploratory factor analysis revealed a high interrelationship among all of the AII items, showing that all 11 items have to be included in the instrument. The AII scores between the atopic and control groups were significantly different ($p < 0.0001$).

The first 4 items of the AII gave a 100% correct response ("no") in healthy subjects (control group), so those 4 items were confirmed as "decisive" responses ("s") (Table 2). The ROC curve was calculated including the entire group of allergic and nonallergic subjects. Results showed an OR of 0.88, with an area under the curve (AUC) of 0.94, and suggested that a cut-off score of 2.69 was able to accurately identify atopic subjects with a sensitivity value of 0.97 and a specificity of 0.91. The TPV was 0.92, and the FPV was 0.97 (95% CI 0.87–0.97, $p = 0.0001$) (Fig. 1).

Using an Excel datasheet, it was possible to fit a formula in which each of the responses obtained from the newly tested subjects (potentially atopic or healthy) could be singularly multiplied by the regression coefficients, including the intercept. In this proposed formula,

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Table 3. Coefficients for logistic regression

	Coefficients			
	estimate	SE	*z* value	*p* value
Intercept	–3.223400	0.499200	–6.457000	0.000000****
r1	3.195600	0.726000	4.402000	0.000011****
r2	0.339900	0.614300	0.553000	0.580040
r3	1.918600	0.595600	3.222000	0.001270***
r4	1.176000	0.722700	1.627000	0.103680
r5	1.347700	0.682300	1.975000	0.048250**
r6	1.699300	0.632300	2.687000	0.007200***
r7	–0.981100	0.825900	–1.188000	0.234870

** $p < 0.01$. *** $p < 0.001$. **** $p < 0.0001$.

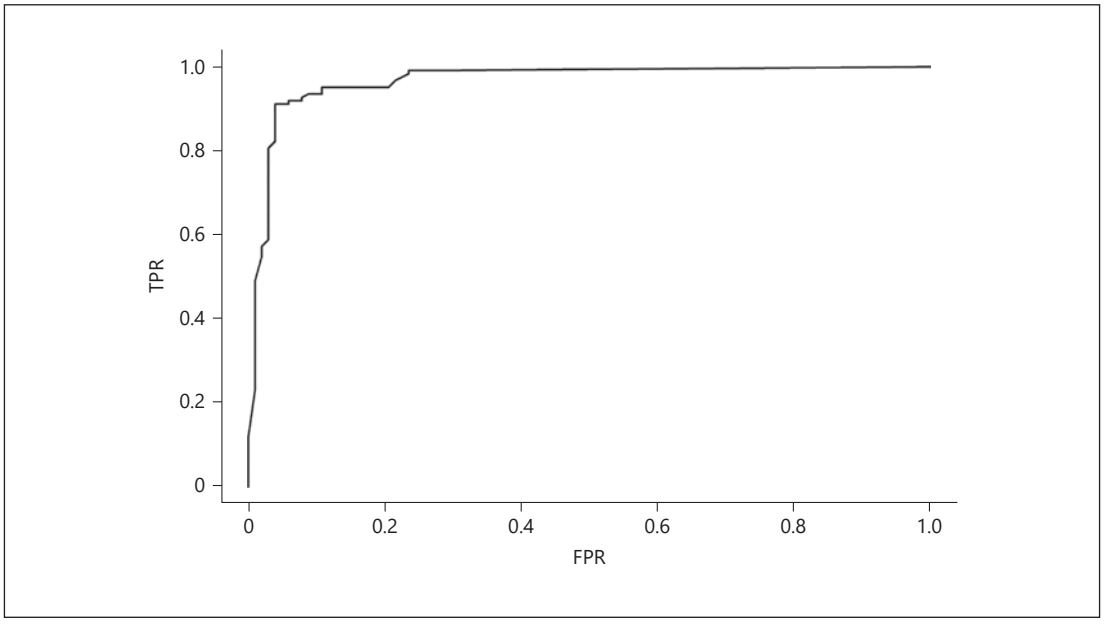

Fig. 1. ROC curve.

the discriminating threshold value became: $Y = \ln (p/(1 - p) = -0.348$, where $Y > 0.348$ identifies the TRUE condition (atopic).

The scores were also recalculated as weighted means, adding the first 4 AII items and weighting all 11 AII items with their accuracy, as reported in Table 2. Logistic regression was carried out with the 7 "probability" items to obtain the regression coefficients and their significance as shown in Table 3. Age and sex did not significantly contribute to any reduction of residual deviance.

A threshold could be established by plotting the Poisson distributions of the responses of atopic and healthy individuals (Fig. 2). Crossing of the 2 plots was confirmed at a value of 2.69, which was selected as the cut-off point, providing a 94% probability of correctly identifying a patient with an atopic condition.

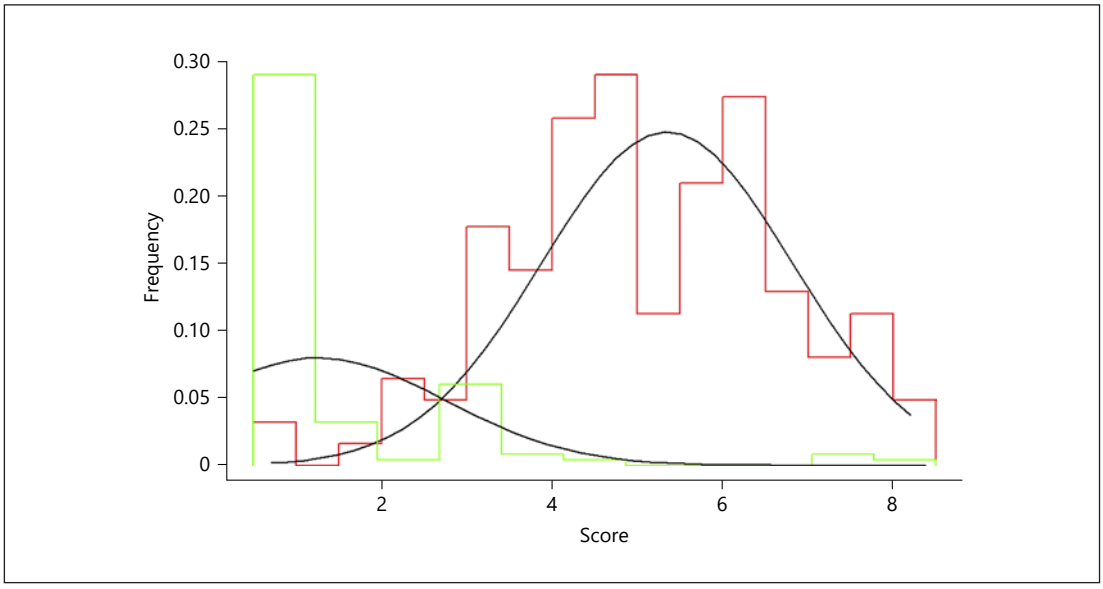

Fig. 2. Plot of the responses calculated by multiplying the binary responses of the 11 variables by their accuracies; separated histograms and fitted Poisson distributions are plotted (red, atopic; green, healthy controls).

Discussion

The impact of atopy on several ENT disorders has not been fully clarified so far, and therefore an easy and rapid inventory that could expedite the assessment of potentially allergic patients and reduce the referral rate to immunoallergologists is highly desirable.

The results showed strong internal consistency and clinical and external validity. Summarizing the results of the statistical analysis, we can conclude that an atopic condition was confirmed if the answer was "yes" to at least one of the decisive questions (s) or to at least 3 probability questions (r), with a high sensitivity and specificity (i.e., 0.97 and 0.91, respectively), a TPV of 0.92, and a FPV of 0.97. A Cronbach α coefficient of 0.88 is generally considered "good" and one greater than 0.9 is deemed "excellent," whereas a value greater than 0.7 is often considered satisfactory. In the present study, the first 4 AII items were able to give a satisfactory test, while the inclusion of at least 1 of the other 7 AII items was able to give a good test, even if the inclusion of all 11 variables gave a result near to excellent ($\alpha = 0.88$).

The strength of this study relies on the unequivocal identification of atopic subjects based on the logistic regression analysis [19]. Furthermore, as far as we know, no other comparable questionnaires are available to act as a "gold standard" to validate the AII. The inventory AII, in fact, differs significantly from the other existing tools as the AII is designed to screen for possibly atopic subjects, while the commonly used questionnaires only allow quantification of the severity of symptoms and monitoring of therapy effects.

Conversely, a limitation of this study is that, with atopy, it is almost impossible to select a control group of unquestionably nonatopic individuals [15] since it is widely accepted that the diagnosis of atopy is complex and it is only confirmed by the expression of atopic symptoms, which might occur later on at any age [23].

The validation analysis allowed us to keep all 11 items, resulting in a questionnaire that could be applied rapidly enough to use for screening. In fact, the data showed that eliminating the questions (r6 and r7) with the lowest accuracy did not provide enough evidence of differences in the results, while causing a significant reduction in sensitivity. We also observed that

item s1 (Do you think you suffer from an allergy or have you received medical treatments for allergies?) had 100% specificity but provided 28% of the false-negative results when asked alone. Even combining the 2 items with the highest accuracy (s1 and r1) resulted in the index not being accurate enough.

Interestingly, the occlusal condition (r1) gave the highest accuracy, OR, and logistic coefficients. While not directly correlated to allergic diseases, the position of the teeth was successfully used to identify the atopic patients in 96% of the cases. The relationship between atopy and tooth position might be explained by the chronic oral breathing in atopic subjects since a low position of the tongue and a narrowing of the palate have been found to be associated with protrusion of the upper incisors [33–36].

As highlighted in the European Academy of Allergy and Clinical Immunology (EAACI) position paper for rhinology in 2011 [19]: "The patients' history is vital in understanding and diagnosing the problem. In rhinitis and rhinosinusitis an accurate history is usually more important than any other investigation."

Our data confirm that atopic patients are easily identifiable when they express the classic symptoms of allergic sensitization (the decisive questions of the AII) but they may be underdiagnosed when their symptoms are related to minimal persistent inflammation of the upper airways due to sensitization to aeroallergens, which is investigated by the probability items. To our knowledge, the AII is the first reliable and simple tool designed specifically for the initial identification of the condition of atopy also in patients accessing the ENT clinic.

Based on the promising results of this study it would be useful and interesting to test the AII in other clinical settings or in more extensive ENT fields in order to select those who should be referred to an immunologist or should be provided an initial symptom-relieving therapy.

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Statement of Ethics

Participation in this study was voluntary for both groups, and the subjects were not compensated. Patients signed a written informed consent form for publication of the results. The research was conducted ethically in accordance with the World Medical Association Declaration of Helsinki of 1975, as revised in 2008; all of the procedures contributing to this work comply with the ethical standards of the relevant national and institutional guidelines on human experimentation and have been approved by the Ethics Committee of the Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico of Milan, Italy (No. 2174-2016). This study also complies with the Standards for Reporting of Diagnostic Accuracy Studies. Written informed consent was obtained from all of the individual participants included in this study.

Conflict of Interest Statement

The authors have no conflict of interests to declare. This paper has not been published elsewhere and it has not been submitted simultaneously for publication elsewhere.

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Author Contributions

Federica Di Berardino and Diego Zanetti conceived and designed this study, directly followed the patients, and wrote this paper. Daniele Monzani and Bruno Rossaro analyzed the data. Giovanna Cantarella and Philippe Dejonckere gave technical and specialist support, and Lorenzo Pignataro reviewed this article.

References

1 Pelikan Z. Role of nasal allergy in chronic secretory otitis media. Curr Allergy Asthma Rep. 2009 Mar;9(2): 107–13.
2 Oh JH, Kim WJ. Interaction Between Allergy and Middle Ear Infection. Curr Allergy Asthma Rep. 2016 Sep; 16(9):66.
3 Martines F, Martines E, Sciacca V, Bentivegna D. Otitis media with effusion with or without atopy: audiological findings on primary school children. Am J Otolaryngol. 2011; 32: 601–606.
4 Cheng X, Sheng H, Ma R, Gao Z, Han Z, Chi F, et al. Allergic rhinitis and allergy are risk factors for otitis media with effusion: A meta-analysis. Allergol Immunopathol (Madr). 2017 Jan - Feb;45(1):25–32.
5 Scadding G. Non-surgical treatment of adenoidal hypertrophy: the role of treating IgE-mediated inflammation. Pediatr Allergy Immunol. 2010 Dec;21(8):1095–106.
6 Di Berardino F, Romagnoli M. Adenoidal hypertrophy and allergic rhinitis. Pediatr Allergy Immunol. 2011 Sep; 22(6):646.
7 Rezende RM, Amato FS, Barbosa AP, Menezes UP, Rezende P, Ferriani VP, et al. Does atopy influence the effectiveness of treatment of adenoid hypertrophy with mometasone furoate? Am J Rhinol Allergy. 2015 Jan-Feb; 29(1):54–6.
8 Schoenwetter WF. Allergic rhinitis: epidemiology and natural history. Allergy Asthma Proc. 2000 Jan-Feb; 21(1):1–6.
9 Sahay S, Gera K, Bhargava SK, Shah A. Occurrence and impact of sinusitis in patients with asthma and/or allergic rhinitis. J Asthma. 2016 Aug;53(6):635–43.
10 Derebery MJ, Berliner KI. Allergy and its relation to Meniere's disease. Otolaryngol Clin North Am. 2010 Oct; 43(5):1047–58.
11 Di Berardino F, Barozzi S, Cesarani A. Allergy and Meniere's disease: a review. Eur Ann Allergy Clin Immunol. 2005 Oct;37(8):299–300.
12 Di Berardino F, Cesarani A. Gluten sensitivity in Meniere's disease. Laryngoscope. 2012 Mar;122(3):700–2.
13 Kravos A, Župevc A, Cizmarevic B, Hocevar-Boltezar I. The role of allergy in the etiology of Reinke's edema on vocal folds. Wien Klin Wochenschr. 2010 May;122(S2 Suppl 2):44–8.
14 Marple BF. Allergic rhinitis and inflammatory airway disease: interactions within the unified airspace. Am J Rhinol Allergy. 2010 Jul-Aug;24(4):249–54.
15 Hoppin JA, Jaramillo R, Salo P, Sandler DP, London SJ, Zeldin DC. Questionnaire predictors of atopy in a US population sample: findings from the National Health and Nutrition Examination Survey, 2005-2006. Am J Epidemiol. 2011 Mar;173(5):544–52.
16 Devenny A, Wassall H, Ninan T, Omran M, Khan SD, Russell G. Respiratory symptoms and atopy in children in Aberdeen: questionnaire studies of a defined school population repeated over 35 years. BMJ. 2004 Aug; 329(7464):489–90.
17 Bousquet J, Schunemann HJ, Fonseca J, Samolinski B, Bachert C, Canonica GW, et al. MACVIA-ARIA Sentinel NetworK for allergic rhinitis (MASK-rhinitis): the new generation guideline implementation. Allergy. 2015 Nov;70(11):1372–92.
18 Samoliński B, Sybilski AJ, Raciborski F, Tomaszewska A, Samel-Kowalik P, Walkiewicz A, et al. Prevalence of rhinitis in Polish population according to the ECAP (Epidemiology of Allergic Disorders in Poland) study. Otolaryngol Pol. 2009 Jul-Aug;63(4):324–30.
19 Scadding G, Hellings P, Alobid I, Bachert C, Fokkens W, van Wijk RG, et al. Diagnostic tools in Rhinology EAACI position paper. Clin Transl Allergy. 2011 Jun;1(1):2.
20 Streiner DL, Norman GR. Health measurement scales: A practical guide to their development and use. Oxford: Oxford University Press; 1995. p. 85–8.
21 Bossuyt PM, Reitsma JB, Bruns DE, et al. STARD Group. STARD 2015: an updated list of essential items for reporting diagnostic accuracy studies. BMJ. 2015;351:h5527.
22 Lieberman P. Validated questionnaire for atopy [cited 2014 February 13]. Available from: http://www.aaaai.org/ask-the-expert/questionnaire-atopy.aspx.
23 Johansson SG, Bieber T, Dahl R, Friedmann PS, Lanier BQ, Lockey RF, et al. Revised nomenclature for allergy for global use: Report of the Nomenclature Review Committee of the World Allergy Organization, October 2003. J Allergy Clin Immunol. 2004 May;113(5):832–6.
24 Zanussi C. Trattato Italiano di allergologia. Selecta Med. 2002;1:410.
25 Johanson SGO. New nomenclature and clinical aspects of allergic disease. In: Pawankar R. et al. (eds) Allergic Frontiers: classifications and pathomechanisms. Springer Eds, Vol. 2. Berlin 2009.

26 Della Torre F, Di Berardino L. Some doubts of the allergist. Eur Ann Allergy Clin Immunol. 2004 Apr;36(4):151–4.
27 Incorvaia C, Frati F, Sensi L, Riario-Sforza GG, Marcucci F. Allergic inflammation and the oral mucosa. Recent Pat Inflamm Allergy Drug Discov. 2007 Feb;1(1):35–8.
28 Di Berardino L, Angrisano A. Comments on BU (biologic units). Allergy. 1997 Jul;52(7):775.
29 Brunetto B, Tinghino R, Braschi MC, Antonicelli L, Pini C, Iacovacci P. Characterization and comparison of commercially available mite extracts for in vivo diagnosis. Allergy. 2010 Feb;65(2):184–90.
30 Di Berardino L, Angrisano A, Gorli L, Cattaneo M, Lodi A. Allergy to house dust and storage mites in children: epidemiologic observations. Ann Allergy. 1987 Aug;59(2):104–6.
31 Wise SK, Lin SY, Toskala E. International consensus statement on allergy and rhinology: allergic rhinitis-executive summary. Int Forum Allergy Rhinol. 2018 Feb;8(2):85–107.
32 Bossuyt PM, Reitsma JB, Bruns DE, Gatsonis CA, Glasziou PP, Irwig L, et al.; STARD Group. STARD 2015: An Updated List of Essential Items for Reporting Diagnostic Accuracy Studies. Clin Chem. 2015 Dec;61(12):1446–52.
33 Grippaudo C, Paolantonio EG, Pantanali F, Antonini G, Deli R. Early orthodontic treatment: a new index to assess the risk of malocclusion in primary dentition. Eur J Paediatr Dent. 2014 Dec;15(4):401–6.
34 Hannuksela A, Väänänen A. Predisposing factors for malocclusion in 7-year-old children with special reference to atopic diseases. Am J Orthod Dentofacial Orthop. 1987 Oct;92(4):299–303.
35 Linder-Aronson S. Adenoids: their effects on mode of breathing and nasal airflow and their relationship to the facial skeleton and dentition. Acta Otolaryngol Suppl. 1970;265:1–132.
36 Rodrigues MM, Passeri LA, Monnazzi MS, Gabrielli MF, Gabrielli MA, Pereira-Filho VA. Evaluation of Nasal Obstruction in Various Sagittal Skeletal Deformity of Jaws. J Craniofac Surg. 2017 Nov;28(8):e790–2.