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Factors contributing to conductance and outcome of specific immunotherapy: Data from the German National Health Interview and Examination Survey 1998

Leif Hommers*, Ute Ellert*, Christa Scheidt-Nave*, Ute Langen*

Background: Allergies are an increasingly relevant public health problem. Specific immunotherapy (sIT) is presently the only causal treatment option. This study aimed to assess the frequency and determinants of sIT use and factors associated with treatment outcome. **Methods:** A cross-sectional analysis based on data from the German National Health Interview and Examination Survey 1998. **Results:** 2727 (39.2%) of study participants reported physician-diagnosed allergic disease. Among these, 16.5% ($n = 296$) stated to have undergone sIT. In this subset 43.4% ($n = 129$) reported improvement of symptoms, 21.9% ($n = 65$) had not changed, and 34.6% ($n = 102$) had discontinued treatment. The majority of patients treated with sIT showed multiple allergic symptoms and sensitisations. Factors significantly correlated with sIT treatment in multivariable analyses included rhinitis, asthma, several sensitisations, higher social status and residence in larger cities. Rhinitis and neurodermatitis were positively, and food allergy was negatively associated with the completion of sIT. No factors predicting improvement due to sIT could retrospectively be identified. **Conclusion:** Treatment with sIT under 'real life' conditions does not exactly follow current clinical guideline recommendations. In addition, patients may be selected for IT by socio-demographic factors. Whether this contributes to considerable discontinuation rates and limited effectiveness as observed here, needs further investigation.

Keywords: allergies, German National Health Interview and Examination Survey 1998, specific immunotherapy

Introduction

Results from epidemiologic studies point towards an increasing prevalence of allergic conditions in western-civilised countries. Germany ranges anywhere in the middle of the other European countries as far as prevalence of allergies is concerned. For example, prevalence estimates for nasal allergies in Germany vary from 13.4 (Erfurt) to 23.0% (Hamburg), whereas in Europe estimates range from 12.1 in Spain (Albacete) to 34.4% in France (Montpellier). For asthma, prevalence estimates in Germany range from 2.1 (Erfurt) to 4.4% (Hamburg), as compared with 2.0 in Estonia (Tartu) to 8.4% in the UK (Cambridge).[1] Prevalence estimates have continuously increased over the last decades. Most recently this was documented for Germany in 1991/92–1998.[2]

Asthma ranges among the chronic conditions with utmost public health impact, due to medical, social and economic sequels.[3] Nevertheless, as documented in the 'Whitebook Allergy in Germany', other allergic conditions, such as allergic rhinitis, also produce high direct, indirect, and intangible costs.

Against this background, primary and secondary prevention concepts, and cost-effective management of patients with allergic diseases are urgently needed. Specific immunotherapy (sIT) is the only causal treatment available so far. The efficacy of sIT has been demonstrated in several randomised controlled studies as documented in a meta analysis by Abramson;[4] main indications include allergic rhinitis, allergic asthma, and insect venom allergy, while contact eczema as a type IV allergy is no indication. Additionally, sIT also seems to prevent the development of asthma among patients suffering from allergic rhinitis.[5] For food allergies avoidance is considered the first choice of treatment. Taken together, sIT has been recommended by numerous international guidelines and position papers[6–8] for the treatment of patients with allergic conditions[6–11] under the following prerequisites: proven IgE-mediated sensitisation (type 1 allergy) and obvious connection between sensitisation and allergic symptoms and availability of standardised or high-quality allergen extracts, proof of efficacy for the planned sIT in the respectively indication, allergen avoidance impossible.

To date, little is known regarding the implementation of guideline recommendations, i.e. the frequency of sIT among eligible patients, and the outcome of sIT under 'real-life' conditions. The current study was undertaken to shed some light on the situation in Germany. Based on data from the 1998 German National Health Survey, we assessed the frequency and determinants of reported sIT use, as well as factors predicting therapeutic outcome in a representative sample of the German adult population.

Methods

Study design and setting

Data from the German National Health Interview and Examination Survey 1998 (NHS98) were used for analysis. Study design, sampling methods, response rates and definition of study characteristics have previously been described in detail.[12] In brief, a representative, regionally stratified random sample of non-institutionalised German adults aged 18–79 years was drawn from population registries. Overall, 61.4% of persons, who were eligible and contactable, participated in the survey. Careful non-response analysis was carried out on

* Department of Epidemiology, Health Monitoring, Robert Koch-Institut, Berlin, Germany

Correspondence: Dr. Ute Langen, Department of Epidemiology, Health Monitoring, Robert Koch-Institut Seestraße 10 D-13353, Berlin, Germany, tel.: +493045473180, fax: +493045473211, e-mail: U.Langen@rki.de

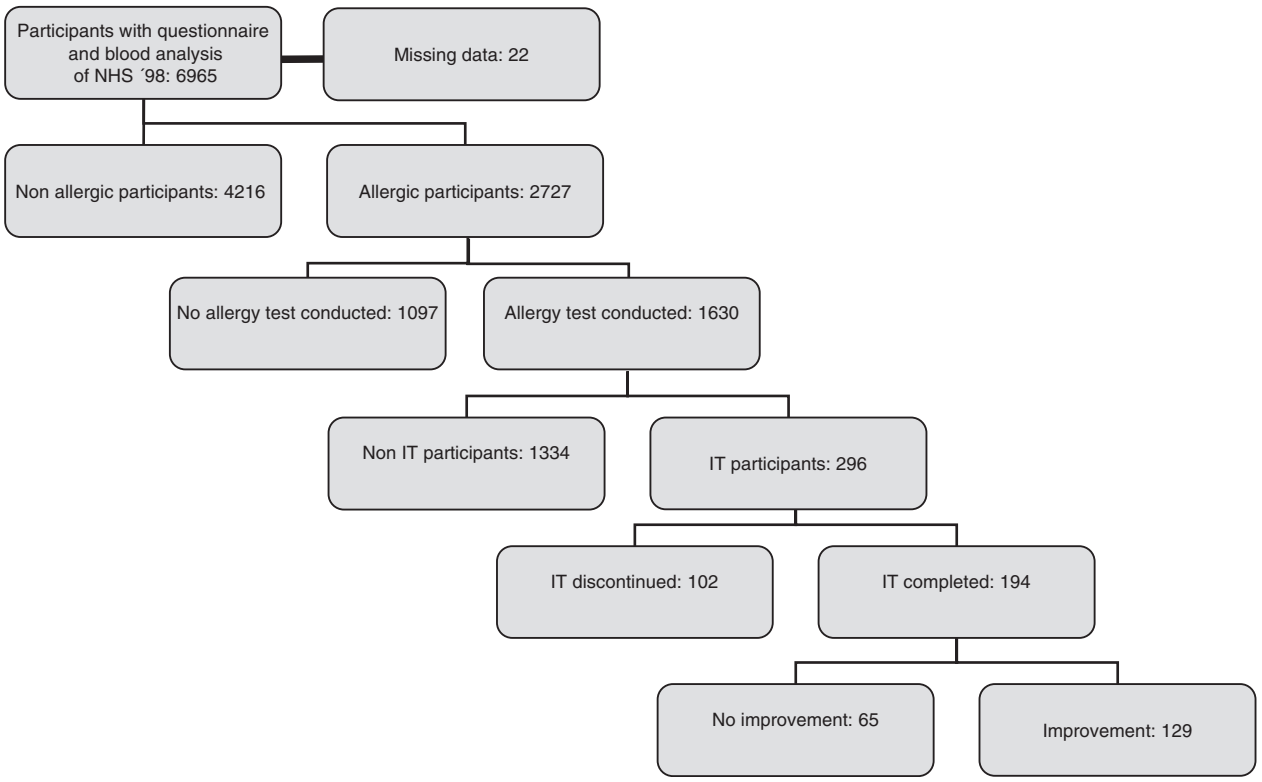

Figure 1 Flow chart of the study population according to the questionnaire structure of the NHS98 (Please note that only persons reporting any allergic condition and the conduction of an allergy test were asked for specific Immunotherapy (sIT) conduction)

the basic information obtained from all but 22.2% of the target population, and weighting factors for 'sex', 'age', 'state', and 'size of town' were calculated, in order to permit the extension of survey data to the German population. If not indicated otherwise, weighted data are presented. The analyses are based on subgroups as shown in figure 1. The study was approved by the Federal data protection officials. Participants were informed in detail about the study goals, interview and examination procedures, as well as, pseudomised data record keeping and analyses. Persons participating in the NHS98 provided written informed consent prior to the interview and examination.

Instruments

Study participants were first asked to complete a self-administered questionnaire covering demographics, education, social status, medical history, and health-related quality of life.[13]

A computer assisted personal interview (CAPI) was then conducted by specifically trained physicians, in order to obtain a detailed medical history. Patients with allergic disease were identified based on the question: 'Have you ever been diagnosed by a doctor with any of the following conditions: ''allergic rhinitis'', ''allergic contact eczema'', ''neurodermatitis'', ''food allergy'', ''urticaria'', and ''other''?' Thus, all these categories were included in the analyses. The age at onset and time of last acute episode were also documented. This information was used to assess the sequence of multiple allergic conditions, i.e. 'onset of at least one allergic condition before allergic rhinitis'.

Persons reporting a medical history of any of the above allergic conditions were asked, whether they had ever undergone allergy testing, and whether test results had revealed a positive sensitisation test against 'pollen', 'animal epithelia', 'mould fungus', 'dust mite', 'food' or 'any other' allergen. They were further asked, whether they had 'ever undergone sIT', 'completed the treatment', and 'whether their condition had improved on completed treatment'.

The wording of the question regarding sIT was 'Desensibilisierung' (desensitisation) which is not the correct term (this would be hyposensitisation, (allergen) immunotherapy, or sIT) but is well known to the patient population and can be expected to result in a good correlation to really having received any kind of sIT.

A medical history of physician-diagnosed bronchial asthma was assessed in a separate question. Persons answering this question affirmatively were not prompted for questions on sIT, unless they also reported a medical history of one or more of the above-mentioned allergic conditions. They were, however, asked whether the doctor's diagnosis had been based on allergy testing, and whether the diagnosis had been specified to 'allergic asthma'. Consistency analysis showed that >94% of asthmatic patients who reported to suffer from allergic asthma also gave the information of suffering from one or more additional allergic conditions.

Study population

Altogether 6965 persons participating in the NHS98 had complete interview data. Among these, 39% ($n = 2727$) reported a medical history of at least one allergic condition (figure 1). Within this subset, 60% ($n = 1630$) stated to have undergone allergy testing and were subsequently asked for having undergone sIT treatment. 296 participants reported a history of sIT resulting in 11% of the allergic population as a whole.

Of those who indicated to have undergone sIT, about one-third ($n = 102$) discontinued treatment. Among those who completed treatment ($n = 194$), two-thirds ($n = 129$) stated to have experienced subjective improvement following sIT.

Table 1 History of allergic disease and sIT treatment among German women and men 18–79 years of age

Characteristic	Women [% (95% CI)] ($N = 3557$)	Men [% (95% CI)] ($N = 3387$)	Population studied [% (95% CI)] ($N = 6965$)
Self-reported medical history of physician-diagnosed allergy (CAPI)			
History of any allergic condition(s)	46.8 (45.2–48.4)	31.3 (29.7–32.9)	39.3 (38.2–40.4)
Single allergic condition	26.7 (25.2–28.2)	20.9 (19.5–22.3)	23.8 (22.8–24.8)
Multiple allergic conditions	20.2 (18.9–21.5)	10.4 (9.4–11.4)	15.3 (14.5–16.1)
All specific allergic conditions covered in the CAPI[a]			
Allergic rhinitis	16.5 (15.3–17.7)	14.6 (13.4–14.8)	15.6 (14.7–16.5)
Allergic contact eczema	21.7 (20.3–23.1)	7.9 (7.0–8.8)	15.0 (14.2–15.8)
Urticaria	10.8 (9.8—11.8)	4.8 (4.1–5.5)	7.9 (7.3–8.5)
Food allergy	7.7 (6.8–8.6)	3.7 (3.1–4.3)	5.7 (5.2–6.2)
Neurodermatitis	4.2 (3.5–4.9)	2.7 (2.2–3.2)	3.5 (3.1–3.9)
Separate CAPI question			
Asthma	6.4 (5.6–7.2)	5.1 (4.4–5.8)	5.7 (5.2–6.2)
As reported by patients with any of the a. m. allergic condition(s)			
Single sensitisation	12.5 (11.4–13.6)	7.3 (6.4–8.2)	9.9 (9.2–10.6)
Multiple sensitisation	10.8 (9.8–11.8)	6.9 (6.0–7.8)	8.9 (8.2–9.6)
Ever received sIT	4.3 (3.6–5.0)	4.3 (3.6–5.0)	4.2 (3.7–4.7)
Received and completed sIT	2.7 (2.2–3.2)	2.8 (2.2–3.4)	2.8 (2.4–3.2)
Improved on completion of sIT	1.7 (1.3–2.1)	2.1 (1.6–2.6)	1.9 (1.6–2.2)

a: It was possible to affirm >1 allergic disease

Statistical analysis

SPPS, version 11.5, was used for statistical analysis. Chi-Squared-tests were used to test for group differences in categorical variables. Multiple logistic regression (MLR) models were fitted to assess independent predictors of sIT conduction, sIT completion, and efficacy among persons with allergic symptoms by using a stepwise forward conditional approach.

Results

Table 1 summarises the observed sex-specific and overall lifetime prevalence of allergic conditions, sensitisations, and sIT among German people. A history of any allergic condition or sensitisation was significantly more prevalent among women; whereas the prevalence of reported sIT did not differ between sexes. The elevated prevalence among women for asthma did not reach statistical significance.

Table 2 presents the distribution of main study characteristics in the study population as well as in the four subsets of study participants defined according to a history of allergic disease and sIT treatment. Compared to the general population, persons with a history of allergic disease were significantly more likely to be women, residents of former West Germany (including West-Berlin) and larger towns or cities, they were also younger and of higher social status. No association with smoking status was observed.

Within the subset of those who had received sIT for allergy treatment, men, younger persons, those of higher social status, and those living in larger towns or cities were over-represented compared to all study participants with a history of allergic disease.

Analysis by social status and age did not reveal a significant effect. Gender-specific analysis showed, that the higher frequency of sIT conduction among men was most pronounced among participants who had never smoked, and were younger, of high social status, from small towns or countryside regions.

Table 3 compares the prevalence of specific types of allergic conditions and sensitisations (overlapping categories) between all persons with a history of allergy and the subsets of persons having received sIT, completed sIT, and subjectively improved on completion of sIT. Among persons who had ever undergone sIT, those with several allergic conditions or multiple sensitisations, and those with asthma, allergic rhinitis, food allergies, and specific sensitisations were significantly over-represented compared with the group of study participants with reported allergies at large. In contrast, allergic contact eczema was under-represented in this group.

We identified a total of 19 persons or a weighted 7% of all persons treated with sIT, who reportedly underwent sIT in the absence of a medical history of asthma or allergic rhinitis. Of these 5 persons reported pollen sensitisation and 13 reported sensitisations against other inhalative allergens as epithelia, dust mite, and mould fungus. Only one person did not report any inhalative sensitisation. Three of these persons reported only allergic contact exzema, two neurodermatitis, and two urticaria. The remaining 12 had multiple allergic diseases. Results in tables 2 and 3 did not basically change when these 19 persons were excluded from analyses.

The mean age gradually decreased from persons with allergic disease to persons with subjective improvement after sIT (data not shown). However, the difference between groups did not reach statistical significance. Gender, social status, and age showed no significant effect.

We calculated a sex-specific multivariate binary logistic regression model using the following social and medical variables (size of town, smoking status, East or West Germany, social status, age, rhinitis, asthma, neurodermatitis,

Table 2 Distribution of main study characteristics in the total population studied and among various subsets of persons with allergic disease and sIT treatment

Characteristic	Total population studied [% (95% CI)] ($N = 6965$)	Persons with allergic disease [% (95% CI)] ($N = 2727$)	Persons with allergic disease ever receiving sIT [% (95% CI)] ($N = 296$)	Persons with allergic disease completing sIT [% (95% CI)] ($N = 195$)	Persons with allergic disease improving on completion of sIT [% (95% CI)] ($N = 129$)
Female	51.2 (50.0–52.4)	61.1 (59.3–62.8)	51.4 (45.7–57.1)	50.5 (43.5–57.5)	54.3 (45.7–62.9)
Male	48.8 (47.6–50.0)	38.9 (37.1–40.7)	48.6 (42.9–54.3)	49.0 (42.0–56.0)	45.7 (37.1–54.3)
≤29 years	18.1 (17.2–19.0)	21.6 (20.1–23.1)	32.1 (26.8–37.4)	29.6 (23.2–36.0)	30.2 (22.3–38.1)
30–39 years	21.9 (20.9–22.9)	26.7 (25.0–28.4)	30.4 (25.2–35.6)	28.6 (22.3–34.9)	31.8 (23.8–39.8)
40–49 years	18.1 (17.2–19.0)	18.3 (16.8–19.8)	16.9 (12.6–21.2)	18.4 (13.0–23.8)	18.6 (11.9–25.3)
≥50 years	41.8 (40.6–43.0)	33.4 (31.6–35.2)	20.6 (16.0–25.2)	22.4 (16.6–28.2)	19.4 (12.6–26.2)
Former East Germany	21.4 (20.4–22.4)	16.4 (15.0–17.8)	14.9 (10.8–19.0)	15.8 (10.7–20.9)	17.1 (10.6–23.6)
Former West Germany	73.9 (72.9–74.9)	79.5 (78.0–81.0)	81.4 (79.7–83.1)	80.6 (75.0–86.2)	79.8 (72.9–86.7)
Low social status	23.0 (22.0–24.0)	18.6 (17.1–20.1)	11.1 (7.5–14.7)	11.7 (7.2–16.2)	14.0 (8.0–20.0)
Medium social status	55.4 (54.2–56.6)	57.9 (56.0–59.8)	56.8 (51.2–62.4)	54.6 (47.6–61.6)	55.0 (46.3–63.7)
High social status	21.6 (20.6–31.3)	23.6 (22.0–25.2)	31.1 (25.8–36.3)	33.2 (26.6–39.8)	31.8 (23.8–39.8)
Countryside	20.5 (19.6–21.4)	18.1 (16.7–19.5)	12.5 (8.7–16.3)	12.2 (7.6–16.8)	10.9 (5.5–16.3)
Small town	21.5 (20.5–22.5)	20.3 (18.8–21.8)	17.9 (13.5–22.3)	19.4 (13.8–25.0)	17.8 (11.2–24.4)
Larger town	27.2 (26.2–28.2)	28.9 (27.2–30.6)	29.7 (24.5–34.9)	28.6 (22.2–34.9)	32.6 (24.5–40.7)
Large city	30.8 (29.7–31.9)	32.7 (30.9–34.5)	40.2 (34.6–45.8)	39.5 (32.6–46.4)	38.8 (30.4–47.2)
Current smoker	32.5 (31.4–33.6)	31.8 (30.1–33.5)	29.4 (24.2–34.6)	26.5 (20.3–32.7)	27.1 (19.4–34.8)
Ex-smoker	21.7 (20.7–22.7)	21.8 (20.3–23.3)	17.9 (13.5–22.3)	17.3 (12.0–22.6)	17.1 (10.6–23.6)
Non-smoker	45.9 (44.7–47.1)	46.3 (44.4–48.2)	52.0 (46.3–57.7)	55.6 (48.6–62.6)	56.6 (48.0–65.2)

food allergy, contact eczema and pollen, epithelial, mould fungus, dust mite, or food sensitisation) to predict 'sIT conduction', 'sIT completion', and 'subjective improvement due to sIT'.

Table 4(a) shows the odds ratios of significant factors in a stepwise forward conditional logistic regression model predicting 'conduction of sIT'. R^2 (Nagelkerkes) using this multivariate model was 35.9% for women and 37.9% for men. The strongest predictors for sIT conduction among women were living in a large city, a high social status, presence of allergic rhinitis and food allergy, and sensitisation against epithelia and pollen. In contrast, presence of allergic contact eczema was a factor negatively associated to conduction of sIT. For men, presence of allergic rhinitis and asthma and sensitisation against dust mite and pollen were the strongest predictors.

Table 4(b) shows the same for 'completion of sIT'. A significant result could only be obtained for women; R^2 (Nagelkerkes) is 12.3%. The strongest predictors for sIT completion among women were presence of allergic rhinitis and neurodermatitis; sensitisation against food was a factor contributing to discontinuation of sIT.

No factors determining the subjective improvement due to sIT was identified.

Discussion

There is mentioning in the 'Whitebook Allergy in Germany'[3] that 250 000 patients per year were starting sIT treatment. Several models for cost-utility analyses were applied, all coming to the conclusion that consequently referring eligible patients to sIT treatment would be cost-effective. However, in lack of population-based data, prevalence estimates applied to the models have been based on clinical studies. To our knowledge, this study represents the first population-based assessment of sIT on a nationwide basis, and specifically provides data on sIT representative to the German general adult population.

On this basis we have been able to show that ~17% of persons reporting one or more allergic conditions had ever undergone sIT, with 43% of these stating subjective improvement on completion of treatment, as opposed to 22% whose condition apparently remained unchanged, and a considerable 35% who discontinued treatment.

Despite the strengths of a population-based data set and large sample size, several methodological limitations have to be kept in mind when interpreting the data. As in any health survey, selective participation and misclassification have to be considered as possible sources of bias in the present study. A comparison of main study characteristics between survey participants and a 16% subset of non-participants did not show any significant differences.[12] However, we cannot exclude that the prevalence of allergic conditions was underestimated in the present analysis, as persons with particularly severe symptoms or acute exacerbations may not have responded to the survey. Misclassification is also possible; as often in survey research, resources did not allow for clinical validation of responses regarding specific medical conditions or treatments. Nevertheless, the observed prevalence rates lend credence to the self-reported information regarding allergic conditions and sensitisations.

There are several deficiencies in the design of the questionnaire that need to be discussed. Respondents reporting a diagnosis of bronchial asthma were not prompted for allergy questions on sensitisation testing and sIT treatment, unless they also reported one or more of the specific allergic conditions

Table 3 Distribution of allergic conditions and time sequence between onset of allergic rhinitis and other allergic conditions among various subsets of persons with allergic disease and sIT treatment

Condition	Persons with allergic disease [% (95% CI)] ($N = 2727$)	Persons with allergic disease ever receiving sIT [% (95% CI)] ($N = 296$)	Persons with allergic disease completing sIT [% (95% CI)] ($N = 196$)	Persons with allergic disease improving on completion of sIT [% (95% CI)] ($N = 129$)
All specific allergic conditions covered in the CAPI[a]				
Allergic rhinitis	40.0 (38.2–41.8)	90.9 (86.7–94.9)	89.8 (85.6–94.0)	89.9 (84.7–95.1)
Allergic contact eczema[b]	38.6 (36.8–40.4)	28.4 (23.3–33.5)	24.0 (18.0–30.0)	25.6 (18.1–33.1)
Urticaria	20.0 (18.5–21.5)	22.3 (17.6–27.0)	23.0 (17.1–28.9)	26.4 (18.8–34.0)
Food allergy	14.7 (13.4–16.0)	28.7 (23.5–33.9)	27.6 (21.3–33.9)	30.2 (22.3–38.1)
Neurodermatitis	8.9 (7.8–10.0)	13.9 (10.0–17.8)	14.3 (9.4–19.2)	14.0 (8.0–20.0)
Number of allergic conditions				
Single allergic condition	81.5 (80.0–83.0)	53.0 (47.3–58.7)	53.6 (46.6–60.6)	51.9 (43.3–60.5)
$\geq$ 2 allergic conditions	18.5 (17.0–20.0)	47.0 (41.3–52.7)	46.4 (39.4–53.4)	48.1 (39.5–56.7)
Second main indication for sIT				
Asthma	11.1 (9.9–12.3)	32.8 (27.5–38.1)	32.7 (26.1–65.4)	31.0 (23.0–39.0)
Time sequence between onset of allergic rhinitis and other allergic conditions				
Other allergic condition present at the onset of rhinitis	13.9 (12.6–15.2)	43.2 (37.6–48.8)	42.3 (35.4–49.2)	45.7 (37.1–54.3)
Other allergic symptom developed after the onset of rhinitis	6.8 (5.9–7.7)	10.1 (6.7–13.5)	9.2 (5.2–13.2)	10.1 (4.9–15.3)
Age at onset of rhinitis (years)	25.5 +– 15.6	19.3 +– 12.6	18.9 +– 12.5	17.9 +– 11.6
Self-reported type of sensitisation (CAPI)				
Pollen sensitisation	27.0 (25.3–28.7)	88.3 (84.6–92.0)	87.1 (82.4–91.8)	87.6 (81.9–93.3)
Epithelial sensitisation	12.4 (11.2–13.6)	40.3 (34.7–45.9)′	38.7 (31.9–45.5)	36.4 (28.1–44.7)
Mould fungus sensitisation	4.9 (4.1–5.7)	15.5 (11.4–19.6)	15.9 (10.8–21.0)	18.6 (11.9–25.3)
Dust mite sensitisation	17.4 (16.0–18.8)	52.9 (47.2–58.6)	51.8 (44.8–58.8)	53.5 (44.9–62.1)
Food sensitisation	8.8 (7.7–9.9)	23.2 (18.4–28.0)	19.5 (14.0–25.0)	20.2 (13.3–27.1)
Number of sensitisations				
Single sensitisation	25.3 (23.7–26.9)	32.1 (26.8–37.4)	36.2 (29.5–42.9)	37.3 (29.0–45.6)
Multiple sensitisation	22.8 (21.3–24.3)	67.2 (61.9–72.5)	62.2 (55.4–69.0)	62.0 (53.6–70.4)

a: It was possible to affirm >1 allergic disease
b: While allergic contact eczema is by no means an indication for sIT treatment, it was one of the five specific allergic conditions participants were prompted for in the CAPI questionnaire with one or more affirmative answers resulting in more detailed questions regarding allergy testing and sIT for allergy treatment. There have been only three patients affirming contact eczema as their only allergy, but all of those three reported sensitisation against ≥1 inhalative allergens

covered in the questionnaire. Results of consistency analyses (94% of asthmatic patients who reported to suffer from allergic asthma were also defined as having allergic disease, based on the allergy filter questions, and were therefore asked for sIT) were, however, reassuring that the described deficiency in the questionnaires did not lead to an unacceptable underestimation of asthmatic patients. Participants with allergies having denied conduction of an allergy test as part of the contingency questions were not further asked for sIT treatment. Consequently, the ultimate frequency of sIT among the German population remains uncertain. Assuming none of those having denied conductance of an allergy test have undergone sIT, 4.2% of the German population have undergone sIT.

Effectiveness of sIT as observed in the present study based on self-reported improvement of symptoms is somewhat less than the 80% efficacy rate in patients with allergic rhinitis and the efficacy rate of nearly reaching 100% in patients with allergies against insect stings (reported in the White-book Allergy in Germany).[3] Since measurement of objective improvement of allergic symptoms was beyond the scope of this study the validity of the variable 'subjective improvement' as reported by the participants remains unclear.

Comparison to international data is difficult, since most studies used clinical parameters to assess efficacy, not effectiveness of sIT. Nevertheless, comparing those persons who successfully finished sIT, the frequency of allergic patients additionally suffering from asthma was almost the same as reported in a meta analysis by Ross *et al.*[14] (62.5% in our study compared with 62.3% in the meta analysis). On the other hand, Vona[15] reported a considerable improvement in

Table 4 Odds ratio (OR), 95% confidence interval (CI) and *P*-value from a multivariate logistic regression analysis for determinants of ever undergoing (a) and completing (b) sIT

Condition	OR women (95% CI)	OR men (95% CI)
(a) Undergoing sIT	$n = 955$	$n = 548$
Place of residence		
Countryside	1	
Small town	1.386 (0.647–2.968)	n. s.
Larger town	1.997 (0.998–3.994)	n. s.
Large city	2.510 (1.290–4.884)	n. s.
Social status		
Low	1	
Medium	2.255 (1.134–4.486)	n. s.
High	2.600 (1.218–5.552)	n. s.
Specific allergic conditions covered in the CAPI[a]		
Rhinitis	3.819 (2.005–7.273)	4.865 (2.367–9.999)
Food allergy	1.571 (1.004–2.459)	n. s.
Contact eczema[b]	0.583 (0.383–0.888)	n. s.
Second main indication for sIT		
Asthma	n. s.	2.698 (1.616–4.502)
Self-reported type of sensitisation (CAPI)		
Dust mite sensitisation	n. s.	3.027 (1.931–4.744)
Epithelial sensitisation	2.081 (1.359–3.186)	n. s.
Pollen sensitisation	4.533 (2.375–8.653)	4.179 (2.233–7.821)
(b) Completion of sIT	$n = 141$	$n = 133$
Specific allergic conditions covered in the CAPI[a]		
Rhinitis	3.148 (1.013–9.779)	
Neurodermatitis	5.325 (1.445–19.621)	
Self-reported type of sensitisation (CAPI)		
Food sensitisations	0.402 (0.184–0.875)	

Explanatory variables in the model include: age, place of residence, former east-versus west Germany, sozial status, smoking status, specific allergic conditions covered in the CAPI interview (allergic rhinitis, allergic contact eczema, urticaria, food allergy and neurodermatitis), asthma and self-reported type of sensitisation (pollen, epithelia, mould fungus, dust mite, or food allergy)
a: It was possible to affirm >1 allergic disease
b: While allergic contact eczema is by no means an indication for sIT treatment, it was one of the five specific allergic conditions participants were prompted for in the CAPI questionnaire, with one or more affirmative answers resulting in more detailed questions regarding allergy testing and sIT for allergy treatment. There have been only three patients affirming contact eczema as their only allergy, but all of those three reported sensitisation against ≥1 inhalative allergens

even 85% of Hungarian patients ($n = 143$) having undergone sIT treatment against dust mite allergy. Our results (54% improvement) did not confirm this level of success among patients with a dust mite allergy on a population basis.

In clinical guidelines allergic rhinitis and asthma are target indications for sIT. In this regard, our observation that allergic rhinitis was found in 90.3% and pollen sensitisation in 88.3% of persons with allergies having undergone sIT, reflects some although not perfect guideline adherence. On the other hand, allergic contact eczema, which is not an indication for sIT at all, was found to be under-represented in the subgroup ever having undergone sIT, but there should not have been any cases at all. We identified a total of 19 persons who reported sIT without a medical history of asthma or rhinitis; however, the vast majority had reported sensitisations ($n = 18$) against inhalative allergens. In this group of patients three reported allergic contact eczema as the only allergic disease. As we had no information whether allergic contact eczema was already present when starting sIT, further evaluation of the appropriateness of sIT or reasons for deviating from guideline recommendations is beyond the scope of the present study.

In univariate analyses, performance of sIT for allergy treatment was significantly associated with multiple versus single sensitisations, as well as with the presence of at least one allergic symptom prior to the onset of allergic rhinitis. These findings suggest, that there is most likely a more severe impact of allergic symptoms on daily life among multi symptomatic and multiple sensitised allergic persons leading to a greater willingness to conduct sIT. The outcome of sIT was independent from the number of allergic symptoms or sensitisations.

Younger people and men were over-represented among persons who had undergone sIT for allergy treatment compared to the entire group of study participants with a medical history of allergic disease, yet age and gender did not remain significant correlates of sIT performance or completion in multiple logistic regression analyses.

Taken together, patients may have been selected for sIT by social factors in order to achieve the highest possible compliance and by symptoms for best possible improvement due to sIT as suggested in national and international sIT guidelines. Alternatively one could consider that patients of higher social status might have consulted their physicians more frequently and that therefore differences in social class are a result of patients self-selection. The higher frequency of younger participants among the sIT group might reflect a trend to intervene as early as possible to prevent disease progression.

Improving completion of sIT would be an effective measure to improve the overall success rate of sIT. Therefore, one major aim of the present study was to identify factors associated with completion versus discontinuation of sIT for allergy treatment. In univariate analysis, the average and median age of onset of asthma, allergic rhinitis and neurodermatitis was lowest among persons who reported successful completion of sIT. In multivariable logistic regression only 'rhinitis' and 'neurodermatitis' were significantly and positively associated with completion of treatment, whereas 'food sensitisations' significantly predicted discontinuation. Whether these findings represent artefacts and whether additional explanatory factors or combination of factors can be identified needs to be investigated in future practice-based studies with more detailed information on the time sequence of conditions and allergy test results.

The observations of the present study refer to the 1998 Health Survey in Germany, and strictly speaking, one would have to interpret the results in the light of guideline recommendations from 1998 or earlier. Recommendations regarding sIT have continually developed with the availability of new allergen preparations and are still developing. Additionally the survey did not distinguish between subcutaneous and sublingual immunotherapy, which at present are recommended with different indications. Changing conditions of the health care system in Germany may also play a role.

In summary, based on population-representative data from the 1998 national health survey, sIT treatment in Germany was found to be conducted in 16.5% of persons with allergic disease, with considerable discontinuation (34,6%) and limited effectiveness based on reported subjective improvement in 43,4%. Most importantly, persons with allergies who reportedly had undergone sIT for allergy treatment had multiple allergic conditions and sensitisations, beyond indications for evidence-based treatment as recommended in current clinical guidelines. Moreover, some socio-demographic factors, such as a higher social status and residence in large cities, were observed to be independently and significantly associated with performance of sIT. This may indicate self-selection due to patient as well as physician factors. We conclude, that sIT for allergy treatment under 'real-life' conditions appears to deviate from current clinical guideline recommendations, and that there is evidence for self-selection of patients regarding treatment decisions. Further practice-based research is needed to evaluate guideline adherence and the effectiveness of treatment, both from the consumer's as well as the provider's perspective. This is all the more true, as guideline recommendations as well as conditions of the health system and medical progress are continuously changing. In this context, the present study serves as a basis for future comparisons.

Key points

- We studied the allergic participants of our latest German population-based health survey, which had undergone sIT.
- We found that one-third of the persons having started sIT did not finish this therapy completely.
- Of those having completed sIT another one-third did not feel that the therapy was effective.
- We have been able to show that the start of sIT therapy depended on age, sex, and social status of the allergic persons.
- It was possible to show that sIT is not exclusively used as recommended in therapy guidelines.

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