

# Nationwide survey on immunotherapy practice by ENT specialists\*

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## Abstract

**Background:** According to the Federal Institution of Health Insurance, ENT doctors perform more skin prick tests for the diagnosis of allergic rhinitis (AR) than other medical specialties in Belgium. However, immunotherapy (IT) is not practiced by all. This study aims to obtain insight into IT practice by ENT doctors, the type of IT performed and the reasons not to perform IT.

**Methodology:** A questionnaire was sent to all registered ENT doctors of Belgium (n = 648), involving questions on type and duration of ENT practice, geography and gender. In addition, the questionnaire informed about diagnosis of AR, indication for IT, type of IT performed, and reasons not to perform IT and referral pattern.

**Results:** The response rate among ENT doctors was 54%, with 7% of responders being excluded as they do not diagnose AR. 81% of Belgian ENT doctors make the indication for IT in AR patients, with 19% neglecting the indication for IT in AR patients. The two main reasons for not indicating IT are lack of expertise and the perception of high costs associated with IT. 70% of ENT specialists are practicing IT themselves, with sublingual IT being mostly performed. Interestingly, IT is mostly frequently performed by those ENT doctors with long-standing ENT practice, in private practice and in Wallonia.

**Conclusion:** Despite the high prevalence of AR in ENT practice, IT is most frequently performed by ENT doctors with longstanding practice, working in private practice and/or in the French speaking part of Belgium. Among the different types of IT, sublingual IT is the most frequently performed means of IT by ENT doctors.

**Key words:** allergic rhinitis, Belgium, ENT, immunotherapy

## Introduction

AR represents a highly prevalent condition in children and adults, significantly affecting the quality of life <sup>(1)</sup>. It is believed that AR plays a pathophysiologic and/or aggravating role in several conditions frequently encountered in ENT practise like otitis media, adenoid hypertrophy, rhinosinusitis, and nasal polyps <sup>(2)</sup>. Therefore, skin prick tests (SPT) are frequently performed by ENT doctors, as they represent the gold standard diagnostic tool for the demonstration of sensitization in patients with symptoms suggestive of AR <sup>(1)</sup>. A survey performed by

the Belgian Federal Institution of Health Insurance (RIZIV) in Belgium in 2009 revealed that most SPTs for inhalant allergens in Belgium are being performed by ENT doctors. As most ENT doctors routinely diagnose AR in their patients, it can be expected that they are fully aware of the therapeutic armamentarium for this chronic condition. There is international consensus about the therapeutic strategy in AR <sup>(1)</sup>, involving 4 cornerstones: information to the patient about the chronicity of the medical condition, evaluation of the feasibility of allergen avoidance, discussion on the different medical treatment options with

pharmacologic therapy and evaluation of the indication for immunotherapy<sup>(3)</sup>. Immunotherapy (IT) for allergic disease involves the administration of increasing amounts of the allergen to which the patient is sensitive, ultimately leading to tolerance. In contrast to medical treatment alleviating symptom severity in AR patients<sup>(4)</sup>, immunotherapy is altering the immune response induced by allergens<sup>(5)</sup>, ultimately leading to the induction of tolerance. Different routes of immunotherapy are available: subcutaneous, sublingual and oral administration of allergens, with each option having its' intrinsic advantages and disadvantages for the patient<sup>(4)</sup>. Meta-analyses have proven long-term efficacy of these different routes of IT<sup>(6)</sup>. There is now growing consensus about IT being indicated in the case of insufficient symptom control in AR by medical treatment and/or dissatisfaction of the patients with medical treatment, occurring in 35% of the patients<sup>(7,8)</sup>.

So far, it is not known to what extent ENT doctors are involved in IT practise in Belgium. This observational study aims at evaluating the percentage of ENT doctors indicating IT, the percentage performing IT, the type of IT performed by ENT doctors, the reasons for not performing IT and referral pattern, in parallel with influencing factors like type of practice, years of ENT experience, gender and geographical differences.

## Materials and methods

### Design, sample and setting

This observational study was conducted between August and December 2011 at the Department of Otorhinolaryngology, Head- and Neck surgery at the University Hospitals of Leuven, Belgium. A self-administrated questionnaire was sent by routine mail to the 648 ENT doctors. Their address was obtained from the Belgian Federal Institution of Health Insurance (RIZIV). The questionnaires were sent along with a short introduction stating the purpose of the study. The specialists were asked to fill out the questionnaire and to send it back to the outpatient ENT clinic of the University Hospitals of Leuven.

Table 1. Profile of ENT doctors studied.

Characteristics	Numbers
Male/ female doctor	146/205
Practice in Flanders/Brussels/Wallonia	160/69/122
Mainly active in Academic Hospital/ General Hospital/ Private Practice	58/227/139
Years of clinical ENT practice: 0-10/11-20/21-30/>30	79/108/102/62

After 4 weeks, the non-responders received a reminder message via ordinary mail.

To prevent any responder bias, 15% of all ENT doctors have been called randomly and was asked the same questions as in the postal questionnaire. The details of the study population can be found in Table 1.

### Questionnaires

The self-report questionnaire used in this study consisted of a total of 10 items and was developed specifically for this study in Dutch and French, being the two official languages of the registered ENT doctors. Based on the geography of the professional address, Dutch questionnaires were sent to Flemish ENT doctors, French to ENT doctors working in Wallonia, and both Dutch and French to doctors in the region of Brussels.

The questionnaire involved the following 4 IT-related yes / no questions (followed by the possible answers):

1. Do you diagnose AR on a regular basis? *Yes/ No.*
2. Do you make the indication for immunotherapy in patients with AR? *Yes/ No.*
3. Do you refer the patient to another doctor for starting immunotherapy? *Yes/ No.*

If yes, to whom? *One option or more: general practitioner, colleague ENT, allergologist, paediatrician, pneumologist, others.*

4. Do you practice immunotherapy yourself? *Yes/ No.*

A/ if yes: a) what type of IT: *subcutaneous, sublingual, oral or transcutaneous.* (One or more options)

b) *How many patients do you treat each year with IT?*

B/ If no:

a) what are the reasons for not indicating subcutaneous IT? (One or more options)

- *I don't have the necessary expertise*
- *difficulties with finding the right indication*
- *too time-consuming for the physician*
- *too expensive for the patient*
- *it takes a long time for any positive result*
- *I am scared for an anaphylactic reaction*
- *difficulties with convincing the patient*
- *efficacy is not proven*
- *others*

b) What are the reasons for not indicating sublingual IT? (*Same options as available in previous question*).

c) What are the reasons for not indicating oral IT? (*Same options as available in previous question*).

In addition to IT specific questions, ENT doctors were asked about the following demographic variables: gender (male/female), year of birth, years of ENT practice (in years), type of hospital (i.e. academic hospital, general hospital or private practice), in which part of Belgium they are mainly working (i.e. Flanders,

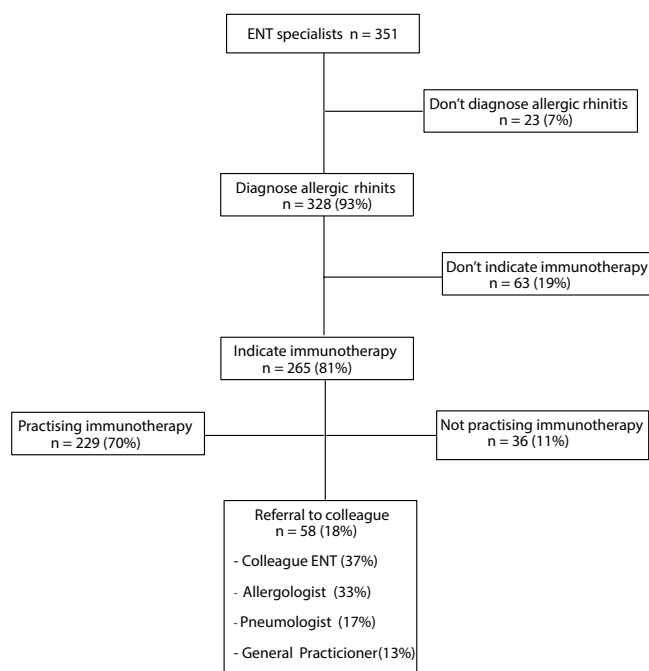


Figure 1. Population of ENT doctors studied in nationwide survey in Belgium on IT practice.

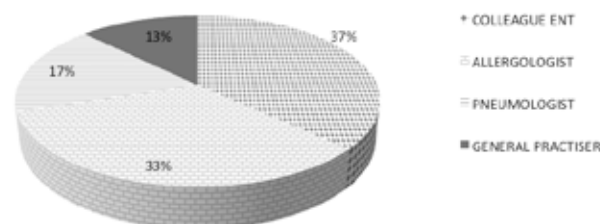


Figure 2. Referral pattern for IT by ENT specialists.

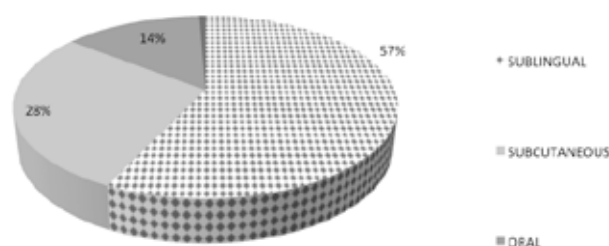


Figure 3. Type of IT performed by ENT specialists.

Brussels, Wallonia) and type of ENT (i.e. general, otolaryngologist, rhinologist, head and neck surgeon).

Every questionnaire received a code, and data were analysed anonymously.

To prevent any bias in responses by responders and non-responders, 15% of all ENT doctors have been called randomly and were asked the same questions as in the postal questionnaire. Because of lack of time of the ENT doctors to answer the questions, only 16 out of 120 questionnaires were answered completely. In addition, only the ENT doctors related to our university hospital were called ( $n = 30$ ).

The questionnaire was approved by the local ethical committee of the University Hospitals in Leuven.

### Statistical analyses

Questionnaires were collected by post. One investigator (MC) checked completeness of the returned questionnaires. All questionnaire responses were verified and registered in computer files. Analyses were performed with the SPSS statistical software package (20.0).

## Results

### Study population

In total, 351 (54%) ENT doctors of Belgium responded to the questionnaire, and their characteristics are listed in Table 1. Seven percent (23/351) of responders were excluded from analysis

as these ENT doctors do not diagnose AR, leaving a total of 328 ENT doctors being studied on IT practice.

To prevent a responder bias, 30 non-responders had been called and were asked the same questions about their IT practice. The responses by phone provided by these so-called non-responders did not differ from the responders, in that also 80% (24/30) of them make the indication for IT. These data have not been taken into account in the analyses.

### IT practice by ENT doctors in Belgium

Nineteen percent (63/328) of the ENT doctors who diagnose AR, do not indicate IT for AR, whereas the majority diagnosing AR indicates IT as therapeutic option (81%, 265/328).

Seventy percent (229/328) of the doctors who diagnose AR are practising IT themselves, whereas 18% (58/328) refer to another physician for IT and 11% (36/328) do not practise IT (Figure 1).

Eighteen percent (58/328) of ENT specialists refer their patient sometimes to another physician for starting with IT. Referring to another ENT colleague (37%) is the most common choice, followed by an allergologist (33%), pneumologist (17%) and general practitioner (13%, Figure 2).

### Type of IT performed by ENT doctors in Belgium

Belgian ENT specialists perform most often sublingual IT (57%, 189/328), followed by subcutaneous (28%, 94/328), oral (14%; 46/328) and transcutaneous IT (1%, 2/328, Figure 3).

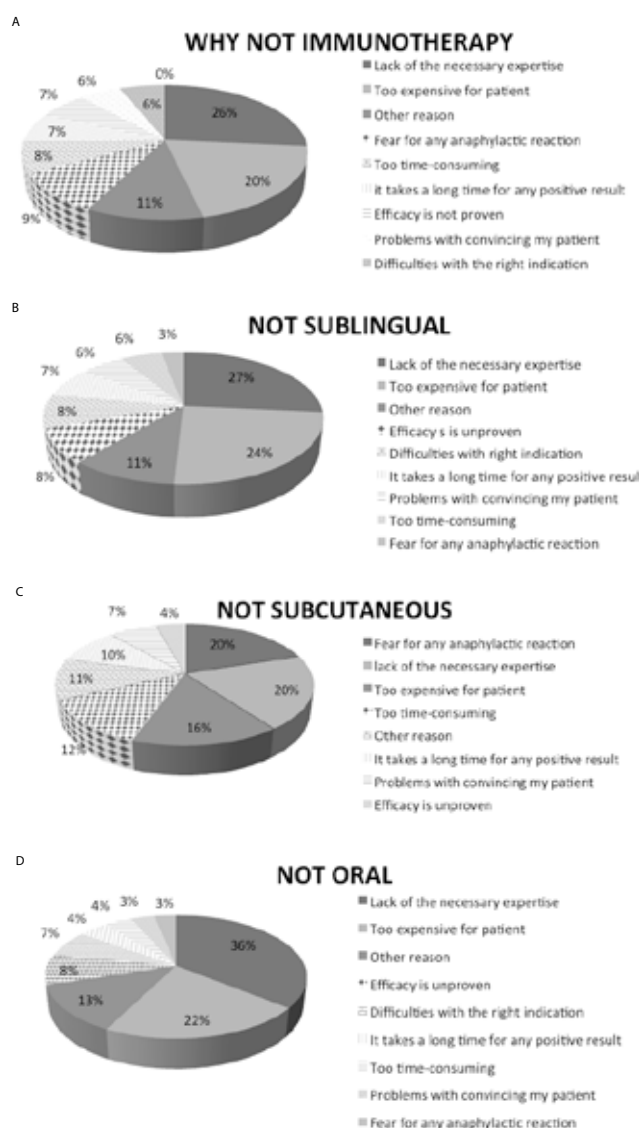


Figure 4. Reasons for not performing IT in general (A), or via sublingual (B), subcutaneous (C) or oral route (D). Please consider omitting titles above each sub-fig, or put: IT in general, sublingual IT, subcutaneous IT, oral IT.

#### Reasons for not starting IT by ENT doctors in Belgium

Lack of the necessary expertise with IT (26%, 92/351) is the main reason for not starting IT by ENT doctors. The second reason is that IT is considered too expensive for the patient (20%, 70/351). Figure 4 provides more detailed information on the different reasons answered by the ENT specialists for not starting IT in general (A) and in relation to sublingual (B), subcutaneous (C) and oral IT (D).

#### Factors influencing IT practice by ENT doctors in Belgium

Upon the evaluation of different factors that may interfere with IT practise by ENT doctors, we found that IT is most frequently performed by ENT doctors in private practice (77% (102/133)),

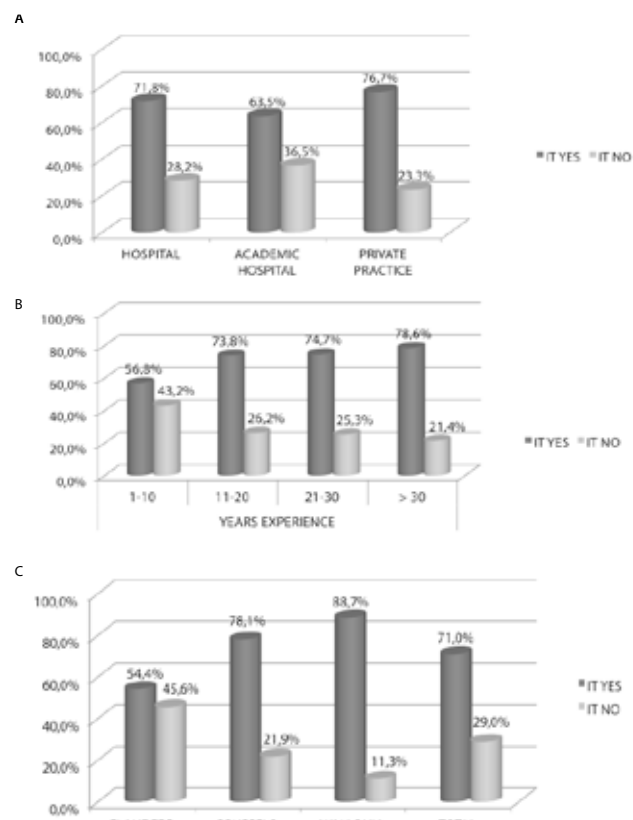


Figure 5. Percentages of ENT doctors performing IT in relation to the type of professional setting (A), years of experience (B) and geography in Belgium (C).

followed by those in general hospitals (72% (155/216)) and academic hospitals (64% (33/52), Figure 5A).

The subsequent factor of influence is the years of clinical ENT practice (Figure 5B). Doctors with more years of experience are practicing IT more frequently in comparison to the younger doctors. Almost 79% (44/56) of ENT specialists who have worked more than 30 years are practicing IT by themselves, in contrast to 57% (42/74) of ENT specialists who worked less than 10 years.

Gender did not interfere with IT performance by ENT doctors as female and male ENT doctors equally performed IT, respectively 73% (101/139) and 70% (132/189).

Interestingly, regional differences were found between the Northern, Central and Southern part of Belgium (Figure 5C). In Flanders (Northern part), 54% (81/149) of ENT specialists are practicing IT compared to 78% (50/64) in Brussels (Central part) and 89% (102/115) in Wallonia (Southern part).

#### Discussion

This study is the first survey to explore IT practice by ENT doctors. We here report that the majority of ENT doctors who

indicate and perform IT mostly perform sublingual IT and show differences in IT practice in relation to the type of ENT practice, duration of ENT practice, and geography. In spite of the large impact of allergic inflammation on general ENT practice <sup>(2)</sup> and the importance of IT as a disease-modifying treatment for AR <sup>(9)</sup>, 20% of ENT doctors do not indicate IT in AR. The most frequently answered reason for not performing IT is the lack of necessary expertise in this area, together with other frequent reasons like costs for the patient, lack of efficacy in polysensitized patients, fear for anaphylactic reactions, the time-consuming nature of IT, and the late onset of efficacy of IT. Most reasons reflect that lack of proper training of a substantial group of ENT doctors in immunotherapy, representing a major challenge for those experts involved in academic and postgraduate training.

In contrast to one fifth of ENT doctors, 80 % of ENT doctors do indicate IT in their patients suffering from AR, and 70% are performing IT themselves. At present, ENT doctors are performing more sublingual IT (SLIT) than subcutaneous IT (SCIT). In spite of the fact that SLIT is not reimbursed by the health insurance in Belgium and hence represents an expensive alternative for SCIT, it takes the lead in IT practise amongst ENT doctors. The fact that SLIT represents the most commonly performed route of IT by ENT doctors is probably related to the fact that SLIT does not imply several additional visits of patients <sup>(10)</sup>, and that no anaphylactic reactions have been reported so far with SLIT <sup>(11,12)</sup>. The fact that several consecutive seasons/years of IT are recommended for full treatment efficacy has given rise to the false belief that the benefits only appear after this long period of treatment. In contrast, studies have shown that clinical benefits start from the first treatment season and even from the first month of treatment <sup>(13-15)</sup>.

Several factors seem to determine to some extent the IT practice of ENT doctors in Belgium. The first factor is the type of ENT practice influencing the frequency of IT practice. Sixty-four percent of the doctors working in an academic hospital are performing IT compared to 72% in a general hospital and 77% in private practice. We may speculate that a different patient-doctor relationship may underlie these differences in practice, and/or different socio-economic implications of patient visits between centers. The duration of ENT practise was positively associated with IT practice. Seventy-nine percent of doctors with more than 30 years of ENT-practice performed IT compared to

57% of those with less than 10 years of ENT practice. The reasons for this observation may be found in the yearlong clinical experience of ENT doctors dealing with chronic upper airway inflammation. Indeed, patients with AR undergoing FESS tend to have a better postoperative outcome when IT had been performed than those undergoing FESS without IT <sup>(16-18)</sup>. Another reason for this observation may be that IT training had been neglected to a large extent during the last decades in the clinical training of ENT specialists. Therefore, young ENT specialists should be encouraged to be trained in IT, as this may help their patients with AR better. The third factor interfering with the frequency of IT was the geographical and linguistic barrier in Belgium, with almost 90% of the French speaking ENT specialists and only 50% of the Flemish speaking ENT specialists performing IT. This difference may be related to the fact that training in IT as well as awareness for the beneficial effects of IT has been higher in the French speaking part of Belgium.

In spite of the high prevalence of AR in daily ENT practice, IT remains a treatment that is not always indicated or performed by ENT doctors. Therefore, optimal patient care in AR can only be obtained when medical doctors diagnosing AR are fully aware of the therapeutic armamentarium and discuss with the patients the different treatment strategies and options. We strongly believe that improving knowledge about medical treatment including immunotherapy amongst ENT doctors will reduce the degree of uncontrolled allergic rhinitis in Belgium.

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## Authorship contribution

MC: study design, questionnaire design, data collection, data analysis, analysis of questionnaires, statistical analysis, telephone survey, literature search, writing manuscript; MJ: data interpretation, correcting manuscript; PR: questionnaire design, data interpretation, correcting manuscript; PWH: study design, questionnaire design, data interpretation, writing manuscript.

## Conflict of interest

All authors state they have no conflict of interest in relation to this study and the results described in the manuscript.

## References

1. Bousquet J, Schünemann HJ, Samolinski B, et al. Allergic rhinitis and its impact on Asthma (ARIA): Achievements in 10 years and future needs. *J Allergy Clin Immunol*. 2012; 130: 1049-1062.
2. Hellings PW, Fokkens WJ. Allergic rhinitis and its impact on otorhinolaryngology. *Allergy*. 2006; 61: 656-664.
3. Kimihiro O, Minoru G. Allergen immunotherapy for allergic rhinitis. *J Nippon Med Sch*. 2010; 77: 285-289.
4. Hellings PW, Fokkens WJ, Akdis C, et al. Uncontrolled allergic rhinitis and chronic rhinosinusitis: where do we stand today? *Allergy* 2013; 68: 1-7.
5. Des Roches A, Paradis L, Menardo J, et al. Immunotherapy with a standardized *Dermatophagoides pteronyssinus* extract. Specific immunotherapy prevents the onset of new sensitizations in children. *J allergy*

- clinImmunol. 1997; 99: 450-453.
6. Dahl R, Kapp A, Colombo G, et al. Sublingual grass allergen tablet immunotherapy provides sustained clinical benefit with progressive immunologic changes over 2 years. *J Allergy Clin Immunol.* 2008; 121: 512.
7. Scadding GK, Richards DH, Price MJ. Patient and physician perspectives on the impact and management of perennial and seasonal allergic rhinitis. *Clin Otolaryngol.* 2000; 25: 551-557.
8. Ciprandi G, Incorvaia C, Scurati S, et al. Patient-related factors in rhinitis and asthma: the satisfaction with allergy treatment survey. *Curr Med Res Opin.* 2011; 27: 1005-1011.
9. Akdis CA. Therapies for allergic inflammation: refining strategies to induce tolerance. *Nat Med.* 2012; 18(5): 736-49.
10. Hsu NM, Reisacher WR. A comparison of attrition rates in patients undergoing sublingual immunotherapy vs subcutaneous immunotherapy. *Int Forum Allergy Rhinol.* 2012; 2: 280-284.
11. Wise SK, Schlosser RJ. Evidence-based practice: sublingual immunotherapy for allergic rhinitis. *Otolaryngol Clin North Am.* 2012; 45: 1045-1054.
12. Mun SJ, Shin JM, Han DH, et al. Efficacy and safety of a once-daily sublingual immunotherapy without escalation regimen in house dust mite-induced allergic rhinitis. *Int Forum Allergy Rhinol.* 2013; 3: 177-183.
13. Didier A, Worm M, Horak F, et al. Sustained 3-year efficacy of pre- and coseasonal 5-grass-pollen sublingual immunotherapy tablets in patients with grass pollen-induced rhinoconjunctivitis. *J Allergy Clin Immunol.* 2011; 128: 559.
14. Passali D, Mösges R, Passali GC, et al. Safety, tolerability and efficacy of sublingual allergoid immunotherapy with three different shortened up-dosing administration schedules. *Acta Otorhinolaryngologica Italica.* 2010; 30: 131-137.
15. Horak F, Ziegelmayer P, Ziegelmayer R, et al. Early onset of action of a 5-grass-pollen 300-IR sublingual immunotherapy tablet evaluated in an allergen challenge chamber. *J Allergy Clin Immunol.* 2009; 124: 471-477.
16. Shangguan C, Wang S, Cai C, Hu Y. Effect of allergy on outcomes after endoscopic sinus surgery in patients with chronic rhinosinusitis. *Lin Chung Er Bi Yan Hou Tou Jing Wai Ke Za Zhi* 2009; 23: 359-363.
17. Guo J, Zhang S, Li X, Luo X. Research on SIT's intervention in NPs after FESS. *Lin Chung Er Bi Yan Hou Tou Jing Wai Ke Za Zhi.* 2010; 24: 406-408.
18. Nishioka GJ, Cook PR, Davis WE, McKinset JP. Immunotherapy in patients undergoing functional endoscopic sinus surgery. *Otolaryngol Head Neck Surg.* 1994; 110: 406-412.

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