# **Position paper**

# EAACI Position Paper on Rhinosinusitis and Nasal Polyps Executive Summary

## W. Fokkens<sup>1</sup>, V. Lund<sup>2</sup>, C. Bachert<sup>3</sup>, P. Clement<sup>4</sup>, P. Helllings<sup>5</sup>, M. Holmstrom<sup>6</sup>, N. Jones<sup>7</sup>, L. Kalogjera<sup>8</sup>, D. Kennedy<sup>9</sup>, M. Kowalski<sup>10</sup>, H. Malmberg<sup>11</sup>, J. Mullol<sup>12</sup>, D. Passali<sup>13</sup>, H. Stammberger<sup>14</sup>, P. Stierna<sup>15</sup>

<sup>1</sup>Chair, Academic Medical Centre, ENT, Amsterdam, the Netherlands, the Netherlands; <sup>2</sup>Co-Chair, University College London, Medical School, Royal National Throat Nose and Ear Hospital, Institute of Laryngology and Otology, London, United Kingdom; <sup>3</sup>Ghent University Hospital, Otorhinolaryngology, Ghent, Belgium; <sup>4</sup>Free University Hospital Brussels, Otorhinolaryngology, Brussels, Belgium; <sup>5</sup>University Hospital Leuven, Otorhinolaryngology, Leuven, Belgium; <sup>6</sup>Uppsala University Hospital, Otorhinolaryngology, Uppsala, Sweden; <sup>7</sup>Queen's Medical Centre, University Hospital, Otorhinolaryngology, Nottingham, United Kingdom; <sup>8</sup>University Hospital Sestre milosrdnice, Otorhinolaryngology, Zagreb, Croatia (Hrvatska); <sup>9</sup>Department of Otorhinolaryngology, Head and Neck Surgery, University Pennsylvania Medical Center, Philadelphia, PA, USA; <sup>10</sup>Department of Clinical Immunology and Allergy, Faculty of Medicine, Medical University, Lodz, Poland; <sup>11</sup>Department of Otorhinolaryngology, University Central Hospital, Helsinki, Finland; <sup>12</sup>Institut d'Investigacions Biomediques August Pi I Sunyer, Barcelona, Spain; <sup>13</sup>Instituto di Discipline Otorinolaringologiche Universita degli Studi di Siena, Sienna, Italy; <sup>14</sup>ENT Department, Karl Franzens University, Graz, Austria; <sup>15</sup>Department of Otorhinolaryngology, Central Hospital, Skovde, Sweden

Key words: clinical protocols; eosinophils; epidemiology; evidence-based medicine; guidelines; immunology; nasal polyps; paranasal sinuses; paranasal sinus diseases; pediatrics; quality-of-life; rhinosinusitis; therapeutics

Wytske Fokkens Academic Medical Centre Department ENT PO Box 22660 1100 DD Amsterdam the Netherlands

Accepted for publication 22 January 2005

# Introduction

Rhinosinusitis is a significant health problem which seems to mirror the increasing frequency of allergic rhinitis and which results in a large financial burden on society (1-3). The last decade has seen the development of a number of guidelines, consensus documents and position papers on the epidemiology, diagnosis and treatment of rhinosinusitis and nasal polyposis (4-6).

Although of considerable assistance, the available consensus documents on chronic rhinosinusitis and nasal polyps do not answer a number of relevant questions that would unify the information and current concepts that exist in epidemiology, diagnosis, treatment and research. To add to this, none of these documents are evidence based.

Evidence-based medicine is an important method of preparing guidelines (7, 8). Moreover, the implementation of guidelines is equally important.

The EP<sup>3</sup>OS document, initiated by the Academy of Allergology and Clinical Immunology (EAACI) and approved by the European Rhinologic Society (ERS), is intended to be state-of-the art for the specialist as well as for the general practitioner:

- to update their knowledge of rhinosinusitis and nasal polyposis;
- to provide an evidence-based documented revision of the diagnostic methods;
- to provide an evidence-based revision of the available treatments;
- to propose a stepwise approach to the management of the disease;
- to propose guidance for definitions and outcome measurements in research in different settings.

This executive summary focuses on definitions, diagnosis and treatment and the relation to allergy and lower airway disease. The whole document is published at the EAACI website (http://www.eaaci.org) and in the Journal Rhinology (Supplement 18, March 2005).

### Definition of rhinosinusitis/nasal polyps

Rhinitis and sinusitis usually coexist and are concurrent in most individuals; thus, the correct terminology is now *rhinosinusitis*.

In 2001 the WHO put together a working group on rhinitis and its impact on asthma (ARIA) (9). In this group rhinitis was classified according to duration and severity. Because rhinitis and sinusitis are so closely linked the definition of CRS/NP in the EPOS document is developed from the ARIA classification of rhinitis and based on symptomatology, duration and severity of disease.

The diagnosis of rhinosinusitis is made by a wide variety of practitioners, including allergologists, otolaryngologists, pulmonologists, primary care physicians and many others. Due to the large differences in technical possibilities to diagnose and treat rhinosinusitis/nasal polyps by various professions, definitions of CRS/NP should be tailored to the individual group.

Clinical definition of rhinosinusitis/nasal polyps

Rhinosinusitis (including nasal polyps) is defined as:

- Inflammation of the nose and the paranasal sinuses characterised by two or more symptoms:
  - blockage/congestion
  - discharge: anterior/post nasal drip
  - facial pain/pressure
  - reduction or loss of smell

and either

- Endoscopic signs:
  - polyps
  - mucopurulent discharge from middle meatus
  - oedema/mucosal obstruction primarily in middle meatus

and/or

- CT changes:
  - mucosal changes within ostiomeatal complex and/ or sinuses

Severity of disease. The disease can be divided into MILD and MODERATE/SEVERE based on total visual analogue scale (VAS) score (0–10 cm): MILD = VAS 0–4, MODERATE/SEVERE = VAS 5–10.

To evaluate the total severity the patient is asked to indicate on a VAS the question:

How troublesome are your symptoms of rhinosinusitis?



*Duration of disease*. The disease can be divided into Acute/Intermittent (<12 weeks with complete resolution of symptoms) and Chronic/Persistent (>12 weeks symptoms with no complete resolution of symptoms).

### **Definition for epidemiology/General Practice**

For epidemiological studies the definition is based on symptomatology without ENT examination or radiology.

Acute/Intermittent Rhinosinusitis is defined as sudden onset of two or more of the symptoms:

- blockage/congestion
- discharge anterior/post nasal drip
- facial pain/pressure
- reduction/loss of smell

for < 12 weeks:

- with symptomfree intervals if the problem is intermittent
- with validation by telephone or interview

Questions on allergic symptoms i.e. sneezing, watery rhinorrhea, nasal itching and itchy watery eyes should be included.

Common cold/viral rhinosinusitis is defined as:

• duration of symptoms for less than 10 days

Acute/Intermittent non-viral rhinosinusitis is defined as:

• increase of symptoms after 5 days or persistent symptoms after 10 days with less than 12 weeks duration

Persistent/Chronic Rhinosinusitis/nasal polyps is defined as:

- nasal congestion/obstruction/blockage with:
  - facial pain/pressure, or
  - discoloured discharge (anterior/posterior-nasal drip), or
  - reduction/loss of smell
- for > 12 weeks
- with validation by telephone or interview.

Questions on allergic symptoms i.e. sneezing, watery rhinorrhea, nasal itching and itchy watery eyes should be included. Also include questions on *intermittent* disease (see definition above).

### **Definition for research**

For research purposes Chronic Rhinosinusitis (CRS) is the major finding and Nasal Polyposis (NP) is considered a subgroup of this entitiy. For the purpose of a study, the differentiation between CRS and NP must be based on out-patient endoscopy. The research definition is based on the presence of polyps and prior surgery.

Definitions when no earlier sinus surgery has been performed

Polyposis bilateral—endoscopically visualised in middle meatus.

Chronic rhinosinusitis bilateral—no visible polyps in middle meatus, if necessary following decongestant.

This definition accepts that there is a spectrum of disease in CRS which includes polypoid change in the sinuses and/or middle meatus but excludes those with polypoid disease presenting in the nasal cavity to avoid overlap.

Definitions when sinus surgery has been performed

Once surgery has altered the anatomy of the lateral wall, the presence of polyps is defined as pedunculated lesions as opposed to cobblestoned mucosa > 6 months after

surgery on endoscopic examination. Any mucosal disease without overt polyps should be regarded as CRS.

### **Rhinosinusitis and Allergy**

Acute rhinosinusitis. Review articles on sinusitis have suggested that atopy predisposes to rhinosinusitis (10). This theory is attractive given the popularity of the concept that disease in the ostiomeatal area contributes to sinus disease in that the mucosa in an individual with allergic rhinitis might be expected to be swollen and more liable to obstruct sinus ostia, reduce ventilation, lead to mucus retention that might be more prone to become infected. Furthermore there has been an increase in the body of opinion that regard the mucosa of the nasal airway as being in a continuum with the paranasal sinuses and hence the term rhinosinusitis (11). The number of studies determining the occurrence of acute rhinosinusitis in patients with and without allergy is very limited.

Savolainen studied the occurrence of allergy in 224 patients with verified acute rhinosinusitis by means of an allergy questionnaire, skin testing, and nasal smears. Allergy was found in 25% of the patients and considered probable in another 6.5%. The corresponding percentages in the control group were 16.5 and 3, respectively. There were no differences between allergic and non-allergic patients in the number of prior acute sinusitis episodes or of previously performed sinus irrigations. Bacteriological and radiological findings did not differ significantly between the groups (12). Alho showed that subjects with allergic IgE-mediated rhinitis had more severe paranasal sinus changes in CT scans than nonallergic subjects during viral colds. These changes indicate impaired sinus functioning and may increase the risk of bacterial sinusitis (13).

In conclusion: although an attractive hypothesis we can repeat the statement made a decade ago, there remain no published prospective reports on the incidence of infective rhinosinusitis in populations with and without clearly defined allergic rhinosinusitis (14).

*Chronic rhinosinusitis*. It has been postulated (15) that swelling of the nasal mucosa in allergic rhinitis at the site of the sinus ostia may compromise ventilation and even obstruct sinus ostia, leading to mucus retention and infection. Furthermore, there has been an increase in the body of opinion that regard the mucosa of the nasal airway as being in a continuum with the paranasal sinuses and hence the term 'rhinosinusitis' was introduced (11). However, critical analysis of the papers linking atopy as a risk factor to infective rhinosinusitis (chronic or acute) reveal that whilst many of the studies suggest a higher prevalence of allergy in patients presenting with symptoms consistent with sinusitis than would be expected in the general population, there may well have been a significant selection process, because the doctors involved often had an interest in allergy (16–21). A number of studies report that markers of atopy are more prevalent in populations with chronic rhinosinusitis. Benninger reported that 54% of outpatients with chronic rhinosinusitis had positive skin prick tests (22). Among CRS patients undergoing sinus surgery, the prevalence of positive skin prick tests ranges from 50 to 84% (12, 23, 24), of which the majority (60%) have multiple sensitivities (24). As far back as 1975, Friedman reported an incidence of atopy in 94% of patients undergoing sphenoethmoidectomies (25).

However, the role of allergy in CRS is questioned by other epidemiologic studies showing no increase in the incidence of infectious rhinosinusitis during the pollen season in pollen-sensitized patients (14). In a small prospective study, no difference in prevalence of purulent rhinosinusitis was found between patients with and without allergic rhinitis (26). Newman et al. reported that whilst 39% of patients with CRS had asthma, raised specific IgE or an eosinophilia, only 25% had true markers to show they were atopic (27). Finally, Emanuel et al. (24)found relatively lower percentages of allergic patients in the group of patients with the most severe sinus disease on CT scan and Iwens et al. (28) reported that the prevalence and extent of sinus mucosa involvement on CT was not determined by the atopic state.

Radiological studies are unhelpful in unravelling the correlation between allergy and rhinosinusitis. High percentages of sinus mucosa abnormalities are found on radiological images of allergic patients, e.g. 60% incidence of abnormalities on CT scans among subjects with ragweed allergy during the season (29). However, one should interpret this data with caution in view of the fact that high percentages of incidental findings are found on radiological images of the sinus mucosa in individuals without nasal complaints, ranging from 24.7% to 49.2% (30–33), that the normal nasal cycle induces cyclical changes in the nasal mucosa volume (34), and that radiological abnormalities contribute minimally to the patient's symptoms (29).

Notwithstanding the lack of hard epidemiologic evidence for a clear causal relationship between allergy and CRS, it is clear that failure to address allergy as a contributing factor to CRS diminishes the probability of success of a surgical intervention (35). Among allergy patients undergoing immunotherapy, those who felt most helped by immunotherapy were the subjects with a history of recurrent rhinosinusitis, and about half of the patients, who had had sinus surgery before, believed that the surgery alone was not sufficient to completely resolve the recurrent episodes of infection (35).

Lower airway involvement in CRS. Recent evidence suggests that allergic inflammation in the upper and lower airways coexist and should be seen as a continuum of inflammation, with inflammation in one part of the airway influencing its counterpart at a distance. The arguments and consequences of this statement are summarized in the ARIA document (9). Rhinosinusitis and lower airway involvement are also frequently associated in the same patients, but their interrelationship is poorly understood.

Studies on radiographic abnormalities of the sinuses in asthmatic patients have shown high prevalences of abnormal sinus mucosa (36, 37). All patients with steroid dependant asthma had abnormal mucosal changes on CT compared to 88% with mild to moderate asthma (38). Again caution should be exercised in the interpretation of these studies. Radiographically detected sinus abnormalities in sensitized patients may reflect inflammation related to the allergic state rather than to sinus infection.

# Diagnosis

Assessment of rhinosinusitis symptoms

Subjective assessment of rhinosinusitis is based on symptoms:

- nasal blockage, congestion or stuffiness
- nasal discharge or postnasal drip, often mucopurulent
- facial pain or pressure, headache
- reduction/loss of smell

Besides these local symptoms, there are distant and general symptoms. Distant symptoms are pharyngeal, laryngeal and tracheal irritation causing sore throat, dysphonia and cough, whereas general symptoms include drowsiness, malaise and fever. Individual variations of these general symptom patterns are many (39–44).

The symptoms are principally the same in intermittent and persistent rhinosinusitis as well as in nasal polyposis, but the symptom pattern and intensity may vary. Acute forms of infections, both acute intermittent and acute exacerbations in persistent, have usually more distinct and often more severe symptoms.

Simple nasal polyps may cause constant non-periodic nasal blockage, which can have a valve-like sensation allowing better airflow in only one direction. Nasal polyps may cause nasal congestion, which can be a feeling of pressure and fullness in the nose and paranasal cavities. This is typical for ethmoidal polyposis, which in severe cases can cause widening of the nasal and paranasal cavities demonstrated radiologically and in extreme cases, hyperteliorism. Disorders of smell are more prevalent in patients with nasal polyps than in other chronic rhinosinusitis patients (45).

*Validation of subjective symptoms assessment.* Validation of the rhinosinusitis symptoms to show the relevance in distinguishing disease modalities and repeatability between ratings of the same patient (intrapatient) and between different patients (interpatient) have been done. Lately, more specific and validated subjective symptom scoring

tools have become available with the development of quality of life (QoL) evaluations. These are either assess general health evaluating (46, 47) or are disease specific (48, 49).

Overall rating of rhinosinusitis severity can be obtained as such or by total symptoms scores, which are summed scores of the individual symptoms scores. These are both commonly used, but according to an old validation study for measuring the severity of rhinitis, scores indicating the course of individual symptoms should not be combined into a summed score, rather the patient's overall rating of the condition should be used (50). QoL methods have produced validated questionnaires which measure the impact of overall rhinosinusitis symptoms on everyday life (48).

### Examination

Anterior rhinoscopy. Anterior rhinoscopy alone is inadequate, but remains the first step in examining a patient with these diseases.

*Endoscopy*. This may be performed without and with decongestion and semi-quantitative scores (41) for polyps, oedema, discharge, crusting and scarring (post-operatively) can be obtained. A number of staging systems for polyps have been proposed (51–53). Johansson showed good correlation between a 0-3 scoring system and their own system in which they estimated the percentage projection of polyps from the lateral wall and the percentage of the nasal cavity volume occupied by polyps. However, they did not find a correlation between size of polyps and symptoms. (Level III).

*Nasal cytology, biopsy and microbiology*. A positive nasal smear may be helpful in indicating the aetiology of disease (54, 55) but a negative smear is not conclusive. The advantage of the technique is its cheapness. However, quantification and changes as a result of therapy in chronic rhinosinusitis/nasal polyposis have not been routinely used.

A biopsy may be indicated to exclude more sinister and severe conditions such as neoplasia and the vasculitides.

Several microbiology studies (56–59) [Evidence Level IIb] have shown a reasonable correlation between specimens taken from the middle meatus under endoscopic control and proof puncture leading to the possibility of microbiological confirmation of both the pathogen and its response to therapy (56–60).

### Imaging

*Plain sinus x-rays.* Plain sinus x-rays are insensitive and of limited usefulness for the diagnosis of rhinosinusitis due to the number of false positive and negative results (61–63).

*Transillumination*. Transillumination was advocated in the 1970 as an inexpensive and efficacious screening modality for sinus pathology (64). The insensitivity and

unspecificity makes it unreliable for the diagnosis of rhinosinusitis (65).

*CT* scanning. CT scanning is the imaging modality of choice confirming the extent of pathology and the anatomy. However, it should not be regarded as the primary step in the diagnosis of the condition but rather corroborates history and endoscopic examination after failure of medical therapy.

A range of staging systems based on CT scanning have been described using stages 0–4 and of varying complexity (27, 51, 66–70). However, the correlation between CT findings and symptom scores has been shown to be consistently poor and is not a good indicator of outcome (71) [Evidence Level IIb]. In addition for ethical reasons a CT scan is generally only performed post-operatively when there are persistent problems and therefore CT staging or scoring can only be considered as an inclusion criterion for studies and not as an outcome assessment.

The Lund-Mackay system relies on a score of 0-2 dependent upon the absence, partial or complete opacification of each sinus system and of the ostiomeatal complex, deriving a maximum score of 12 per side (51).

This has been validated in several studies (72) [Evidence Level IIb] and was adopted by the Rhinosinusitis Task Force Committee of the American Academy of Otolaryngology Head and Neck Surgery in 1996 (6).

*MRI*. MRI is not the primary imaging modality in chronic rhinosinusitis and is usually reserved in combination with CT for the investigation of more serious conditions such as neoplasia.

### Quality of Life

During the last decade more attention has been paid to not only symptoms but also to patient's quality of life (QoL) (49). However, it is of interest that the severity of nasal symptoms do not always correlate with QoL scales (73) [Evidence Level IIb]. The QOL questionnaires can provide either general (generic) or disease specific health assessment.

*General health status instruments.* Generic measurements enable the comparison of patients suffering from chronic rhinosinusitis with other patient groups. Of these the Medical Outcomes Study Short Form 36 (SF36) (46) is by far the most widely used and well validated and this has been used both pre- and post-operatively in chronic rhinosinusitis. (74, 75) [Evidence Level IIa,IIb].

In a generic SF-36 survey the scores of chronic rhinosinusitis patients were compared to those of a healthy population. The results showed statistically significant differences in seven of eight domains (76). Gliklich and Metson (77) have reported that patients with chronic rhinosinusitis have more bodily pain and worse social functioning than for example patients with chronic obstructive pulmonary disease, congestive heart failure, or back pain.

Winstead and Barrett (75) confirmed a similar degree of impact on general quality of life in chronic rhinosinusitis with the SF-36. Following endoscopic sinus surgery they demonstrated a return to normality in all eight domains six months post-operatively which was maintained at twelve months.

Radenne et al. have studied the QoL of nasal polyposis patients using a generic SF-36 questionnaire (73). Polyposis impaired the QoL more than for example perennial rhinitis. Treatment significantly improved the symptoms and the QoL of the polyposis patients. FESS surgery on asthmatic patients with massive nasal polyposis improved nasal breathing and QoL, and also the use of asthma medications was significantly reduced (78).

Disease specific health status instruments. Several disease specific questionnaires for evaluation of quality of life in chronic rhinosinusitis have been published. In these questionnaires specific symptoms for rhinosinusitis are included. Such areas include headache, facial pain or pressure, nasal discharge or postnasal drip, and nasal congestion.

*Rhinosinusitis outcome measure (RSOM)*. This contains 31 items classified into 7 domains and takes approximately 20 minutes to complete (79). Modifications of this test are the Sinonasal Outcome Test 20 (SNOT 20) which is validated and easy to use (80) and has been used in a number of studies both medical and surgical (71, 74) [Evidence Levels Ib, IIb]; the Sinonasal Outcome Test 16 (SNOT 16) (81) and the 11 point Sinonasal Assessment Questionnaire (SNAQ-11) (82).

In a recent randomised study of patients with chronic rhinosinusitis/nasal polyposis, treatment was either endoscopic sinus surgery or three months of a macrolide antibiotic such as erythromycin (74). Patients were followed up at 3, 6, 9 and 12 months with a variety of parameters including visual analogue scores of nasal symptoms, SNOT 20, SF-36, nitric oxide measurements of upper and lower respiratory tract expired air, acoustic rhinometry, saccharine clearance test and nasal endoscopy. The study showed that there had been improvement in all subjective and objective parameters (P < 0.01) but there was no difference between the medical and surgical groups except that total nasal volume as measured by acoustic rhinometry was greater in the surgical group. This study shows the usefulness of objective measurement in confirming subjective impressions (Evidence Level 1b).

*Chronic Sinusitis Survey (CSS)*. This is a 6 item duration based monitor of sinusitis specific outcomes which has both systemic and medication-based sections (83). In common with other questionnaires, it is rather better at determining

the relative impact of chronic rhinosinusitis compared to other diseases than as a measure of improvement following therapeutic intervention but can be a useful tool (49, 84) [Evidence Level IIb].

Mean scores one year after endoscopic frontal sinus surgery showed a significant improvement in symptoms of pain, congestion, and drainage as measured by the Chronic Sinusitis Survey. Medication use was also significantly reduced (85).

Other disease specific tests are the Rhinosinusitis Disability Index (RSDI) (48, 86), the Chronic Rhinosinusitis Type Specific Questionnaire (87) and the Rhinitis Symptom Utility Index (RSUI) (88).

The well known Rhinoconjunctivitis quality of life questionnaire (RQLQ) focuses on allergy and is of less relevance in chronic rhinosinusitis and nasal polyposis (89).

*General.* Most questionnaires concentrate on the duration of the symptoms and not on the severity of the symptoms. A QoL questionnaire developed by Damm et al includes the severity of the symptom scale (43). The domains in the questionnaire are the overall quality of life, nasal breathing obstruction, post-nasal drip or discharge, dry mucosa, smell, headache and asthmatic complaints.

# Evidence based schemes for diagnostic and treatment

### Introduction

The following schemes for diagnosis and treatment are the result of a critical evaluation of the available evidence.

#### Table 1. Therapy in acute/intermittent rhinosinusitis

Therapy	Level	Grade of recommendation	Relevance
antibiotic (90).	1a (49 studies)	А	yes: after 5 days, or in
topical steroid	1b (1 study not yet published)	В	severe cases yes
addition of topical steroid to antibiotic (91–94)	lb	А	yes
oral steroid (95, 96)	no evidence (1 study +, one –)	D	no
addition of oral antihistamine in allergic patients (97)	2b	В	no
nasal saline douche (98, 99)	no evidence	D	no
decongestion (100-102)	no evidence	D	yes as symtomatic relief
mucolytics (103, 104)	no evidence	D	no
bacterial lysates (105, 106)	2b	В	no
phytotherapy (107, 108)	2b	В	no

Table 2. Therapy in chronic rhinosinusitis\*

Therapy	Level	Grade of recommendation	Relevance
oral antibiotic therapy short term <2 weeks (109–113)	III	С	no
oral antibiotic therapy long term ~12 weeks (74, 114–118)	III	С	yes
antibiotics – topical (119, 120–123).	III	D	no
steroid - topical (122, 124-127)	lb	А	yes
steroid – oral	IV	D	no
nasal saline douche (128–131)	III no data on single use	С	yes, for symptomatic relief
decongestant oral/topical	no data on single use	D	no
mucolytics (132)	III	С	no
antimycotics - systemic	no data	D	no
antimycotics - topical (133-135)	lb (—)	D	no
oral antihistamine added in allergic patients	no data	D	no
allergen avoidance in allergic patients	IV	D	yes
proton pump inhibitors (136-138)	Ш	С	no
bacterial Lysates (139)	2b	С	no
immunotherapy	no data	D	no
phytotherapy	no data	D	no

\*Some of these studies also included patients with nasal polyposis in addition to CRS.

\*Acute exacerbations of CRS should be treated like acute rhinosinusitis.

Table 3. Postoperative treatment in chronic rhinosinusitis\*

Therapy	Level	Grade of recommendation	Relevance
oral antibiotics short term <2 weeks (112, 140–142)	IV	D	immediately post-operative, if pus was seen during operation
oral antibiotics long term $\sim$ 12 weeks (114–117)	111	С	yes
topical steroids (143)	1b (negative)	D	yes: immediately post-operative no: long term therapy
oral steroids	no data available	D	yes: immediately post-operative no: long term therapy
nasal douche	no data available	D	yes: immediately post-operative no: long term therapy

\*Some of these studies also included patients with nasal polyposis in addition to CRS.

Tables 1–5 give the level of evidence and grade of recommendation for the available therapy. Under relevance it is indicated whether the group of authors think this treatment to be of relevance in the indicated disease.

Table 4. The	erapy in	nasal	polyposis
--------------	----------	-------	-----------

Therapy	Level	Grade of recommendation	Relevance
oral antibiotics short	no data	D	no
term <2 weeks	available		
oral antibiotic long	III	С	yes
term $\sim$ 12 weeks (74, 118)			
topical antibiotics	no data available		no
topical steroids (144-146)	l b (>10)	А	yes
oral steroids (147–150)	III	С	yes
nasal douche	III no data	D	yes for
	in single use		symptomatic
			relief
decongestant topical/oral	no data	D	no
	in single use		
mucolytics	no data	D	no
antimycotics – systemic	no data	D	no
antimycotics -	III (2)	D	no
topical (151, 152)			
oral antihistamine in	lb (1)	В	no
allergic patients (153)			
capsaicin (154–156)	II	В	
proton pump inhibitors (157)	II	С	no
immunotherapy	no data	D	no
phytotherapy	no data	D	no

Table 5. Postoperative care in nasal polyposis\*

Therapy	Level	Grade of recommendation	Relevance
oral antibiotic short term <2 weeks	no data available	D	immediately postoperative, if pus was seen during operation
oral antibiotic long term $\sim$ 12 weeks (74)	Ш	С	yes
topical antibiotics	no data available	D	no
topical steroid after polypectomy (158–162)	lb	А	yes
topical steroid after FESS (143)	lb (negative)	D	yes
oral steroid (163)	III	С	short time in high dose long time low dose
nasal douche	no data available	D	yes, for immediate
use no for long time use decongestant – topical/oral	no data available	D	no

### Evidence based diagnosis and management scheme for GPs

Scheme for GP for adults with acute/intermittent rhinosinusitis

*Diagnosis*. Symptoms:

• facial pain or headache (for adults) especially unilaterally, plus one or more of the following

### Fokkens et al.

- nasal obstruction
- smell disturbance

## Treatment:

- mild: start with symptomatic relief, analgesics
- moderate/severe: additional topical steroids

Failure of treatment for moderate/severe disease:

- persistence of symptoms after 5 days of therapy
- or increasing symptoms for 2 days during therapy

Recheck the diagnosis and, if necessary, refer to an ENT-surgeon.

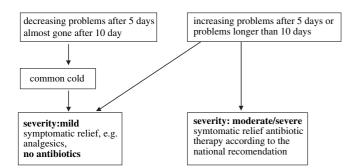


Figure 1. Treatment scheme for GP to use with adults with acute intermittent rhinosinusitis.

Signs of potential complications requiring immediate referral:

- eye swollen/red eyelids;
- displaced globe;
- double vision;
- ophthalmoplegia
- unable to test vision
- reduced vision acuity;
- severe unilateral or bilateral frontal headache;
- frontal swelling;
- signs of meningitis or focal neurologic signs.

Scheme for GP for CRS/NP in adults

### Diagnosis.

Symptoms present longer than 12 weeks:

- nasal obstruction; plus one or more additional symptom;
  - discoloured discharge
  - frontal pain, headache
  - smell disturbance

Additional diagnostic information:

• questionnaire for allergy should be added and, if positive, allergy testing should be performed.

Not recommended: plain x-ray.

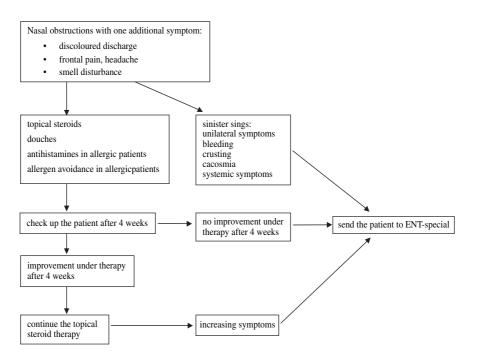


Figure 2. Treatment scheme for GP: therapy for CRS/NP in adults.

CT-scan is also not recommended unless additional problems such as:

- very severe disease
- immuncompromised patient
- signs of complications
- operation recommended

Severity of symptoms:

• (following the VAS score for the total severity) mild/ moderate/severe.

Signs of potential complications requiring immediate referral:

- swelling of eye or lids/eye redness
- displaced globe
- double vision
- reduced vision
- severe unilateral frontal headache
- frontal swelling
- signs of meningitis or focal neurologic signs

### Therapy:

- topical steroids
- nasal douches
- antihistamines in allergic patients
- allergen avoidance in allergic patients

# Evidence based diagnosis and management scheme for Non-ENT specialist for adults with CRS/NP

Diagnosis

Symptoms present longer than 12 weeks:

- nasal obstruction; plus one or more additional symptom:
  - discoloured discharge
  - frontal pain, headache
  - smell disturbance

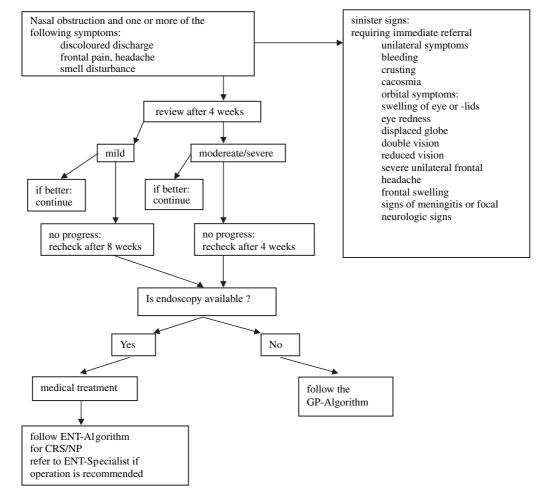


Figure 3. Treatment scheme for Non-ENT specialists: therapy for CRS/NP in adults.

### Fokkens et al.

Additional diagnostic information:

- anterior rhinoscopy, inspection with otoscope or ideally nasal endoscopy (if available)
- review primary care physician's diagnosis and treatment
- questionnaire for allergy should be added and, if positive, allergy testing should be performed, if it is not done yet

Not recommended: plain x-ray.

CT-scan is also not recommended unless additional problems such as:

- very severe disease
- immuncompromised patients
- signs for complications

Severity of symptoms:

• (following the VAS score for the total severity) mild/ moderate/severe.

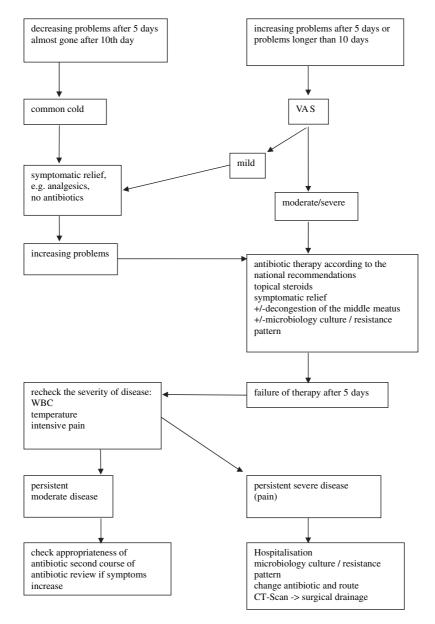


Figure 4. Treatment scheme for ENT-specialists for adults with acute rhinosinusitis.

# Treatment:

- topical steroids;
- nasal douches;
- antihistamines and allergen avoidance in allergic patients.

# Evidence based diagnosis and management scheme for ENT specialists

Scheme for ENT-Specialist for adults with acute rhinosinusitis

# Diagnosis.

Symptoms:

- facial pain (for adults) especially unilaterally; plus one or more of the following symptoms
- nasal obstruction
- smell disturbance
- nasal discharge

### Signs:

- nasal examination (swelling, redness, pus)
- oral examination: posterior discharge
- exclude dental infection
- ENT-examination including nasal endoscopy

Not recommended: plain x-ray.

CT-scan is also not recommended unless additional problems such as:

- very severe diseases,
- immuncompromised patients;
- signs for complications.

Severity of symptoms:

• mild/moderate/severe.

### Treatment:

Initial treatment depending on the severity of the disease:

- VAS: mild  $\rightarrow$  follow initial treatment for common cold
- moderate → follow initial treatment for common cold with short follow up
- severe  $\rightarrow$  follow initial treatment as listed below:

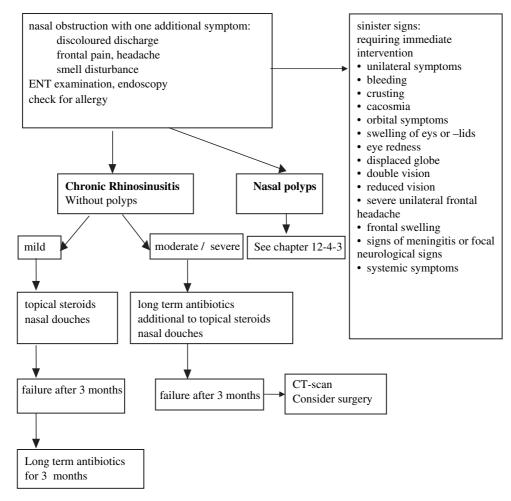
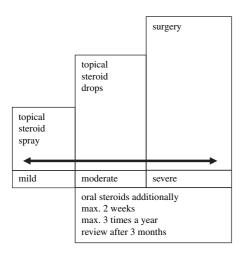


Figure 5. Treatment scheme for ENT-Specialists for adults with CRS.



*Figure 6.* Use of corticosteriod treatment for adults with nasal polyposis.

Signs of potential complications requiring immediate intervention:

- eye swollen/red eye or lids
- displaced globe
- double vision
- ophthalmoplegia
- unable to test vision
- reduced vision
- severe unilateral frontal headache
- frontal swelling
- signs of meningitis or focal neurologic signs

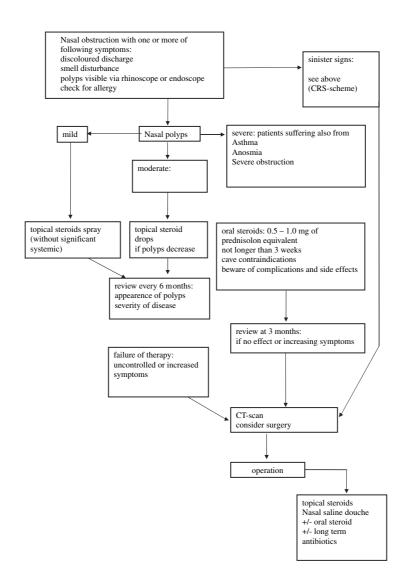


Figure 7. Treatment scheme for ENT-Specialists for adults with nasal polyps.

Scheme for ENT-Specialists for adults with CRS

Diagnosis.

Symptoms present longer than 12 weeks:

- nasal obstruction; plus one or more of the following symptoms:
  - discoloured discharge
  - frontal pain, headache
  - smell disturbance

# Sign:

- ENT examination, endoscopy
- review primary care physician's diagnosis and treatment
- questionnaire for allergy and if positive, allergy testing if it has not already been done

# Severity of the symptoms:

• (following the VAS score for the total severity) mild/ moderate/severe.

# Treatment:

- topical steroids;
- douches;
- antihistamines in allergic patients;
- allergen avoidance in allergic patients.

# Scheme for ENT-Specialists for adults with NP

### Diagnosis.

Symptoms for longer than 12 weeks:

- nasal obstruction; plus one or more of the following symptoms
- discolourered discharge
- frontal pain
- smell disturbance

Sign:

- ENT examination, endoscopy;
- review primary care physician's diagnosis and treatment;
- questionnaire for allergy and if positive, allergy testing if not already done.

### Severity of the symptoms:

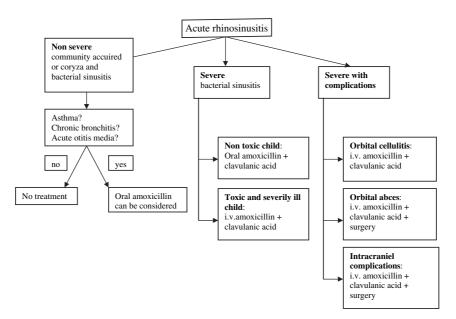
• (following the VAS score for the total severity) mild/ moderate/severe.

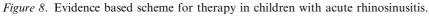
### Treatment:

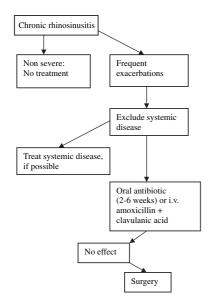
- topical steroids (drops preferred);
- nasal douches;
- antihistamines in allergic patients;
- allergen avoidance in allergic patients.

### Evidence based schemes for therapy in children

The following schemes should help different disciplines in the treatment of rhinosinusitis in children. The recommendations are based on the available evidence, but the choices need to be made depending on the circumstances of the individual case.







*Figure 9.* Evidence based scheme for therapy in children with chronic rhinosinusitis.

### **Research needs and priorities**

Although much work has been done on chronic rhinosinusitis and nasal polyps there are many questions still unanswerd. The following suggestions should highlight some areas of interest for further research.

### References

- Durr DG, Desrosiers MY, Dassa C. Impact of rhinosinusitis in health care delivery: the Quebec experience. J Otolaryngol 2001;30:93–7.
- Goetzel RZ, Hawkins K, Ozminkowski RJ, Wang S. The health and productivity cost burden of the 'top 10' physical and mental health conditions affecting six large US employers in 1999. J Occup Environ Med 2003;45:5– 14.
- Ray NF, Baraniuk JN, Thamer M, Rinehart CS, Gergen PJ, Kaliner M, et al. Healthcare expenditures for sinusitis in 1996: contributions of asthma, rhinitis, and other airway disorders. J Allergy Clin Immunol 1999;103(3 Pt 1):408–14.
- New guidelines for sinusitis target prescribing practices. Dis Manag Advis 2004;10:27–30.
- Anon JB, Jacobs MR, Poole MD, Ambrose PG, Benninger MS, Hadley JA, et al. Antimicrobial treatment guidelines for acute bacterial rhinosinusitis. Otolaryngol Head Neck Surg 2004;130(1 Suppl):1–45.

- Rhinosinusitis Task Force Committee. Report of the Rhinosinusitis Task Force Committee Meeting. Alexandria, Virginia, August 17, 1996. Otolaryngol Head Neck Surg 1997;117(3 Pt 2): S1–68.
- Sackett DL, Rosenberg WM, Gray JA, Haynes RB, Richardson WS. Evidence based medicine: what it is and what it isn't. Bmj 1996;**312**:71–2.
- Shekelle PG, Woolf SH, Eccles M, Grimshaw J. Clinical guidelines: developing guidelines. Bmj 1999;318: 593-6.
- Bousquet J, Van Cauwenberge P, Khaltaev N. Allergic rhinitis and its impact on asthma. J Allergy Clin Immunol 2001;108(5 Suppl):S147–334.
- Kaliner M. Treatment of sinusitis in the next millennium. Allergy Asthma Proc 1998;19:181–4.
- Lanza DC, Kennedy DW. Adult rhinosinusitis defined. Otolaryngol Head Neck Surg 1997;117(3 Pt 2):S1–7.
- Savolainen S. Allergy in patients with acute maxillary sinusitis. Allergy 1989;44:116–22.

- 1. A prospective population study of a group of ageand sex-matched controlled atopic and non-atopic individuals to consider the incidence of all upper respiratory tract symptoms including acute and chronic rhinosinusitis over a 5 year period.
- 2. A long-term follow-up of a cohort of patients with nasal polyposis to study the natural history of the condition (a randomised medical and surgical arm could be done at the same time).
- 3. A study of the benefit of long term macrolide therapy in patients with chronic rhinosinusitis with and without nasal polposis (this needs repeating to verify the work already published on this).
- 4. Studies should be performed to compare nasal steroids as a single modality of treatment with antibiotics in patients with intermittent or persistent rhinosinusitis.
- 5. There is an urgent need for randomized placebo controlled trials to study the effect of antibiotics in chronic rhinosinusitis and exacerbations of chronic rhinosinusitis.
- 6. To provide good evidence for the use of local antibiotic treatment in acute exacerbations of chronic rhinosinusitis, further studies with better characterized patients are needed.
- 7. Comparison of surgical and medical treatment modalities in CRS with and without NP.
  - Alho OP, Karttunen TJ, Karttunen R, Tuokko H, Koskela M, Suramo I, et al. Subjects with allergic rhinitis show signs of more severely impaired paranasal sinus functioning during viral colds than nonallergic subjects. Allergy 2003;58:767–71.
  - Karlsson G, Holmberg K. Does allergic rhinitis predispose to sinusitis? Acta Otolaryngol Suppl 1994;515:26–8 discussion 29.
  - Stammberger H. Functional endoscopic sinus surgery. Philadelphia: B.C. Decker, 1991.
  - Slavin RG. Sinusitis in adults and its relation to allergic rhinitis, asthma, and nasal polyps. J Allergy Clin Immunol 1988;82(5 Pt 2):950–6.
  - 17. Hamilos DL, Leung DY, Wood R, Meyers A, Stephens JK, Barkans J, et al. Chronic hyperplastic sinusitis: association of tissue eosinophilia with mRNA expression of granulocytemacrophage colony-stimulating factor and interleukin-3. J Allergy Clin Immunol 1993;92(1 Pt 1):39–48.

- Hamilos DL, Leung DY, Wood R, Cunningham L, Bean DK, Yasruel Z, et al. Evidence for distinct cytokine expression in allergic versus nonallergic chronic sinusitis. J Allergy Clin Immunol 1995;96:537–44.
- Rachelefsky GS, Goldberg M, Katz RM, Boris G, Gyepes MT, Shapiro MJ, et al. Sinus disease in children with respiratory allergy. J Allergy Clin Immunol 1978;61:310–4.
- Shapiro GG. Role of allergy in sinusitis. Pediatr Infect Dis 1985;4(6 Suppl):S55– 9.
- Shapiro GG, Virant FS, Furukawa CT, Pierson WE, Bierman CW. Immunologic defects in patients with refractory sinusitis. Pediatrics 1991;87:311–6.
- Beninger M. Rhinitis, sinusitis and their relationship to allergies. Am J Rhinol 1992;6:37–43.
- Grove R, Farrior J. Chronic hyperplastic sinusitis in allergic patients: a bacteriologic study of 200 operative cases. J Allergy Clin Immunol 1990;11:271–276.
- Emanuel IA, Shah SB. Chronic rhinosinusitis: allergy and sinus computed tomography relationships. Otolaryngol Head Neck Surg 2000;123:687–91.
- Friedman WH. Surgery for chronic hyperplastic rhinosinusitis. Laryngoscope 1975;85(12 pt 1):1999–2011.
- Hinriksdottir I, Melen I. Allergic rhinitis and upper respiratory tract infections. Acta Otolaryngol Suppl 1994;515:30–2.
- Newman LJ, Platts-Mills TA, Phillips CD, Hazen KC, Gross CW. Chronic sinusitis. Relationship of computed tomographic findings to allergy, asthma, and eosinophilia. Jama 1994;271:363–7.
- Iwens P, Clement PA. Sinusitis in allergic patients. Rhinology 1994;32:65– 7.
- Naclerio RM, de Tineo ML, Baroody FM. Ragweed allergic rhinitis and the paranasal sinuses. A computed tomographic study. Arch Otolaryngol Head Neck Surg 1997;123:193–6.
- Moser FG, Panush D, Rubin JS, Honigsberg RM, Sprayregen S, Eisig SB. Incidental paranasal sinus abnormalities on MRI of the brain. Clin Radiol 1991;43:252–4.
- Lloyd GA. CT of the paranasal sinuses: study of a control series in relation to endoscopic sinus surgery. J Laryngol Otol 1990;104:477–81.

- 32. Havas TE, Motbey JA, Gullane PJ. Prevalence of incidental abnormalities on computed tomographic scans of the paranasal sinuses. Arch Otolaryngol Head Neck Surg 1988;114:856–9.
- Patel K, Chavda SV, Violaris N, Pahor AL. Incidental paranasal sinus inflammatory changes in a British population. J Laryngol Otol 1996;110:649–51.
- Zinreich SJ, Kennedy DW, Kumar AJ, Rosenbaum AE, Arrington JA, Johns ME. MR imaging of normal nasal cycle: comparison with sinus pathology. J Comput Assist Tomogr 1988;12:1014–9.
- Lane AP, Pine HS, Pillsbury HC III. Allergy testing and immunotherapy in an academic otolaryngology practice: a 20-year review. Otolaryngol Head Neck Surg 2001;124:9–15.
- Salvin RG, Cannon RE, Friedman WH, Palitang E, Sundaram M. Sinusitis and bronchial asthma. J Allergy Clin Immunol 1980;66:250–7.
- Schwartz HJ, Thompson JS, Sher TH, Ross RJ. Occult sinus abnormalities in the asthmatic patient. Arch Intern Med 1987;147:2194–6.
- Bresciani M, Paradis L, Des Roches A, Vernhet H, Vachier I, Godard P, et al. Rhinosinusitis in severe asthma. J Allergy Clin Immunol 2001;107:73–80.
- Berg O, Carenfelt C. Analysis of symptoms and clinical signs in the maxillary sinus empyema. Acta Otolaryngol 1988;105:343–9.
- Williams JW Jr, Simel DL, Roberts L, Samsa GP. Clinical evaluation for sinusitis. Making the diagnosis by history and physical examination. Ann Intern Med 1992;117:705–10.
- Lund VJ, Kennedy DW. Quantification for staging sinusitis. The Staging and Therapy Group. Ann Otol Rhinol Laryngol Suppl 1995;167:17–21.
- Spector SL, Bernstein IL, Li JT, Berger WE, Kaliner MA, Schuller DE, et al. Parameters for the diagnosis and management of sinusitis. J Allergy Clin Immunol 1998;102(6 Pt 2):S107– 44.
- 43. Damm M, Quante G, Jungehuelsing M, Stennert E. Impact of functional endoscopic sinus surgery on symptoms and quality of life in chronic rhinosinusitis. Laryngoscope 2002;**112**:310–5.
- Dykewicz MS. 7. Rhinitis and sinusitis. J Allergy Clin Immunol 2003; 111(2 Suppl):S520–9.
- 45. Vento SI, Ertama LO, Hytonen ML, Wolff CH, Malmberg CH. Nasal polyposis: clinical course during 20 years. Ann Allergy Asthma Immunol 2000;85:209–14.

- Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. Med Care 1992;**30**:473–83.
- Anderson RT, Aaronson NK, Wilkin D. Critical review of the international assessments of health-related quality of life. Qual Life Res 1993;2:369–95.
- Benninger MS, Senior BA. The development of the Rhinosinusitis Disability Index. Arch Otolaryngol Head Neck Surg 1997;123:1175–9.
- Metson RB, Gliklich RE. Clinical outcomes in patients with chronic sinusitis. Laryngoscope 2000;110(3 Pt 3):24–8.
- Linder A. Symptom scores as measures of the severity of rhinitis. Clin Allergy 1988;18:29–37.
- Lund VJ, Mackay IS. Staging in rhinosinusitus. Rhinology 1993;31:183–4.
- Lildholdt T, Rundcrantz H, Lindqvist N. Efficacy of topical corticosteroid powder for nasal polyps: a doubleblind, placebo-controlled study of budesonide. Clin Otolaryngol 1995;20:26– 30.
- Johansson L, Akerlund A, Holmberg K, Melen I, Stierna P, Bende M. Evaluation of methods for endoscopic staging of nasal polyposis. Acta Otolaryngol 2000;120:72–6.
- 54. Godthelp T, Holm AF, Fokkens WJ, Doornenbal P, Mulder PG, Hoefsmit EC, et al. Dynamics of nasal eosinophils in response to a nonnatural allergen challenge in patients with allergic rhinitis and control subjects: a biopsy and brush study. J Allergy Clin Immunol 1996;97:800–11.
- Meltzer EO, Orgel H, Jalowaski A. Nasal cytology. In: Nacleio RDS, Mygind N, editors. Rhinitis: mechanisms of management. New York: Marcel Dekker, 1999.
- Klossek JM, Dubreuil L, Richet H, Richet B, Sedallian A, Beutter P. Bacteriology of the adult middle meatus. J Laryngol Otol 1996;110:847–9.
- Gold SM, Tami TA. Role of middle meatus aspiration culture in the diagnosis of chronic sinusitis. Laryngoscope 1997;107(12 Pt 1):1586–9.
- Vogan JC, Bolger WE, Keyes AS. Endoscopically guided sinonasal cultures: a direct comparison with maxillary sinus aspirate cultures. Otolaryngol Head Neck Surg 2000;122:370–3.
- Casiano RR, Cohn S, Villasuso E III, Brown M, Memari F, Barquist E, et al. Comparison of antral tap with endoscopically directed nasal culture. Laryngoscope 2001;111:1333–7.

- Talbot GH, Kennedy DW, Scheld WM, Granito K. Rigid nasal endoscopy versus sinus puncture and aspiration for microbiologic documentation of acute bacterial maxillary sinusitis. Clin Infect Dis 2001;33:1668–75.
- Jonas I, Mann W. Misleading x-ray diagnosis due to maxillary sinus asymmetries (author's transl). Laryngol Rhinol Otol (Stuttg) 1976;55:905–13.
- McAlister WH, Lusk R, Muntz HR. Comparison of plain radiographs and coronal CT scans in infants and children with recurrent sinusitis. AJR Am J Roentgenol 1989;153:1259–64.
- Iinuma T, Hirota Y, Kase Y. Radioopacity of the paranasal sinuses. Conventional views and CT. Rhinology 1994;**32**:134–6.
- Landman MD. Ultrasound screening for sinus disease. Otolaryngol Head Neck Surg 1986;94:157–64.
- Otten FW, Grote JJ. The diagnostic value of transillumination for maxillary sinusitis in children. Int J Pediatr Otorhinolaryngol 1989;18:9–11.
- Friedman WH, Katsantonis GP, Sivore M, Kay S. Computed tomography staging of the paranasal sinuses in chronic hyperplastic rhinosinusitis. Laryngoscope 1990;100:1161–5.
- Kennedy DW. Prognostic factors, outcomes and staging in ethmoid sinus surgery. Laryngoscope 1992;102(12 Pt 2 Suppl 57):1–18.
- Glicklich R, Metson R. A comparison of sinus computed tomography (CT) staging system for outcomes research. Am J Rhinol 1994;8:291–297.
- Jorgensen RA. Endoscopic and computed tomographic findings in ostiomeatal sinus disease. Arch Otolaryngol Head Neck Surg 1991;117:279–87.
- Gaskins RE. A surgical staging system for chronic sinusitis. Am J Rhinol 1992;6:5–12.
- Browne J, Hopkins J, Hopkins C, Slack R, van der Meulen J, Lund V, et al. The National Comparative Audit of Surgery for Nasal Polyposis and Chronic Rhinosinusitis. Royal College of Surgeons of England, 2003.
- Oluwole M, Russell N, Tan L, Gardiner Q, White P. A comparison of computerized tomographic staging systems in chronic sinusitis. Clin Otolaryngol 1996;21:91–5.
- Radenne F, Lamblin C, Vandezande LM, Tillie-Leblond I, Darras J, Tonnel AB, et al. Quality of life in nasal polyposis. J Allergy Clin Immunol 1999;104:79–84.

- 74. Ragab SM, Lund VJ, Scadding G. Evaluation of the medical and surgical treatment of chronic rhinosinusitis: a prospective, randomised, controlled trial. Laryngoscope 2004;114:923–30.
- 75. Winstead W, Barnett SN. Impact of endoscopic sinus surgery on global health perception: an outcomes study. Otolaryngol Head Neck Surg 1998;119:486–91.
- Durr DG, Desrosiers MY, Dassa C. Quality of life in patients with rhinosinusitis. J Otolaryngol 1999;28:108–11.
- Gliklich RE, Metson R. The health impact of chronic sinusitis in patients seeking otolaryngologic care. Otolaryngol Head Neck Surg 1995;113:104–9.
- Uri N, Cohen-Kerem R, Barzilai G, Greenberg E, Doweck I, Weiler-Ravell D. Functional endoscopic sinus surgery in the treatment of massive polyposis in asthmatic patients. J Laryngol Otol 2002;116:185–9.
- Piccirillo JFED, Haiduk A et al. Psychometric and clinimetric validity of the 3-item rhinosinusitis outcome measure (RSOM-31). Am J Rhinol 1995;9:297– 306.
- Piccirillo JF, Merritt MG Jr, Richards ML. Psychometric and clinimetric validity of the 20-Item Sino-Nasal Outcome Test (SNOT-20). Otolaryngol Head Neck Surg 2002;126:41–7.
- Anderson ER, Murphy MP, Weymuller EA Jr Clinimetric evaluation of the Sinonasal Outcome Test-16. Student Research Award 1998. Otolaryngol Head Neck Surg 1999;121:702–7.
- Fahmy FF, McCombe A, McKiernan DC. Sino nasal assessment questionnaire, a patient focused, rhinosinusitis specific outcome measure. Rhinology 2002;40:195–7.
- Gliklich RE, Metson R. Techniques for outcomes research in chronic sinusitis. Laryngoscope 1995;105(4 Pt 1):387–90.
- Gliklich RE, Metson R. Effect of sinus surgery on quality of life. Otolaryngol Head Neck Surg 1997;117:12–7.
- Metson R, Gliklich RE. Clinical outcome of endoscopic surgery for frontal sinusitis. Arch Otolaryngol Head Neck Surg 1998;124:1090–6.
- Senior BA, Glaze C, Benninger MS. Use of the Rhinosinusitis Disability Index (RSDI) in rhinologic disease. Am J Rhinol 2001;15:15–20.
- Hoffman SR, Mahoney MC, Chmiel JF, Stinziano GD, Hoffman KN. Symptom relief after endoscopic sinus surgery: an outcomes-based study. Ear Nose Throat J 1993;72:419–20.

- Revicki DA, Leidy NK, Brennan-Diemer F, Thompson C, Togias A. Development and preliminary validation of the multiattribute Rhinitis Symptom Utility Index. Qual Life Res 1998;7:693–702.
- Juniper EF, Guyatt GH. Development and testing of a new measure of health status for clinical trials in rhinoconjunctivitis. Clin Exp Allergy 1991;21:77–83.
- Williams JW Jr, Aguilar C, Cornell J, Chiquette E., Dolor RJ, Makela M, Holleman DR, et al. Antibiotics for acute maxillary sinusitis (Cochrane Review). Cochrane Database Syst Rev 2003(4).
- 91. Meltzer EO, Charous BL, Busse WW, Zinreich SJ, Lorber RR, Danzig MR. Added relief in the treatment of acute recurrent sinusitis with adjunctive mometasone furoate nasal spray. The Nasonex Sinusitis Group. J Allergy Clin Immunol 2000;106:630–7.
- 92. Nayak AS, Settipane GA, Pedinoff A, Charous BL, Meltzer EO, Busse WW, et al. Effective dose range of mometasone furoate nasal spray in the treatment of acute rhinosinusitis. Ann Allergy Asthma Immunol 2002;89:271– 8.
- 93. Dolor RJ, Witsell DL, Hellkamp AS, Williams JW Jr, Califf RM, Simel DL. Comparison of cefuroxime with or without intranasal fluticasone for the treatment of rhinosinusitis. The CAFFS Trial: a randomized controlled trial. Jama 2001;286:3097–105.
- 94. Barlan IB, Erkan E, Bakir M, Berrak S, Basaran MM. Intranasal budesonide spray as an adjunct to oral antibiotic therapy for acute sinusitis in children. Ann Allergy Asthma Immunol 1997;78:598–601.
- 95. Gehanno P, Beauvillain C, Bobin S, Chobaut JC, Desaulty A, Dubreuil C, et al. Short therapy with amoxicillinclavulanate and corticosteroids in acute sinusitis: results of a multicentre study in adults. Scand J Infect Dis 2000;**32**:679–84.
- 96. Klossek JM, Desmonts-Gohler C, Deslandes B, Coriat F, Bordure P, Dubreuil C, et al. Treatment of functional signs of acute maxillary rhinosinusitis in adults. Efficacy and tolerance of administration of oral prednisone for 3 days. Presse Med 2004;33:303–9.
- 97. Braun JJ, Alabert JP, Michel FB, Quiniou M, Rat C, Cougnard J, et al. Adjunct effect of loratadine in the treatment of acute sinusitis in patients with allergic rhinitis. Allergy 1997;**52**:650–5.

- Adam P, Stiffman M, Blake RL Jr A clinical trial of hypertonic saline nasal spray in subjects with the common cold or rhinosinusitis. Arch Fam Med 1998;7:39–43.
- 99. Axelsson A, Grebelius N, Jensen C, Melin O, Singer F. Treatment of acute maxillary sinusitis. IV. Ampicillin, cephradine and erythromycinestolate with and without irrigation. Acta Otolaryngol 1975;**79**:466–72.
- 100. Inanli S, Ozturk O, Korkmaz M, Tutkun A, Batman C. The effects of topical agents of fluticasone propionate, oxymetazoline, and 3% and 0.9% sodium chloride solutions on mucociliary clearance in the therapy of acute bacterial rhinosinusitis in vivo. Laryngoscope 2002;112:320–5.
- 101. Wiklund L, Stierna P, Berglund R, Westrin KM, Tonnesson M. The efficacy of oxymetazoline administered with a nasal bellows container and combined with oral phenoxymethyl-penicillin in the treatment of acute maxillary sinusitis. Acta Otolaryngol Suppl 1994;**515**:57–64.
- McCormick DP, John SD, Swischuk LE, Uchida T. A double-blind, placebocontrolled trial of decongestant-antihistamine for the treatment of sinusitis in children. Clin Pediatr (Phila) 1996;35:457–60.
- 103. Van Bever HP, Bosmans J, Stevens WJ. Nebulization treatment with saline compared to bromhexine in treating chronic sinusitis in asthmatic children. Allergy 1987;42:33–6.
- 104. Tarantino V, Stura M, Marenco G, Leproux GB, Cremonesi G. Advantages of treatment with bromhexine in acute sinus inflammation in children. Randomized double-blind study versus placebo. Minerva Pediatr 1988;40:649–52.
- 105. Serrano E, Demanez JP, Morgon A, Chastang C, Van Cauwenberge P. Effectiveness of ribosomal fractions of Klebsiella pneumoniae, Streptococcus pneumoniae, Streptococcus pyogenes, Haemophilus influenzae and the membrane fraction of Kp (Ribomunyl) in the prevention of clinical recurrences of infectious rhinitis. Results of a multicenter double-blind placebo-controlled study. Eur Arch Otorhinolaryngol 1997;**254**:372–5.
- 106. Habermann W, Zimmermann K, Skarabis H, Kunze R, Rusch V. Reduction of acute recurrence in patients with chronic recurrent hypertrophic sinusitis by treatment with a bacterial immunostimulant (Enterococcus faecalis Bacteriae of human origin.

Arzneimittelforschung 2002;52:622-7.

- 107. Federspil P, Wulkow R, Zimmermann T. Effects of standardized Myrtol in therapy of acute sinusitis-results of a double-blind, randomized multicenter study compared with placebo. Laryngorhinootologie 1997;**76**:23–7.
- 108. Gabrielian ES, Shukarian AK, Goukasova GI, Chandanian GL, Panossian AG, Wikman G, et al. A double blind, placebo-controlled study of Andrographis paniculata fixed combination Kan Jang in the treatment of acute upper respiratory tract infections including sinusitis. Phytomedicine 2002;9:589–97.
- 109. Legent F, Bordure P, Beauvillain C, Berche P. A double-blind comparison of ciprofloxacin and amoxycillin/clavulanic acid in the treatment of chronic sinusitis. Chemotherapy 1994;40(Suppl 1):8–15.
- 110. McNally PA, White MV, Kaliner MA. Sinusitis in an allergist's office: analysis of 200 consecutive cases. Allergy Asthma Proc 1997;18:169–75.
- 111. Subramanian HN, Schechtman KB, Hamilos DL. A retrospective analysis of treatment outcomes and time to relapse after intensive medical treatment for chronic sinusitis. Am J Rhinol 2002;16:303–12.
- 112. Namyslowski G, Misiolek M, Czecior E, Malafiej E, Orecka B, Namyslowski P, et al. Comparison of the efficacy and tolerability of amoxycillin/clavulanic acid 875 mg b.i.d. with cefuroxime 500 mg b.i.d. in the treatment of chronic and acute exacerbation of chronic sinusitis in adults. J Chemother 2002;14:508–17.
- 113. Huck W, Reed BD, Nielsen RW, Ferguson RT, Gray DW, Lund GK, et al. Cefaclor vs amoxicillin in the treatment of acute, recurrent, and chronic sinusitis. Arch Fam Med 1993;2:497–503.
- 114. Nishi K, Mizuguchi M, Tachibana H, Ooka T, Amemiya T, Myou S, et al. Effect of clarithromycin on symptoms and mucociliary transport in patients with sino-bronchial syndrome. Nihon Kyobu Shikkan Gakkai Zasshi 1995;**33**:1392–1400.
- 115. Gandhi A, Brodsky L, Ballow M. Benefits of antibiotic prophylaxis in children with chronic sinusitis: assessment of outcome predictors. Allergy Proc 1993;14:37–43.
- Ichimura K, Shimazaki Y, Ishibashi T, Higo R. Effect of new macrolide roxithromycin upon nasal polyps associated with chronic sinusitis. Auris Nasus Larynx 1996;23:48–56.

- 117. Hashiba M, Baba S. Efficacy of longterm administration of clarithromycin in the treatment of intractable chronic sinusitis. Acta Otolaryngol Suppl 1996;**525**:73–8.
- Scadding GK, Lund VJ, Darby YC. The effect of long-term antibiotic therapy upon ciliary beat frequency in chronic rhinosinusitis. J Laryngol Otol 1995;109:24–6.
- Scheinberg PA, Otsuji A. Nebulized antibiotics for the treatment of acute exacerbations of chronic rhinosinusitis. Ear Nose Throat J 2002;81:648–52.
- 120. Mosges R, Spaeth J, Berger K, Dubois F. Topical treatment of rhinosinusitis with fusafungine nasal spray. A double-blind, placebo-controlled, parallel-group study in 20 patients. Arzneimit-telforschung 2002;**52**:877–83.
- Leonard DW, Bolger WE. Topical antibiotic therapy for recalcitrant sinusitis. Laryngoscope 1999;109:668–70.
- 122. Sykes DA, Wilson R, Chan KL, Mackay IS, Cole PJ. Relative importance of antibiotic and improved clearance in topical treatment of chronic mucopurulent rhinosinusitis. A controlled study. Lancet 1986;2:359–60.
- 123. Desrosiers MY, Salas-Prato M. Treatment of chronic rhinosinusitis refractory to other treatments with topical antibiotic therapy delivered by means of a large-particle nebulizer: results of a controlled trial. Otolaryngol Head Neck Surg 2001;125:265–9.
- 124. Parikh A, Scadding GK, Darby Y, Baker RC. Topical corticosteroids in chronic rhinosinusitis: a randomized, double-blind, placebo-controlled trial using fluticasone propionate aqueous nasal spray. Rhinology 2001;**39**:75–9.
- 125. Lavigne F, Cameron L, Renzi PM, Planet JF, Christodoulopoulos P, Lamkioued B, et al. Intrasinus administration of topical budesonide to allergic patients with chronic rhinosinusitis following surgery. Laryngoscope 2002;112:858–64.
- 126. Cuenant G, Stipon JP, Plante-Longchamp G, Baudoin C, Guerrier Y. Efficacy of endonasal neomycin-tixocortol pivalate irrigation in the treatment of chronic allergic and bacterial sinusitis. ORL J Otorhinolaryngol Relat Spec 1986;48:226–32.
- 127. Lund VJ, Black JH, Szabo LZ, Schrewelius C, Akerlund A. Efficacy and tolerability of budesonide aqueous nasal spray in chronic rhinosinusitis patients. Rhinology 2004;42:57–62.

- 128. Bachmann G, Hommel G, Michel Ol. Effect of irrigation of the nose with isotonic salt solution on adult patients with chronic paranasal sinus disease. Eur Arch Otorhinolaryngol 2000;257:537–41.
- 129. Taccariello M, Parikh A, Darby Y, Scadding G. Nasal douching as a valuable adjunct in the management of chronic rhinosinusitis. Rhinology 1999;**37**:29–32.
- 130. Rabago D, Zgierska A, Mundt M, Barrett B, Bobula J, Maberry R. Efficacy of daily hypertonic saline nasal irrigation among patients with sinusitis: a randomized controlled trial. J Fam Pract 2002;**51**:1049–55.
- 131. Shoseyov D, Bibi H, Shai P, Shoseyov N, Shazberg G, Hurvitz H. Treatment with hypertonic saline versus normal saline nasal wash of pediatric chronic sinusitis. J Allergy Clin Immunol 1998;101:602–5.
- 132. Szmeja Z, Golusinski W, Mielcarek-Kuchta D, Laczkowska-Przybylska J. Use of mucolytic preparations (Mucosolvan) in selected diseases of the upper respiratory tract. Part II. Otolaryngol Pol 1997;51:480–6.
- 133. Ponikau JU, Sherris DA, Kita H, Kern EB. Intranasal antifungal treatment in 51 patients with chronic rhinosinusitis. J Allergy Clin Immunol 2002:110:862–6.
- 134. Weschta M, Rimek D, Formanek M, Polzehl D, Podbielski A, Riechelmann H. Topical antifungal treatment of chronic rhinosinusitis with nasal polyps: a randomized, double-blind clinical trial. J Allergy Clin Immunol 2004;113:1122–8.
- 135. Ponikau JU, Sherris DA, Weaver A, Kita H. Treatment of chronic rhinosinusitis with intranasal amphotericin B: A randomized, placebo-controlled, double-blind pilot trial. J Allergy Clin Immunol 2005;115:125–31.
- 136. Weaver EM. Association between gastroesophageal reflux and sinusitis, otitis media, and laryngeal malignancy: a systematic review of the evidence. Am J Med 2003;115(Suppl 3A):81S–89S.
- 137. Phipps CD, Wood WE, Gibson WS, Cochran WJ. Gastroesophageal reflux contributing to chronic sinus disease in children: a prospective analysis. Arch Otolaryngol Head Neck Surg 2000;126:831–6.
- Ulualp SO, Toohill RJ, Hoffmann R, Shaker R. Possible relationship of gastroesophagopharyngeal acid reflux with pathogenesis of chronic sinusitis. Am J Rhinol 1999;13:197–202.

- 139. Heintz B, Schlenter WW, Kirsten R, Nelson K. Clinical efficacy of Broncho-Vaxom in adult patients with chronic purulent sinusitis–a multi-centric, placebo-controlled, double-blind study. Int J Clin Pharmacol Ther Toxicol 1989;27:530–4.
- 140. Matthews BL, Kohut RI, Edelstein DR, Rybak LP, Rapp M, McCaffrey TV, et al. Evaluation of cefixime in the treatment of bacterial maxillary sinusitis. South Med J 1993;86:329–33.
- 141. Pakes GE, Graham JA, Rauch AM, Collins JJ. Cefuroxime axetil in the treatment of sinusitis. A review. Arch Fam Med 1994;3:165–75.
- 142. Fombeur JP, Barrault S, Koubbi G, Laurier JN, Ebbo D, Lecomte F, et al. Study of the efficacy and safety of ciprofloxacin in the treatment of chronic sinusitis. Chemotherapy 1994;40(Suppl 1):24–8.
- 143. Dijkstra MD, Ebbens FA, Poublon RM, Fokkens WJ. Fluticasone propionate aqueous nasal spray does not influence the recurrence rate of chronic rhinosinusitis and nasal polyps 1 year after functional endoscopic sinus surgery. Clin Exp Allergy 2004;34:1395– 400.
- 144. Mygind N, Pedersen CB, Prytz S, Sorensen H. Treatment of nasal polyps with intranasal beclomethasone dipropionate aerosol. Clin Allergy 1975;5:159–64.
- 145. Penttila M, Poulsen P, Hollingworth K, Holmstrom M. Dose-related efficacy and tolerability of fluticasone propionate nasal drops 400 microg once daily and twice daily in the treatment of bilateral nasal polyposis: a placebocontrolled randomized study in adult patients. Clin Exp Allergy 2000;**30**:94– 102.
- 146. Hadfield PJ, Rowe-Jones JM, Mackay IS. A prospective treatment trial of nasal polyps in adults with cystic fibrosis. Rhinology 2000;38:63–5.
- 147. Lildholdt T, Rundcrantz H, Bende M, Larsen K. Glucocorticoid treatment for nasal polyps. The use of topical budesonide powder, intramuscular betamethasone, and surgical treatment. Arch Otolaryngol Head Neck Surg 1997;**123**:595–600.
- 148. Lildholdt T, Fogstrup J, Gammelgaard N, Kortholm B, Ulsoe C. Surgical versus medical treatment of nasal polyps. Acta Otolaryngol 1988;105:140–3.
- van Camp C, Clement PA. Results of oral steroid treatment in nasal polyposis. Rhinology 1994;**32**:5–9.

- 150. Damm M, Jungehulsing M, Eckel HE, Schmidt M, Theissen P. Effects of systemic steroid treatment in chronic polypoid rhinosinusitis evaluated with magnetic resonance imaging. Otolaryngol Head Neck Surg 1999;120:517–23.
- Ricchetti A, Landis BN, Maffioli A, Giger R, Zeng C, Lacroix JS. Effect of anti-fungal nasal lavage with amphotericin B on nasal polyposis. J Laryngol Otol 2002;116:261–3.
- 152. Hartsel SC, Benz SK, Ayenew W, Bolard J. Na+, K+ and Cl- selectivity of the permeability pathways induced through sterol-containing membranevesicles by amphotericin B and other polyene antibiotics. Eur Biophys J 1994;23:125–32.
- 153. Haye R, Aanesen JP, Burtin B, Donnelly F, Duby C. The effect of cetirizine on symptoms and signs of nasal polyposis. J Laryngol Otol 1998;112:1042–6.
- 154. Filiaci F, Zambetti G, Luce M, Ciofalo A. Local treatment of nasal polyposis with capsaicin: preliminary findings. Allergol Immunopathol (Madr) 1996;24:13–8.
- 155. Baudoin T, Kalogjera L, Hat Jl. Capsaicin significantly reduces sinonasal polyps. Acta Otolaryngol 2000;**120**:307–11.
- 156. Zheng C, Wang Z, Lacroix JS. Effect of intranasal treatment with capsaicin on the recurrence of polyps after polypectomy and ethmoidectomy. Acta Otolaryngol 2000;**120**:62–6.
- 157. Passali D, Bernstein JM, Passali FM, Damiani V, Passali GC, Bellussi L. Treatment of recurrent chronic hyperplastic sinusitis with nasal polyposis. Arch Otolaryngol Head Neck Surg 2003;**129**:656–9.
- Drettner B, Ebbesen A, Nilsson M. Prophylactive treatment with flunisolide after polypectomy. Rhinology 1982;20:149–58.
- 159. Virolainen E, Puhakka H. The effect of intranasal beclomethasone dipropionate on the recurrence of nasal polyps after ethmoidectomy. Rhinology 1980;**18**:9–18.
- Karlsson G, Rundcrantz H. A randomized trial of intranasal beclomethasone dipropionate after polypectomy. Rhinology 1982;20:144–8.

- 161. Dingsor G, Kramer J, Olsholt R, Soderstrom T. Flunisolide nasal spray 0.025% in the prophylactic treatment of nasal polyposis after polypectomy. A randomized, double blind, parallel, placebo controlled study. Rhinology 1985;23:49–58.
- 162. Hartwig S, Linden M, Laurent C, Vargo AK, Lindqvist N. Budesonide nasal spray as prophylactic treatment after polypectomy (a double blind clinical trial). J Laryngol Otol 1988;102:148–51.
- 163. Stevens MH. Steroid-dependent anosmia. Laryngoscope 2001;**111**:200–3.