# ULTRASOUND IN THE MANAGEMENT OF ACUTE RHINOSINUSITIS PATIENTS IN PRIMARY CARE

**Helena Varonen**

ACADEMIC DISSERTATION

To be presented, by the permission of the Medical Faculty of the University of Helsinki, for public examination in the Auditorium of the Ear, Nose and Throat Hospital, University of Helsinki on March 14th , 2003 at 12 o'clock noon.

HELSINKI 2003

Supervised by

Professor Marjukka Mäkelä
Department of Medicine
University of Helsinki

and

Docent Seppo Savolainen
Department of Medicine
University of Kuopio

Reviewed by

Docent Seppo Y.T. Junnila
Department of Medicine
University of Turku

and

Professor Jouko Suonpää
Department of Medicine
University of Turku

## CONTENTS

## ABSTRACT

Acute maxillary sinusitis (AMS) is a common infectious disease in primary care and a diagnostic challenge to the physician. Sinus ultrasound has been introduced to help in screening the acute rhinosinusitis patients. Ultrasound has many qualities: it is harmless, rapid and convenient to the patient.

This thesis evaluates sinus ultrasound as a diagnostic tool in primary care. The accuracy of ultrasound was assessed by systematic review and meta-analysis and by empiric studies. The clinical outcomes in ultrasound positive and negative patients were studied in a randomized controlled trial. The views of patients and physicians were examined in surveys and focus group interviews.

Most patients with suspected AMS primarily hope for a specific diagnosis and wish to receive information from the physician. They respect the use of diagnostic imaging to achieve a reliable diagnosis. Very few patients are aware that acute rhinosinusitis can be a self-limiting disease, and many fear potential complications.

Primary care physicians consider AMS a difficult diagnosis, and they are dissatisfied with the current management. They feel obliged to prescribe unnecessary antibiotics for rhinosinusitis because of patient expectations and lack of good diagnostic device.

Ultrasound is a highly user-dependent method. With practice and training a physician can detect fluid in maxillary sinuses by sinus ultrasound as reliably as by radiographs. A back wall echo in sinus ultrasound examination is a reliable sign of fluid in the sinus. Only half of patients with clinically diagnosed AMS have fluid retention in sinus ultrasound examination. Sinus ultrasound is less expensive than the other additional diagnostic options for patients with suspected AMS.

National Library of Medicine Classification: WV 345

Medical Subject Headings: ultrasonography; diagnosis; maxillary sinusitis; primary health care; clinical trials; meta-analysis; sensitivity and specificity; Finland

## LIST OF THE ORIGINAL PUBLICATIONS

This thesis is based on the following original publications, referred to in the text by their Roman numerals I to V. In addition, some previously unpublished data are presented.

I. Varonen H, Mäkelä M, Savolainen S, Läärä E, Hilden J. Comparison of ultrasound, radiography, and clinical examination in the diagnosis of acute maxillary sinusitis: a systematic review. J Clin Epidemiol 2000;53:940-8.

II. Laine K, Määttä T, Varonen H, Mäkelä M. Diagnosing acute maxillary sinusitis in primary care: a comparison of ultrasound, clinical examination and radiography. Rhinology 1998;36:2-6.

III. Varonen H, Savolainen S, Kunnamo I, Heikkinen R, Revonta M. Acute rhinosinusitis in primary care: A comparison of symptoms, signs, ultrasound and radiography. Rhinology 2003; (In press).

IV. Varonen H, Kunnamo I, Savolainen S, Mäkelä M, Ruotsalainen J, Malmberg H. Treatment of acute rhinosinusitis diagnosed by clinical criteria or ultrasound in primary care: A placebo-controlled randomized trial. Scand J Prim HC 2003; (In press)

V. Varonen H, Sainio S. Patients' and physicians' views on the management of acute maxillary sinusitis (Manuscript).

## ABBREVIATIONS

| | |
|---|---|
| AMS | Acute maxillary sinusitis |
| RCT | Randomized controlled trial |
| ENT | Ear, nose and throat |
| CT | Computed tomography |
| MRI | Magnetic resonance imaging |
| LR+ | Positive likelihood ratio |
| LR- | Negative likelihood ratio |
| CRP | C-reactive protein |
| ESR | Erythrocyte sedimentation rate |
| SF-36 | The Medical Outcomes Study 36-item Short-Form Health Survey |

## TERMS

| | |
|---|---|
| Rhinosinusitis | Acute inflammation – with or without infection, of the nose and the paranasal sinuses. |
| Sinusitis | Inflammation of the paranasal sinus mucosa. Occurs in the maxillary, ethmoidal, sphenoidal or frontal sinus. |
| Acute maxillary sinusitis | Sinusitis with fluid retention in the maxillary sinus and with symptoms lasting less than four weeks. |
| Meta-analysis | A quantitative method for combining effects across several similar studies. |
| ROC-curve | Receiver operating characteristic curve, a statistical method to assess the diagnostic performance of a test. The tradeoffs between sensitivity and specificity of a test are visualized. |
| SROC-curve | Summary receiver operating characteristic curve, a statistical method to combine several diagnostic studies into one graph. |
| Sensitivity | Proportion of true positives among all patients with a condition. |
| Specificity | Proportion of true negatives among all patients without a condition. |
| Likelihood ratio | Expresses the likelihood that a given test result would be expected in a patient with a target disorder compared with the likelihood that the same result would be expected in a patient without the target disorder. |
| Technology assessment in health care | Analysis of medical, social, ethical, and economic implications of use of a health technology. |

# 1. INTRODUCTION

Use of ultrasound is becoming more widespread in primary care diagnostics (Kunnamo 1996). Ultrasound has many good properties: it is harmless, convenient to the patient and the results are available rapidly. Sinus ultrasound was first described by Mann (Mann 1975). In Finland, Revonta presented sinus ultrasound in a monograph: the accuracy was similar or better than that of sinus radiography (Revonta 1980). Since then, a large number of studies have assessed the accuracy of sinus ultrasound; most of them in secondary care settings.

"Sinuses" are a common complaint in primary care. The physician's challenge is to decide whether the patient with a runny nose and pain in the cheeks needs antibiotics or not, and whether symptomatic treatment is indicated. The diagnostic criteria for acute maxillary sinusitis (AMS) are not well established. Most often it is defined as an inflammation of the paranasal sinus mucosa with retention in the sinuses.

The treatment recommendations for AMS also vary. In the Netherlands the preferred strategy is watchful waiting (Stalman et al. 1997b), while in the United States the diagnosis is made on clinical grounds and antibiotics are often recommended in first place (Balk et al. 2001,Brooks et al. 2000). Unnecessary prescribing of antibiotics for viral upper respiratory tract infections, including acute rhinosinusitis, is considered a vast public health problem (Barden et al. 1998,Finkelstein et al. 2001,Guillemot et al. 1998,Macfarlane et al. 1997,Steffensen et al. 1997,Unsworth and Walley 2001). The growth of antimicrobial resistance is its feared consequence (Huovinen and Cars 1998).

The aim of this study was to assess whether sinus ultrasound could improve the diagnostics of AMS in primary care. The accuracy of ultrasound was estimated by a

systematic review and meta-analysis and by empiric studies. The clinical outcomes in ultrasound positive and negative rhinosinusitis patients were studied in a randomized controlled trial. The value and use of a diagnostic method do not depend only on the accuracy and efficacy. This thesis also included studies on the acceptability of sinus ultrasound from the perspective of both patients and physicians, and the additional costs sinus ultrasound incurs.

# 2. REVIEW OF THE LITERATURE

## *2.1 Acute rhinosinusitis*

### 2.1.1 Definition

Sinusitis is defined as an inflammation of the paranasal sinus mucosa (Gwaltney 1996,Shapiro and Rachelefsky 1992). Sinusitis occurs in the maxillary, ethmoidal, sphenoidal or frontal sinus, or overall in the sinuses (pansinusitis). Sinusitis may have an infectious aetiology, or it may be due to allergy or chronic nasal disorders (Druce 1992,Klossek and Chidiac 2001). AMS is the fourth common reason for consultation in Finnish primary care (Seppo Y.T. Junnila, personal communication). In this thesis AMS refers to an infection of the maxillary sinuses where retention in the sinuses has been verified. Very often the diagnosis is based on clinical examination alone, in which case the diagnosis is acute rhinosinusitis.

Rhinosinusitis is the broad definition for any inflammation – with or without infection – of the nose and the paranasal sinuses. Rhinosinusitis typically starts as a form of common cold, and most cases of acute rhinosinusitis resolve spontaneously in less than a week. Patients with rhinosinusitis consult physicians for various reasons: severe symptoms,

desire for rapid relief, need for sick leave, or fear of complications. The challenge in primary care is to detect among all acute rhinosinusitis patients those cases that benefit from antibacterial treatment.

### 2.1.2 Incidence and prevalence

In the MIKSTRA Study including 30 Finnish health centres, 7777 patients consulted during one week for infectious diseases and 12% were diagnosed as having AMS (Rautakorpi et al. 2001). Calculated from these figures, in the population of 820 000 inhabitants the yearly incidence of AMS was 5.9%. However, the yearly incidence is probably lower because the study was conducted in November when the incidence of AMS is higher than during the summer months.

When broader criteria for sinusitis are used than those for AMS, the prevalence is higher. In Canada the yearly prevalence of rhinosinusitis has been estimated to be 135 patients per 1000 (Durr et al. 2001). The prevalence of pathological lesions in the sinuses is still higher than symptomatic rhinosinusitis: up to 40% of patients in the general adult population have pathology in the maxillary sinuses (Gordts et al. 1996,Tarp et al. 2000). The patients in these studies had magnetic resonance imaging (MRI) because of a suspected intracranial neurological disease.

### 2.1.3 Predisposing factors

One of the major predisposing factors for AMS is ostiomeatal complex dysfunction. Many reasons may cause swelling of the mucosa: viral infections, allergy and hyper-responsiveness. The ostium has a diameter of only 6-8 millimetres (Lang 1989), and it can be easily obstructed (Drettner and Lindholm 1967). When the sinus is no longer well ventilated, the ciliary beating and clearance are diminished and secretion is gathered to sinus. Together with decreased oxygen pressure these factors can lead to tissue inflammation in the sinus (Slavin 1988). If the patient cannot resist the viruses and bacteria with humoral factors (e.g. immunoglobulins, proteases, and lymphocytes), infection can result.

It has been proposed that allergy is a predisposing factor for AMS. The underlying inflammation is possibly in the ostiomeatal area, which occurs more frequently in allergic persons (Settipane 1999). Allergy is more common in patients with AMS than in controls (Savolainen 1989). In spite of this, it is not known whether allergy increases the frequency or duration of bacterial sinusitis.

Asthma and sinusitis are both diseases of the respiratory epithelium. Crater et al reported (Crater et al. 1999) that asthmatic patients had more mucosal thickening than controls in the nasal passages and sphenoidal, ethmoidal, and frontal sinuses. On the other hand, patients with asthma and control subjects had similar changes in the maxillary sinus mucosa.

Chronic disorders that predispose to infectious diseases (such as diabetes, HIV, cystic fibrosis and immunodeficiency disorders) also increase the incidence of AMS (Jackson and Rice 1987,Rombaux et al. 1997). Septum deviation may cause obstruction in the ostiomeatal area (Kaliner

[1998a)]. In intensive care patients, mechanical ventilation via a nasotracheal intubation tube increases the risk of nosocomial sinusitis [(Holzapfel et al. 1999)].

### 2.1.4 Bacteriology

There is cumulating evidence that symptomless sinuses may not be sterile but can be colonized with bacteria under normal circumstances [(Brook 1981,Jiang et al. 1999)]. Bacteria are common in the ostiomeatal area: Savolainen et al [(Savolainen et al. 1986)] reported in a study on healthy young adults that the most common aerobic bacteria in nasal cavity were *Staphylococcus epidermidis* (79%), diphtheroids (42%), *Staphylococcus aureus* (34%). *Propionibacterium acnes* was the most commonly cultured anaerobe (74.5%). Potential pathogens *Haemophilus influenzae* and *Streptococcus pneumoniae* were found in 5% and 0.5% of cultures, respectively. [(Savolainen et al. 1986)]. Klossek et al have described similar results in healthy adults [(Klossek et al. 1996)].

Several studies have focused on bacteria cultured from maxillary sinus aspirates in AMS patients [(Berg et al. 1988,Gwaltney et al. 1992,Jousimies-Somer et al. 1988,Penttilä et al. 1997)]. The most common pathogens include *Haemophilus influenzae* (30-50%), *Streptococcus pneumoniae* (30-40%), *Moraxella catarrhalis* (12-20%), and *Streptococcus pyogenes* (up to 3%) [(Hansen et al. 1995,Jousimies-Somer et al. 1988, 1989,Klossek et al. 1996,Ylikoski et al. 1989)]. Other pathogens, such as other *Streptococcus* species and *Neisseria* species, are found less frequently [(Axelsson and Brorson 1973,Jousimies-Somer et al. 1988,Klossek et al. 1996,Ylikoski et al. 1989)]. *Streptococcus pneumoniae* and *Haemophilus influenzae* were the most common pathogens found in the nasopharynx specimens of primary care AMS patients [(Lindbaek et al. 2001)]. Anaerobic infections are common

in chronic and dental sinusitis [Brook et al. 1997,Su et al. 1983], and fungi can cause sinusitis in patients with immunodeficiency or diabetes [Herr 1991].

### 2.1.5 Aetiology of rhinosinusitis as a basis for therapy

Rhinosinusitis has several possible origins. The preferred treatment strategy depends on the physician's conception of the aetiology and severity of rhinosinusitis (Table 1).

Table 1. Possible aetiologies of rhinosinusitis, their typical occurrence, and preferred treatment.

| Aetiology | Typical occurrence | Treatment |
|---|---|---|
| Non-allergic inflammation | Related to a specific cause | Decongestants, nasal steroids |
| Allergic inflammation | Seasonal | Antihistamine, nasal steroids |
| Viral | As a form of common cold | Symptomatic: Decongestants |
| Bacterial | After viral rhinosinusitis | Antimicrobial |
| Structural | After trauma or congenitally | Surgical |

Rhinoviruses are common in the sinus epithelium of rhinosinusitis patients [Gwaltney et al. 1992,Pitkäranta et al. 2001], and they may cause AMS in up to 50% of the cases [Pitkäranta et al. 1997]. Viral rhinosinusitis is a frequent finding in the early days of common cold [Puhakka et al. 1998]. It typically resolves in a few days and warrants symptomatic treatment, if any. In a study by Lindbaek et al, antibiotics were no better than placebo in rhinosinusitis patients with mucosal thickening as the only abnormal finding in CT [Lindbaek et al. 1998].

It has been estimated that 0.5 – 2.0% of cases with viral rhinosinusitis develop into bacterial infection [Berg et al. 1986,Gwaltney 1996]. While antibiotics are generally not effective for patients with common cold, there is evidence that they may help those with bacteria in nasopharyngeal secretions [Kaiser et al. 1996]. Bacterial sinusitis may also improve without medication. Generally, two thirds of patients with radiologically confirmed AMS recover in two weeks when given placebo [van Buchem et al. 1997]. Fear of complications and search for faster relief from symptoms are among factors that make physicians choose antibiotics when bacterial AMS is suspected [Piccirillo et al. 2001,Poole 1999].

## *2.2 Diagnostic methods*

Sinus puncture was earlier considered the gold standard in the diagnosis of sinusitis [Evans Fo et al. 1975]. However, it is an invasive technique, sometimes painful and not ideal for use in primary care. It can be recommended if the patient has severe sinus pain because the puncture gives immediate pain relief. Nowadays the primary care physician must choose other strategies for diagnosing the majority of cases with acute rhinosinusitis.

### 2.2.1 Symptoms, signs and clinical examination

Many symptoms are related to acute rhinosinusitis (Table 2). Several studies have tried to find correlation between certain symptoms and bacterial sinusitis, but with weak results [Axelsson and Runze 1976,Berg and Carenfelt 1988,Blomgren et al. 2002,Hansen et al. 1995,Kenny et al. 2001,Williams et al. 1992b].

Axelsson and Runze posed 69 questions on history to patients with suspected sinusitis and compared symptoms with radiography findings. Most symptoms that are

conventionally supposed to indicate sinusitis were as common in patients with radiologically normal sinuses [Axelsson and Runze 1976].

Table 2. Symptoms related to AMS.

| General symptoms | Local symptoms |
|---|---|
| Cough | Nasal obstruction |
| Thick nasal voice | Nasal discharge |
| Fatigue | Unilateral facial pain |
| Headache | Sinus pain |
| Fever | Maxillary toothache |
| Hoarseness | Postnasal drip |
| Malaise | Hyposmia (Impaired sense of smell) |
| Bad taste in mouth | |
| Dizziness | |

Clinical examination of a patient with suspected AMS generally includes inspection of throat and tonsils to notice throat infections and postnasal drip. Ears are examined and maxillary sinuses palpated or tapped with fingers. Anterior rhinoscopy is performed to visualize polyps, obstruction, septum deviation or secretion in nasal cavities. In bacterial sinusitis purulent discharge may be visible in the middle meatus [Berg et al. 1981], but it is not easy to visualize this area without using decongestants.

The items of clinical examination have been compared with a reference standard in several studies. Williams et al compared clinical examination and radiography in 247 male patients [Williams et al. 1992b]. They found five independent predictors for sinusitis in logistic

regression analysis: maxillary toothache, purulent nasal secretion, poor response to nasal decongestants, abnormal transillumination, and coloured nasal discharge.

Combining these items improved sensitivity but the specificity remained low. Thus, clinical examination is a sensitive test and can be best used to rule out sinusitis (Jaeschke et al. 1994,Williams and Simel 1993). If the patient has none of the five predictive factors, sinusitis can be ruled out with certainty. A recent review assessed the studies on clinical examination, and the following symptoms and signs were associated with acute purulent sinusitis: purulent secretion, pain in the teeth, pain when bending forward, and a two-phased illness history (Lindbaek and Hjortdahl 2002). However, clinical examination is unspecific and produces several false positive diagnoses. A more specific test than clinical criteria would be needed to identify bacterial AMS.

### 2.2.2 Transillumination

Transillumination (diaphanoscopy) is a method to visualize sinuses with a transilluminator (Evans et al. 1975). In a dark room the transilluminator is placed infraorbitally or in the patient's mouth and the illumination of maxillary sinuses is judged as opaque, dull or normal. The accuracy of transillumination is not very high (Gwaltney et al. 1981,Williams et al. 1992b). Another problem is that the examination is time-consuming: the physician must stay in the dark room for at least 10 minutes before the examination to adapt his eyes. However, transillumination is harmless and commonly used in North America, sometimes also in Finland. A similar diaphanoscopy method with infrared light has been described in Germany (Wittek and Beuthan 1990).

### 2.2.3 Sinus radiography

Basic radiographic examination of the paranasal sinuses includes the occipitomental view described by Waters in 1915 (Waters and Waldron 1915). It can be complemented with occipitofrontal, lateral and axial views (Dolan and Smoker 1983). Earlier, a fifth view was recommended to visualize even better the retention in sinuses (Axelsson et al. 1970b). This occipitomental view is taken with the patient in lying position the affected side downwards.

A single Waters' view correlates well with four paranasal views (Williams et al. 1992a), and it can be used instead of multiple views especially in uncomplicated primary care sinusitis cases (Hayward et al. 1990,Williams et al. 1992a).

Studies assessing the sensitivity and specificity of radiography compared with sinus puncture are presented in Table 3. Generally, air-fluid levels can be accurately detected in radiography; mucosal thickening and opacification correlate less well with puncture findings (Kay et al. 1984). Complete opacification is another typical pathological finding in sinus radiography, and it may be due to sinusitis or other causes, such as tumours (Burke et al. 1994). Mucosal thickening of the sinuses may be a sign of sinusitis but it is commonly seen also in healthy individuals.

Table 3. Results of studies comparing radiography with sinus puncture

| Study | N | Prev | Sens | (95% CI) | Spec | (95% CI) | LR+ | LR - |
|---|---|---|---|---|---|---|---|---|
| McNeill 1963 (McNeill 1962) | 242 | 0.61 | 0.76 | (0.71-0.82) | 0.76 | (0.70-0.81) | 3.1 | 0.3 |
| Revonta 1980 I (Revonta 1980) | 170 | 0.46 | 0.87 | (0.82-0.92) | 0.91 | (0.87-0.95) | 9.9 | 0.1 |
| Revonta 1980 II (Revonta 1980) | 60 | 0.58 | 0.80 | (0.70-0.90) | 0.80 | (0.71-0.89) | 2.9 | 0.5 |
| Kuusela et al. 1982 (Kuusela et al. 1983) | 156 | 0.53 | 0.83 | (0.77-0.89) | 0.72 | (0.65-0.79) | 2.9 | 0.2 |
| van Buchem et al.1995 (van Buchem L et al. 1995) | 62 | 0.26 | 0.63 | (0.50-0.75) | 0.91 | (0.84-0.98) | 7.2 | 0.4 |
| Savolainen et al. 1997 (Savolainen et al. 1997b) | 234 | 0.80 | 0.93 | (0.90-0.96) | 0.62 | (0.55-0.68) | 2.4 | 0.1 |

N = number of patients
Prev = prevalence
Sens = sensitivity
95% CI = 95% confidence intervals
Spec= specificity
LR = likelihood ratio

In clinical practice, sinus radiography has several limitations. First, it is not available in all primary care sites, especially during on-call hours. Second, radiography involves the risk of radiation to eye lenses involving potential cataract formation (Mafee 1993,Roberts et al. 1995). If the examination is repeated many times, radiation may pose a real risk. Third, radiography is costly. The current guidelines especially in North America do not recommend primary use of radiography for suspected sinusitis (Brooks et al. 2000,Hickner et al. 2001,Klossek and Chidiac 2001,Low et al. 1997).

### 2.2.4 Ultrasound

Mann et al reported in 1970s that use of ultrasound might reduce the diagnostic error in paranasal sinus disease[(Mann 1980, 1975, 1976,Mann et al. 1977,Mann et al. 1976)]. The point in sinus ultrasound examination is that air in a healthy sinus immediately reflects the ultrasound back to the probe while secretion carries the ultrasound to the bony back wall of the diseased sinus and back to the probe. Sinus ultrasound presents a back wall echo when the sinus is filled with secretion. One dimensional A-mode and two-dimensional B-mode scans are used for sinus ultrasound [(Revonta 1980)].

Ultrasound was a welcome novelty to sinusitis diagnosis because it had several advantages compared with radiography: absence of ionizing radiation, short duration of the testing, and convenience for the patient [(Druce 1988)]. Revonta compared sinus ultrasound with sinus puncture and reported the results in a monograph [(Revonta 1980)]. The accuracy compared with sinus radiography was similar or better. The detection of back wall echo was a reliable sign of secretion in the sinus. Another monograph from Sweden later reported similar findings [(Jannert et al. 1981)].

Studies comparing ultrasound with sinus puncture in adult maxillary sinusitis are presented in Table 4. The accuracy of ultrasound has been moderate or good in studies where the patient population has consisted of acute patients with suspected rhinosinusitis either in ENT outpatient clinic or primary care.

Table 4. Results of studies comparing ultrasound with sinus puncture.

| Study | N | Prev | Sens | (95% CI) | Spec | (95% CI) | LR+ | LR- |
|---|---|---|---|---|---|---|---|---|
| Revonta 1980 I (Revonta 1980) | 170 | 0.46 | 0.87 | (0.82-0.92) | 0.91 | (0.87-0.95) | 9.9 | 0.1 |
| Revonta 1980 II (Revonta 1980) | 200 | 0.53 | 0.92 | (0.88-0.95) | 0.81 | (0.75-0.86) | 4.7 | 0.1 |
| Revonta 1980 III (Revonta 1980) | 60 | 0.58 | 0.94 | (0.88-1.00) | 0.72 | (0.61-0.83) | 3.4 | 0.1 |
| Kuusela et al. 1982 (Kuusela et al. 1983) | 156 | 0.53 | 0.71 | (0.64-0.78) | 0.64 | (0.56-0.71) | 1.9 | 0.5 |
| van Buchem et al.1995 (van Buchem L et al. 1995) | 48 | 0.27 | 0.54 | (0.40-0.68) | 0.94 | (0.88-1.00) | 9.4 | 0.5 |
| Savolainen et al.1997 (Savolainen et al. 1997b) | 234 | 0.80 | 0.81 | (0.76-0.86) | 0.72 | (0.67-0.78) | 2.9 | 0.3 |
| Haapaniemi et al. 2001 (Haapaniemi and Laurikainen 2001) | 206 | 0.66 | 0.77 | (0.72-0.82) | 0.49 | (0.43-0.55) | 1.5 | 0.5 |

N = number of patients
Prev = prevalence
Sens = sensitivity
95% CI = 95% confidence intervals
Spec = specificity
LR = likelihood ratio

Studies of sinus ultrasound that have used radiography, computed tomography or endoscopy as a reference standard have reported conflicting results. Some studies have shown good accuracy (Bauer et al. 1983,Berger 1986,Dobson et al. 1996,Ghatasheh and Smadi 2000,Karantanas and Sandris 1997,Lichtenstein et al. 1998,Tiedjen et al. 1998), while others (Berg and Carenfelt 1985,Jensen and von Sydow 1987,Pfleiderer et al. 1984,Rohr et al. 1986,Vento et al. 1999) have concluded that the accuracy of ultrasound is not adequate. Ultrasound has not been accurate in demonstrating mucosal thickening, polyps and cysts in the sinuses, especially in patients with chronic sinusitis (Berg and Carenfelt 1985,Jensen and von Sydow 1987,Pfleiderer et al. 1984,Rohr et al. 1986,Vento et al. 1999). Neither is the diagnostic

accuracy of ultrasound good in allergic patients: in the study of Shapiro et al in patients with allergic rhinitis the sensitivity of ultrasound varied from 44% to 61%, depending on the criteria applied to the radiograph [Shapiro et al. 1986a]. On the other hand, fluid in frontal sinuses can also be detected accurately by ultrasound [Suonpää and Revonta 1989].

Studies of sinus ultrasound in children have also reported conflicting results [Haapaniemi 1997,Reilly et al. 1989,Revonta et al. 1980,Shapiro et al. 1986b]. Ultrasound can be used to detect fluid also in sinuses of children [Revonta et al. 1980] but its ability to evaluate mucosal thickening in small, developing paranasal sinuses has been low [Reilly et al. 1989,Shapiro et al. 1986b].

Puhakka et al compared sinus ultrasound with MRI in patients with common cold. Ultrasound had a sensitivity of 64% and a specificity of 95% [Puhakka et al. 2000].

### 2.2.5 Computed tomography

Computed tomography (CT) gives a detailed image of the paranasal sinuses, but because of limited availability, costs, and radiation exposure it is not recommended as a diagnostic method for acute rhinosinusitis [Benninger et al. 1997,Brooks et al. 2000,Gwaltney et al. 1995,Klossek and Chidiac 2001]. In a general practice study, 63% of patients with a clinical diagnosis of sinusitis had changes in coronal CT images. The majority had changes in more than one sinus: the most common combination was maxillary and ethmoid sinus [Lindbaek et al. 1996c].

CT has been used as a reference standard in several studies on diagnosing sinusitis [Burke et al. 1994,Karantanas and Sandris 1997,Lucchin et al. 1996,Pfister et al. 1994,Roberts et al. 1995,Tiedjen et al. 1998]. Its value as a reference standard is limited by false-positive findings: pathological changes are

common also in CT images of healthy individuals [Calhoun et al. 1991,Gwaltney et al. 1994]. Roberts et al examined the average radiation exposure of coronal CT scanning and found it was 218 times the dose for a plain sinus radiograph [Roberts et al. 1995].

### 2.2.6 Magnetic resonance imaging

Magnetic resonance imaging (MRI) provides better visualization of soft tissue than CT, and it is used to diagnose e.g. fungal infections [Zinreich 1993]. MRI is also indicated in the diagnosis of complications of paranasal infections [Dessi et al. 1999,Jones et al. 1995]. Similar to CT and sinus radiography, it produces a number of false positive diagnoses. In MRI studies on patients with no symptoms of sinusitis, 32% to 60% of patients had mucosal thickening, opacification, fluid or polyps in their sinuses [Gordts et al. 1996,Jones et al. 1997,Tarp et al. 2000]. For costs and availability, MRI is not an option for primary care sinusitis diagnosing.

### 2.2.7 Laboratory tests

Savolainen et al compared erythrocyte sedimentation rate (ESR), white blood cell count (WBC) and C-reactive protein (CRP) with radiography and sinus puncture [Savolainen et al. 1997a]. These conventional blood tests were not helpful in diagnosing sinusitis. When sinusitis was caused by *Haemophilus influenzae* or *Moraxella catarrhalis* the CRP levels were not elevated. However, high CRP levels (>40 mg/l) were related to rhinosinusitis caused by *Streptococcus pneumoniae* or *S. pyogenes* [Savolainen et al. 1997a]. ESR and CRP were not found to be helpful as diagnostic tools in a thesis on frontal sinusitis [Antila 1999].

Lindbaek et al [Lindbaek et al. 1996b] and Hansen et al [Hansen et al. 1995] compared simple laboratory tests with computed tomography in patients with suspected rhinosinusitis. Linbaek et al concluded that ESR >10 had a sensitivity of 70% and specificity of 57%. Hansen et al found that the combination of ESR >11 and CRP >11 had a sensitivity of 82% and specificity of 57%. The high false positive rate makes these simple laboratory tests impractical for use in primary care.

## *2.3 Treatment of rhinosinusitis*

### 2.3.1 Antibiotic treatment

Stalman et al combined three placebo-controlled studies in a meta-analysis and found no significant efficacy in the antibiotics [Stalman et al. 1997c]. Later, larger meta-analyses have detected a small treatment effect. Although up to two thirds of rhinosinusitis patients recover spontaneously, antibiotics are still considered indicated in bacterial rhinosinusitis [Benninger et al. 2000,De Ferranti et al. 1998,Williams et al. 2000]. The advantages of antibiotic therapy include shorter duration of symptoms, less severe disease pattern and reduced risk of complications. On the other hand, there is evidence that side effects may equal or exceed the marginal benefits of antibiotic therapy [Ioannidis et al. 2002]. Six studies comparing antibiotics and placebo have been published (Table 5).

Table 5. Placebo-controlled studies on antibiotics for sinusitis

| Study | Diagnostic criteria | Treatments | Main result |
|---|---|---|---|
| Rantanen et al. 1973 (Rantanen and Arvilommi 1973) | Clinical, Sinus puncture | Doxycyclin (n=32)<br>Placebo (n=20) | No significant differences between antibiotic and placebo |
| Gananca et al. 1973 (Gananca and Trabulsi 1973) | Clinical, Culture | Cyclacillin (n=30)<br>Placebo (n=20) | Recovery time shorter in patients in the cyclacillin group |
| Norrelund 1978 (Norrelund 1978) | Clinical | Pivampicillin (n=73)<br>Placebo (n=67) | No significant differences between antibiotic and placebo |
| Lindbaek et al. 1996 (Lindbaek et al. 1996a) | CT: fluid level or total opacification | Penicillin V (n=41)<br>Amoxicillin (n=45)<br>Placebo (n=44) | Improved by day 10<br>Antibiotic: 86 %<br>Placebo: 57% |
| van Buchem et al. 1997 (van Buchem et al. 1997) | Radiography | Amoxicillin (n=108)<br>Placebo (n=106) | Improved by two weeks:<br>Antibiotic: 83 %<br>Placebo: 77% |
| Stalman et al. 1997 (Stalman et al. 1997b) | Clinical | Doxycycline (n=98)<br>Placebo (n=94) | No significant differences between antibiotic and placebo |

When different antibiotics have been compared, no large discrepancies in efficacy have existed (Adelglass et al. 1998,Calhoun and Hokanson 1993,Camacho et al. 1992,Dubois et al. 1993,Federspil and Bamberg 1981,Gehanno et al. 1996,Gehanno and Berche 1996,Ioannidis et al. 2001,Karma et al. 1991,Lasko et al. 1998,Nord 1988,Sorri et al. 1981,Williams et al. 1995,von Sydow et al. 1982). First-line antibiotics are as effective as more expensive wide-spectrum antibiotics in the initial treatment of acute rhinosinusitis (De Ferranti et al. 1998). A

meta-analysis from the Netherlands concluded that while there are no major differences in the effect of different antibiotics for AMS, the cheapest should be chosen [De Bock et al. 1997].

There are several recommendations of the optimal treatment duration for AMS. Earlier, treatment duration of 10 to 14 days was preferred [Evans 1994]. In recent guidelines shorter courses of antibiotics are favoured, mainly to diminish the quantity of antibiotics prescribed and to prevent microbial resistance [Pichichero 2000,Pichichero and Cohen 1997]. There is evidence from controlled trials that a three to five days' regimen of antibiotics is as effective as 10 days [Ioannidis et al. 2001,Sher et al. 2002,Williams et al. 1995].

### 2.3.2 Non-antibiotic medications

Vasoconstrictors are often prescribed for a patient with rhinosinusitis to relieve nasal obstruction although controlled trials have produced little evidence of their efficacy as primary treatment for rhinosinusitis. Axelsson et al compared nasal decongestant treatment alone or in combination with antibiotics or sinus irrigation, and the combination therapies gave better results than decongestants alone [Axelsson et al. 1970a]. Patients also use nasal vasoconstrictors as self-medication for rhinosinusitis symptoms.

Oral vasoconstrictors such as pseudoephedrine are effective alone or in combination with antihistamines for symptoms of rhinitis [Bertrand et al. 1996,Roth et al. 1977]. Combination therapies are widely used also for rhinosinusitis although they often cause side effects in therapeutic doses [Malm 1994].

There is growing evidence that intranasal corticosteroids have a role in the treatment of rhinosinusitis. The addition of intranasal corticosteroid spray to antibiotic treatment significantly improves the outcomes in acute rhinosinusitis (Dolor et al. 2001,Meltzer et al. 2000,Meltzer et al. 1993). The patients in these studies have had either a recurrent sinusitis or sinusitis with allergy. In a study on patients with common cold fluticasone propionate treatment tended to prevent paranasal sinusitis; however, the differences were not statistically significant (Puhakka et al. 1998).

### 2.3.3 Sinus puncture

Sinus puncture has a long history: In 1707 William Cowper developed a method to drain sinuses: a tooth was removed and the sinus drained through the alveolus (Blevald 1957). After this, John Hunter (1728 – 1793) recommended opening the antrum via middle meatus, and Gooch (died 1780) and Mikulicz (1896) introduced antral puncture through the inferior meatus. Sinus puncture became a common method for the diagnosis and treatment of sinus infections (Bailey 1983). It was also used to take bacterial specimens by Nordic physicians since 1940s (Urdal and Berdal 1949). There is evidence from one study that sinus puncture every other day controls the symptoms of sinusitis equally well or better than antibiotics (Axelsson et al. 1971).

One problem with sinus puncture has been that inserting the local anesthetic with a cotton-tipped applicator is sometimes painful. EMLA cream inserted with a syringe to the inferior meatus might provide better and faster anesthesia (Joki-Erkkilä et al. 2002). In primary care, sinus puncture is nowadays used mainly to treat patients with chronic sinusitis or severe purulent sinusitis. In Salo area health centre in 2001, during the 2500 visits due to sinusitis

207 sinus punctures were performed in a population of 46 000 (Seppo Y.T. Junnila, personal communication).

## *2.4 Complications of sinusitis*

The most common complication of AMS is pansinusitis in which the infection spreads widely to other paranasal sinuses (Brook et al. 1980). It has been suspected that recurrent episodes of acute sinusitis may develop into chronic sinusitis. On the other hand, it is possible that chronic sinusitis is instead related to other factors, such as certain micro-orgasnisms or allergy (Gwaltney 1996). Whether the development of chronic sinusitis could be prevented by medications or by use of sinus irrigations is not known (Druce and Slavin 1991,Kaliner 1998b). Chronic sinusitis causes a burden of disease that often leads to sinonasal surgery (Penttilä et al. 1997).

In bacterial sinusitis the infection can spread into nearby tissues. It has been demonstrated in animal models that *Streptococcus pneumoniae* can cause meningitis following intranasal infections via a non-haematogeneous route (Marra and Brigham 2001). In spite of this, severe complications are rare in adult maxillary sinusitis (Lindbaek et al. 1997). Possible complications include cellulites and abscess, rarely meningitis, cavernous sinus thrombosis, and osteomyelitis (Kern 1984,Quick and Payne 1972,Swift and Gill 1994). Severe, even life-threatening complications of AMS are more common in children than in adults (Hytönen et al. 2000,Pitkäranta et al. 2000).

## *2.5 Costs of management of rhinosinusitis*

According to an estimate made in the United States in 1996 there were 26.7 million health care visits per year because of sinusitis amounting to an expenditure of $5.8 billion (Ray et al. 1999). In Norway, acute sinusitis generated a cost of 192 million NOK per year, and 75% of this was due to sick leave (Lindbaek et al. 1997).

An evidence report from the United States included a full cost-effectiveness analysis on the management of AMS (Balk et al. 2001;Diagnosis and treatment of uncomplicated acute sinusitis in children 2000). It concluded that the most cost-effective strategy for AMS is to use clinical criteria for diagnosis and treat these cases with first-line antibiotics (amoxicillin or folate inhibitors). In mild and moderate cases the cost-effectiveness of symptomatic treatment came very close to antibiotic treatment. The report also assessed the cost-effectiveness of ultrasound and concluded that it was close to that of radiography. Ultrasound was used in a different manner than in Finland: it was a not an examination performed by a primary care physician during consultation but a specialist examination requiring appointment. Hence, the base case value for sinus ultrasound was $150 as opposed to $103 for sinus radiography.

Another cost-effectiveness analysis from the Netherlands compared clinical strategies that included 1. wait and see for one week, 2. prescribe antibiotics selectively, 3. prescribe antibiotics immediately or 4. perform further diagnostics. It ended up in a different conclusion than the study from the USA: postponing antibiotics for one week was the most effective strategy (De Bock et al. 2001).

## 2.6 Patient perspectives on rhinosinusitis

Patient perspectives on the diagnosis and treatment of rhinosinusitis have not been studied much (Atkins and Larson 1992). A Canadian study compared the quality of life in chronic rhinosinusitis to normative values measuring it with SF-36. The conclusion was that chronic inflammation affects the quality of life of patients with rhinosinusitis and represents an important health burden (Durr et al. 2001).

Benninger and Senior developed a disease-specific instrument for rhinosinusitis (Rhinosinusitis Disability Index). This instrument has 30 questions that assess the emotional, functional and physical well being of the patient (Benninger and Senior 1997). However, the ability of this instrument to measure changes in disease status has been questioned (Kinney 2002).

Little is known about the social aspects and rhinosinusitis. Sinusitis is more frequent in women: in most studies two thirds of the patients are women. One explanation for this is increased mucosal thickening caused by hormonal factors. Pregnant women also have a higher incidence of sinusitis (Sorri et al. 1980). Another explanation is the higher frequency of upper respiratory tract infections as a result of spending more time in the company of small children. To prevent common cold and rhinosinusitis, one should meet a variety of people. Diverse social networks have been linked to a greater resistance to upper respiratory illness (Cohen et al. 1997).

## *2.7 Physician perspectives: current management of rhinosinusitis*

In primary care the diagnosis of sinusitis is most often based on symptoms and clinical examination. More than 90 % of Finnish patients with suspected sinusitis receive a course

of antibiotics at their first visit to a primary care physician when the diagnosis is based on clinical examination only (Mäkelä and Leinonen 1996). A recent study from France reported that primary care physicians almost always base their treatment decision on the signs and symptoms the patient presents. Clinical examination was not always performed, only 65% of the physicians reported that they examined the nasal cavities, and the examination was a diagnostic factor in 15% of cases (Pessey et al. 2000).

A retrospective analysis in United States indicated that family practitioners relied on four factors (sinus tenderness, facial pressure, postnasal drainage and coloured basal discharge) to differentiate AMS from viral rhinosinutis (Hueston et al. 1998). Clinical examination also remains the preferred diagnostic strategy in guidelines (Table 6), especially in North America (Druce 1991,Engels et al. 2000,Gwaltney et al. 1995,Oppenheimer 1992,Richtsmeier 1992).

Table 6. Recommendations in national guidelines on the diagnosis of AMS

| Country, year, ref. | Recommended diagnostic strategy |
|---|---|
| United States 2001 (Pediatrics 2001) | Children </= 6, clinical criteria, >6 imaging methods may be necessary |
| France 2001 (Klossek and Chidiac 2001) | History and physical examination |
| United States 2000 (Brooks et al. 2000) | History and physical examination, diagnostic imaging only in atypical cases and treatment failures |
| Finland 1999 ([Finnish Otolaryngological Association 1999) | Clinical examination and sinus radiography or ultrasound |
| Canada 1997 (Low et al. 1997) | History and findings on physical examination |
| United States | History and physical findings |

1995 (Gwaltney et al. 1995)

Primary care physicians are criticised for diagnosing sinusitis too often and prescribing antibiotics for it although they are less well equipped than specialists to reach the correct diagnosis (Gleeson 1992). Differentiating between bacterial and viral sinusitis is not easy using clinical criteria alone (Kumlien 1993), and diagnosing acute sinusitis is often considered problematical among primary care physicians (Stalman et al. 1997a). In Norway, 79% of general practitioners stated in a survey in 1993 that the diagnosis of sinusitis is more uncertain than that of otitis media. Norwegian primary care physicians regarded CRP as a helpful additional examination. Ultrasound was not available to primary care physicians in Norway (Lindbaek and Hjortdahl 1993).

# 3. AIMS OF THE STUDY

## *3.1 General aims*

This study aims at assessing the validity and usefulness of ultrasound in the diagnosis of acute rhinosinusitis in adult patients in primary care. Using the methods of health technology assessment (Kearney 1996), the accuracy, practicability, costs and implications to patients and physicians of sinus ultrasound are studied.

### *3.2 Specific aims*

The specific objectives of this study are:

1. To compare sinus ultrasound with other possible diagnostic methods (sinus radiography, symptoms and clinical signs) for acute rhinosinusitis in primary care.

2. To study the accuracy of sinus ultrasound in primary care settings.

3. To compare the effect of antibiotics and placebo in the treatment of ultrasound positive and negative rhinosinusitis patients.

4. To describe the additional costs that sinus ultrasound produces in primary care.

5. To describe and analyse the attitudes and expectations the primary care patients have towards diagnostic methods for acute rhinosinusitis.

6. To describe and analyse the attitudes and values the primary care physicians have in the diagnosis of acute rhinosinusitis.

## 4. SUBJECTS AND METHODS

### *4.1 Data collection and inclusion criteria*

This thesis is based on five original studies (Table 6). Several study approaches have been used: systematic review and meta-analysis, two clinical diagnostic comparisons, placebo-controlled randomized clinical trial, and survey and qualitative focus groups interviews both on sinusitis patients and on physicians.

Table 6. Design, subjects, and setting of the included studies.

| Study | Number of subjects | Setting |
|---|---|---|
| 1. Systematic review and meta-analysis (I) | 11 studies comprising 1144 patients | Studies in primary care or outpatient clinics |
| 2. Diagnostic study comparing ultrasound and sinus puncture (II) | 39 patients | Two health centres (Nurmijärvi and Kajaani) |
| 3. Combined diagnostic-therapeutic randomized controlled trial (III and IV) | 150 patients | Nine health centres (Karstula, Saarijärvi, Halikko, Salo, Katriina, Simo, Kuivaniemi, Heinävesi and Tikkurila) |
| 4. Survey and focus groups on patients (V) | 177 patients in survey and 22 in focus groups | Four health centres (Joensuu, Nurmijärvi, Kankaanpää and Tikkurila) and two private clinics |
| 5. Survey and focus groups on physicians (V) | 245 physicians in survey and 20 in focus groups | A random sample (10%) of primary care physicians Focus groups in four health centres (Joensuu, Nurmijärvi, Kankaanpää and Tikkurila) |

### 4.1.1 Systematic review (I)

To find articles on the diagnosis of sinusitis we searched the Medline database from 1966 to April 1999 and the Finnish medical database, Medic, from 1977 onwards using a variety of both Medical Subject Heading (MeSH) terms and textword options. Database searches were complemented with other search methods: reference lists of pertinent articles and reviews were searched, hand searches were done on four journals and experts were contacted to find all relevant studies, including unpublished data.

We included studies that compared a diagnostic method with a reference standard. As reference methods we accepted sinus puncture or computed tomography. Our target population was adults with a suspected AMS (symptoms for less than three months) in primary care or a comparable setting. If the setting was not clearly stated, we accepted the study if the population consisted of acute patients with no diagnostic procedures carried out before the methods under study. We accepted articles in English, German, French, Scandinavian languages, and Finnish. We excluded studies on chronic sinusitis or otherwise selected patient populations (e.g., consisting solely of allergic or patients referred to surgery).

### 4.1.2 Diagnostic comparisons (II,III)

Ultrasound was studied in two primary care studies. In Nurmijärvi and Kajaani health centres (II) consecutive acute patients over 15 years of age suspected of having AMS were included. The patient, nurse, or primary care physician all could have raised the

suspicion of AMS. Patients were excluded for the following reasons: symptoms over 30 days, pregnancy, previous maxillary surgery or unwillingness to participate.

After informed consent from the patient, the physician on duty took the patient's history, performed clinical and ultrasound examinations, and recorded the clinical diagnosis based on this information. Sinus radiographs were taken subsequently. Thereafter, one of the two principal investigators (Karri Laine or Tuomo Määttä) recorded a short history, performed anterior rhinoscopy and ultrasound examination and irrigated the sinuses. The principal investigator did not receive any information from the on-duty physician; however, he did have the sinus radiographs at his disposal.

The other diagnostic comparison was a part of a multi-centre study on the management of rhinosinusitis (see 4.1.3) (III). All patients with suspected AMS were examined with ultrasound, and the ultrasound results shown on the screen of the device were frozen and printed. The printouts were later read by an ear, nose and throat (ENT) specialist (Matti Revonta) without knowledge of the clinical situation. The interpretations were compared with those of the primary care physicians. At Karstula health centre, all patients had a sinus radiograph taken.

### 4.1.3 Randomized controlled trial (IV)

The study took place in nine health centres in Finland from November 1998 to October 1999 (Halikko, Heinävesi, Katriina, Karstula, Kuivaniemi, Saarijärvi, Salo, Simo, and Tikkurila). An ENT specialist (Seppo Savolainen, Matti Revonta or Heikki Kiukaanniemi)

gave a small group tutorial of 1.5 hours on sinus ultrasound to 60 physicians in the participating health centres.

The study covered adult patients (over 18 years of age) with a clinical diagnosis of AMS. The minimum criteria for a clinical diagnosis of AMS were at least three symptoms and one out of three signs typical to AMS. Reasons for exclusion included duration of AMS symptoms for more than 30 days, anti-microbial treatment during the last month, pregnancy or breastfeeding, an acute phase of a diagnosed chronic maxillary sinusitis, clinical suspicion of dental or frontal sinusitis or pansinusitis or suspicion of a severe complication, and previous sinus surgery.

The physicians discussed the study with the patients, recorded history and clinical findings, and handed out the study medication if the patient fulfilled the criteria of AMS. Patients assessed their symptoms before consultation with a three-step scale (1=no, 2=little, 3=much). A symptom score of the twelve symptoms was counted by giving 2 points for ‘much’ answers and 1 point for ‘little’ answers. The points for the three most important symptoms (maxillary pain, postnasal drip and cough) were doubled. The maximum symptom score was thus 30. The patients received diaries for recording their symptoms daily over two weeks. The same list of 12 symptoms with a 3-step scale as in the initial patient form was used.

The patients were randomized to one of four treatment options, all for seven days: amoxicillin 750 mg x 2, penicillin V 1500 IU x 2, doxycyclin 100 mg x 2 or placebo 1x2. The placebo group was doubled: two patients out of five received placebo. The treatments

were previously randomized in blocks of 20 consecutive patients at the Pharmacy of the military Hospital in Helsinki and distributed in identical sealed bottles.

Two weeks (14-16 days) after the initial consultation, the researcher (HV) interviewed the patients by telephone asking about subjective symptoms, their severity, possible side effects and the patient's estimate of recovery or recurrence. The interviewer did not know the patient’s history, treatment or the result of the ultrasound examination.

After one year the researcher (HV) checked the patient records to register recurrent or chronic sinusitis in the study patients. Recurrent sinusitis was defined as another episode of sinusitis diagnosed by a primary care physician. Chronic sinusitis was defined as sinusitis with symptoms lasting for more than three months.

### 4.1.4 Costs

Symptoms, signs and clinical examination are the basic evaluations for acute rhinosinusitis. If the diagnosis is inconclusive, additional testing is considered. Sinus ultrasound is an additional examination for the diagnosis of AMS in primary care. Other possible additional methods in Finland include sinus radiography (one to four views), bacteriological culture or CRP. For this thesis, the information on the market prices of the additional examinations was collected and the average costs in a health centre were estimated.

Introducing ultrasound as a new diagnostic device incurs costs for a health centre. The average costs per physician were estimated by allocating them on a three-year schedule (Jefferson et al. 1996).

### 4.1.5 Survey studies (V)

To study and compare the perceptions of physicians and patients, we designed a survey addressing both groups. We posed a same set of questions to both patients and physicians and compared their responses. Also additional separate questions to patients and physicians were included. From March to May in 1997 patients with suspected AMS were recruited to the survey in six study centres, including two small rural health centres, two large urban health centres and two private health care units. The primary care physicians explained the purpose of the study to the patient and oral informed consent was obtained. The survey questionnaire and a cover letter were handed out to all consecutive patients who consulted because of suspected AMS.

The physician survey sample was a random sample of all Finnish primary care physicians. It consisted of approximately 10% of all full-time health centre physicians, those born on 11$^{th}$, 13$^{th}$, 15$^{th}$ or 31$^{st}$ day of each month. The addresses were retrieved from the register of physicians kept up by Finnish Medical Association. The non-responders were reminded once to return the questionnaire.

### 4.1.6 Focus groups (V)

To obtain a full picture of what patients and physicians think about AMS, we also used qualitative methods [Delbanco 1996,Fitzpatrick and Boulton 1994,Morgan 1993,Pope and Mays 1995,Segesten 1997,Sixma et al. 1998]. We utilized triangulation: survey and focus group results were compared with and complemented by each other. Patients and physicians were interviewed in the same health centres but in individual groups. We conducted the focus group interviews during April and August 1997 in health centre meeting rooms by two moderators, the primary researcher and another investigator who had an education in the social sciences. The patients were recruited among the survey respondents by telephone (by HV). We tried to form heterogeneous groups (different age groups, males and females), to obtain a variety of points of view.

The focus group interviews were semi-structured, and the topics included practices in diagnosing and treating sinusitis. In the patient groups, expectations and preferences were discussed. In the physician groups the topics included the thinking underlying the practice, the influence of colleagues, patients, research information and other factors on decision-making, and ideas on improving practice in the management of sinusitis.

Both patient and physician focus group sessions were ended with a discussion on a study by van Buchem et al [van Buchem et al. 1997] in which amoxicillin and placebo were equal in the treatment of radiologically diagnosed AMS. A summary of this study was given to the participants, questions were clarified, and the paper was discussed.

The researchers made notes of the discussions and other observations such as group dynamics and different forms of communication. The focus group discussions were audiotaped and transcribed. The transcripts were interpreted first by both researchers

independently and themes were searched for and coded. Later the interpretations were compared and discussed, and transcripts were read again to formulate the conclusions. The survey results were compared with the focus group findings to assess the reliability of the results.

## *4.2. Diagnostic criteria*

### 4.2.1 Clinical criteria

The minimum criterion for clinical diagnosis of AMS in studies III and IV was the presence of at least three symptoms and one clinical sign. Data were collected on 12 symptoms related to AMS (nasal obstruction, nasal discharge, headache, postnasal drip, cough, sinus pain, unilateral facial pain, maxillary toothache, hyposmia, anosmia, malaise and fever), and three clinical signs (purulent secretion in the nasal cavity, discharge in the pharynx and tenderness in sinus tapping).

### 4.2.2 Ultrasound

In both diagnostic comparisons an A-mode ultrasound was used (Sinuscan 102 , Oriola, Finland). The frequency of the unfocused transducer was 3 MHz and the diameter of the piezoelectric disc was 8 mm. The criterion for AMS was a back wall echo on the screen of the device at a distance of 3.5 cm or more, indicating fluid in the maxillary sinus. None of the other findings were considered sinusitis.

In the Nurmijärvi-Kajaani study (II) the physicians were also able to classify mucosal thickening or unclear findings. In the analysis, sinuses with only mucosal thickening were classified as normal and those with unclear findings were excluded. In the multi-centre study (III) the physicians classified the results of both maxillary sinuses as sinusitis or non-sinusitis.

### 4.2.3 Radiography

In the Nurmijärvi-Kajaani study (II) the radiographic examination consisted of three standard projections (occipitofrontal, occipitomental and lateral projections). The radiographs were later interpreted by a radiologist under blinded conditions. The radiologist had neither the clinical information, nor the results of sinus irrigations or ultrasound examinations.

In the multi-centre study (III) patients in Karstula had a sinus radiography taken (occipitomental projection) within 15 minutes to 1 hour from the ultrasound examination. Two ENT specialists (MR and SS) interpreted the radiographs independently and without knowledge of the clinical situation or the ultrasound result. Criteria for AMS were either total opacification, an air–fluid level, or mucosal thickening of 6 mm or more (Revonta and Suonpää 1981).

### 4.2.4 Sinus puncture

In the Nurmijärvi-Kajaani study (II) sinus irrigation was performed as soon as possible after the ultrasound and radiographic examinations. A topical anaesthesia (lidocain 4%, adrenaline 0,1%) was used and antral lavage was performed with at least 100 ml of warm 0,9 % saline solution. If the antral lavage contained either purulent or mucopurulent material, the patient was diagnosed as having AMS. The puncture material categories were: + for width of floccule <0,5 cm, ++ for width of floccule 0,5-2 cm and +++ for width of floccule >2 cm or purulent fluid.

## *4.3 Statistical methods*

### 4.3.1 Meta-analysis

We followed the methodology proposed by the Cochrane Methods Working Group (Cochrane Methods Working Group 1997). From primary data in original articles we calculated the sensitivity, specificity, and their confidence intervals for the diagnostic method under study. We also calculated the prevalence of sinusitis in each study population and the positive and negative likelihood ratios (Jaeschke et al. 1994) for the diagnostic method in each study. We categorized the original studies by the type of reference standard used and performed summary analysis within each group. We calculated the summary sensitivities, specificities, and likelihood ratios and their confidence intervals while weighting the studies by inverse variance (Petitti 1994).

For diagnostic test meta-analysis (Irwig et al. 1995,Irwig et al. 1994), we formed summary receiver operating characteristic curves (Hilden 1991) (SROC) by using the Meta-test software produced by Joseph Lau, and by modifying the method introduced by Moses, Shapiro, and

Littenberg [Littenberg and Moses 1993,Moses et al. 1993] using zero as the slope parameter. As a summary estimate we used the Q* value, the point where the SROC curve shoulders up to the desirable northwest corner [Moses et al. 1993]. Q* is the point on the SROC curve in which the sensitivity and the specificity are equal.

### 4.3.2 Diagnostic comparisons

We calculated the sensitivity and specificity, their confidence intervals, and positive and negative likelihood ratios [Sackett et al. 1991] for ultrasound compared with the reference standard.

We calculated Cohen's Kappa [Guggenmoos-Holzmann 1996] statistics for the comparison of the interpretations of ultrasound performed by primary care physicians and specialists. For statistical analyses we used StatView 5.0 software.

### 4.3.3 Sample size calculation for the RCT

Previous studies have shown that approximately 75 – 80% of patients with AMS treated with placebo recover in two weeks [Stalman et al. 1997c,van Buchem et al. 1997]. To find a 15% treatment difference from 75% to 90% at the significance level of $\alpha$= 0.05 and $\beta$=0.20 (power = 0.80), a sample size of 98 patients in each treatment arm was needed [Pocock 1990].

### 4.3.4 Statistics for comparisons

In the RCT we analysed the data by intention to treat for the main outcomes. Differences in proportions in study groups were tested with $\chi^2$ or Fischer's exact test. Duration of sinusitis was analysed only in patients who recovered fully during the two-week follow up. We investigated differences in symptom scores between the groups by descriptive statistics, unpaired t-tests and the Mann-Whitney U-test. All reported p values are two sided.

In surveys the responses were cross-tabulated and the groups compared. We used descriptive statistics and tested differences in proportions in study groups with $\chi^2$ or Fischer's exact test. We analysed all data with StatView 5.0.1 software (SAS Institute Inc.).

## *4.4. Ethics*

The ethical committee of the National Research and Development Centre for Welfare and Health (Stakes) and the local ethical committees at study centres accepted all study protocols. The patients received written information of the studies and their possible harmful effects. The patients in the clinical studies (II, III and IV) and the focus group participants (V) gave their written informed consent.

# 5. RESULTS

## *5.1. Ultrasound in the diagnosis of acute sinusitis: a systematic review (I)*

### 5.1.1 Search results

The database searches (Medline and Medic) yielded 1103 references: 168 abstracts were printed for further examination and 49 studies concerning the diagnosis of maxillary sinusitis in adults were retrieved. The results of the literature searches are presented in Table 7 and the primary reasons for study exclusion in Table 8.

Table 7. Results of the literature searches

| Source | No. of reports found |
|---|---|
| Medline | 30 |
| Medic | 1 |
| Reference searches | 12 |
| Hand searches | 0 |
| Personal contact | 6 |
| Total | 49 |

Table 8. Reasons for exclusion

| Primary reasons for exclusion | No. of reports |
|---|---|
| Selected patient population | 12 |
| Inadequate data | 10 |
| Chronic sinusitis | 6 |
| Unacceptable reference method | 8 |
| Retrospective study | 2 |
| Total | 38 |

Eleven articles met our inclusion criteria, with two pairs of duplicate publications, those of Kuusela [Kuusela et al. 1983, 1982] and Hansen [Hansen et al. 1996, 1995]. Table 9 gives the characteristics of the settings and the patient populations of the included studies.

Table 9. Characteristics of patient populations of included studies

| Year | Authors (ref) | Setting | Patients, N | Age, (percentage of males) | Duration of symptoms |
|---|---|---|---|---|---|
| 1963 | McNeill (Mcneill 1962) | ENT clinic | 150 | 10 to over 50, (52 %) | NA |
| 1980 | Revonta (Revonta 1980) | ENT clinic | 215 | adults | NA |
| 1982 | Kuusela et al. (Kuusela et al. 1983) | Military clinic | 105 | 17-28, (100%) | NA |
| 1985 | Berg et al. (Berg and Carenfelt 1985) | ENT clinic | 105 | 10-75, mean 37, (33 %) | < 3 months |
| 1988 | Berg et al. (Berg and Carenfelt 1988) | Emergency ward | 155 | adults, mean 38, (38% ) | < 3 months |
| 1995 | Hansen et al. (Hansen et al. 1995) | General practice | 174 | 19-62, (30%) | < 1 month |
| 1995 | van Buchem et al. (van Buchem et al. 1995) | General practice | 40 | over 18, (33%) | NA |
| 1997 | Savolainen et al. (Savolainen et al. 1997b) | Military clinic | 161 | 17-68, (81%) | < 1 month |
| 1998 | Laine et al. (Laine et al. 1998) | General practice | 39 | 16-68, median 37 (33%) | < 1 month |

NA = data not available

ENT clinic = ear, nose, and throat clinic

### 5.1.2 Methodological quality of included trials

The methodological characteristics of the included trials are collected in Table 10. The patients studied were seldom described in detail (e.g., age, severity of disease, duration of symptoms, dropouts). The presentation of results varied and several types of categories and tabulations were used. Sensitivity and specificity were reported in most cases but likelihood ratios in one case only. Sometimes it was difficult to determine the quality of blinding.

Table 10. Methodological characteristics of included studies. The three columns from the right refer to the Cochrane working group standards 1, 2 and 4; violation of 3, 5 and 6 meant exclusion.

| Year | Authors | Diagnostic method | Reference standard | Test and ref.standard measured independently of each other? | Category * | Test measured blind of all clinical information? |
|---|---|---|---|---|---|---|
| 1963 | McNeill (Mcneill 1962) | clin.exam, x-ray | x-ray, SP | No | NA | NA |
| 1980 | Revonta (Revonta 1980) | u-sound, x-ray | SP, x-ray | Yes | I | No |
| 1982 | Kuusela et al. (Kuusela et al. 1983) | u-sound, x-ray | SP | NA | NA | NA |
| 1985 | Berg et al. (Berg and Carenfelt 1985) | clin.exam, u-sound | x-ray or SP | Yes | II | NA |
| 1988 | Berg et al. (Berg and Carenfelt 1988) | clin.exam | SP | NA | NA | Not feasible |
| 1995 | Hansen et | clin.exam | CT (SP for a | Yes | II | Not feasible |

| | | | | | | |
|---|---|---|---|---|---|---|
| | al. (Hansen et al. 1995) | | subgroup) | | | |
| 1995 | van Buchem et al. (van Buchem et al. 1995) | u-sound, x-ray | SP | Yes | I | No |
| 1997 | Savolainen et al. (Savolainen et al. 1997b) | u-sound, x-ray | SP | Yes | I | No |
| 1998 | Laine et al. (Laine et al. 1998) | u-sound, x-ray | SP | Yes | I | No |

* Categories:
I Test measured independently of reference standard and reference standard independently of test (MOST VALID).
II Test measured independently of reference standard but not vice versa.
NA = data not available.
SP= sinus puncture.
CT= computed tomography.

### 5.1.3 Meta-analysis: sinus puncture as reference standard

In the comparisons with sinus puncture as the reference, radiography was the most accurate diagnostic method for AMS. Radiography had both good sensitivity and specificity in the diagnosis of AMS (Table 11). In the two primary care studies (that of van Buchem et al. and that of Laine et al.) the sensitivity was lower than in the hospital-based studies.

The overall results of ultrasound compared with puncture were not much weaker than those of radiography (Table 11) but they were more heterogeneous. Revonta [Revonta 1980] achieved better results than the other authors.

The summary Q* values of radiography and ultrasound were comparable, 0.82 (95 % CI 0.78 – 0.85) for radiography and 0.80 (95 % CI 0.76 – 0.83) for ultrasound (Table 11).

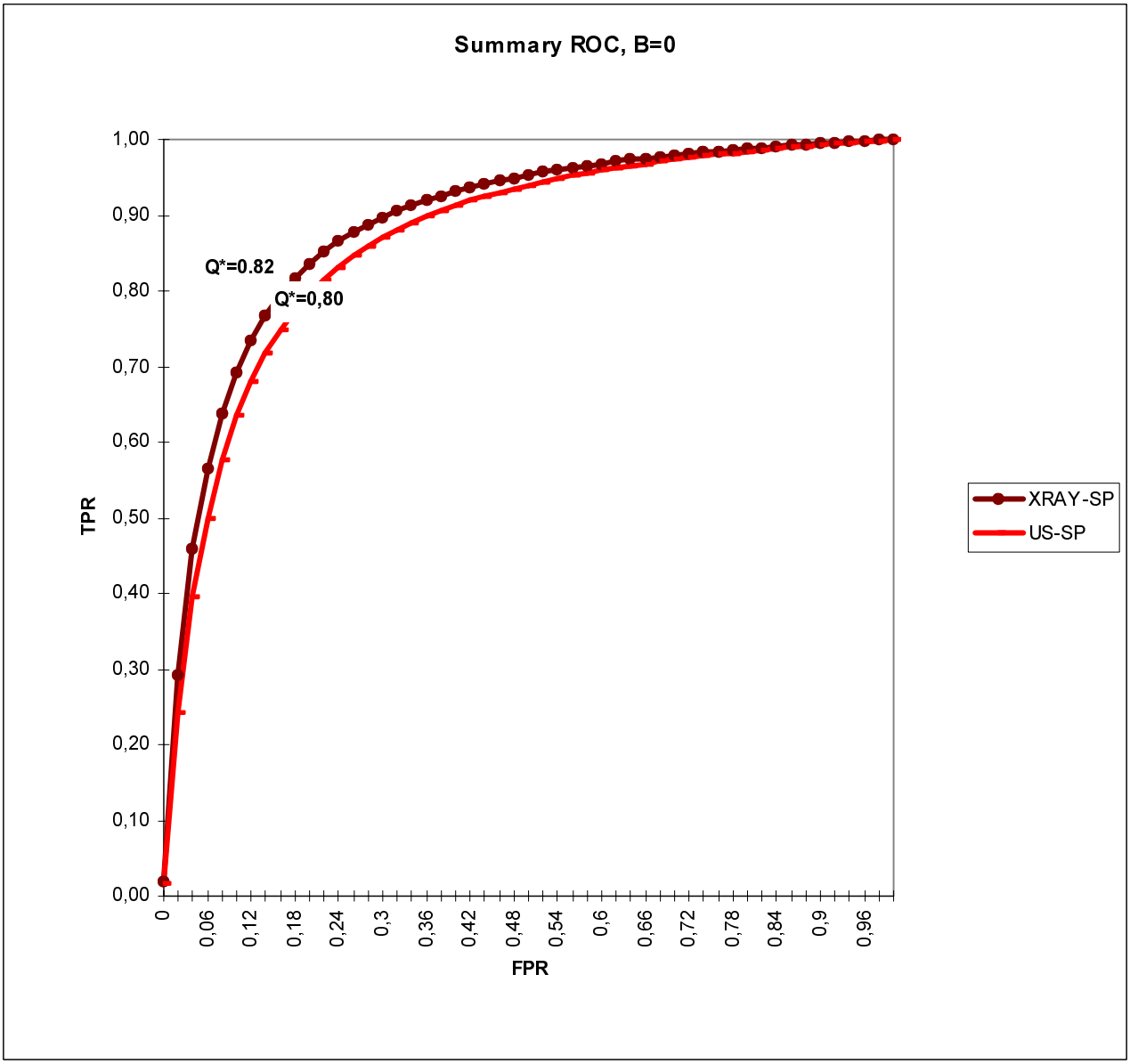
Table 11. Results obtained with summary statistics.

| Comparison | Sinuses in meta-analysis, N | Weighted mean Sensitivity (95% CI) | Weighted mean Specificity (95% CI) | Q* point on summary ROC line (sensitivity =specificity) (95% CI) |
|---|---|---|---|---|
| Radiography-Puncture | 996 | 0.87 (0.85-0.88) | 0.89 (0.88 – 0.91) | 0.82 (0.78-0.85) |
| Ultrasound-Puncture | 940 | 0.85 (0.84-0.87) | 0.82 (0.80-0.83) | 0.80 (0.76-0.83) |

N= number of sinuses.

The SROC curves for radiography and ultrasound compared with sinus puncture are presented in Figure 1.

Figure 1. SROC curves for sinus ultrasound and sinus radiography compared with sinus puncture.




## *5.2. Accuracy of ultrasound in primary care setting (II, III)*

### 5.2.1 Ultrasound compared with sinus puncture (II)

The Nurmijärvi-Kajaani study (II) included 39 patients with a clinically suspected sinusitis, 26 women (67%) and 13 men (33%). The age range of the patients was from 16 to 68 years, and the median was 37 years. 72 sinuses were punctured in 39 patients. Two of the 78 sinuses could not be punctured and for four sinuses the ultrasound result was unclear or lacking.

The sensitivity of ultrasound was 61% and specificity 53% (Table 12). The results were not dependent on the severity of findings on sinus irrigation. This was verified by testing different cut-off points in the interpretation of sinus irrigation findings. The sensitivity of ultrasound was comparable to that of specialist's interpretation of radiographs (61%) but radiographs had a very high specificity (98%).

Table 12. The accuracy of general practitioner ultrasound compared with sinus puncture.

| Ultrasound | Sinus puncture + | Sinus puncture - | Total |
|---|---|---|---|
| + | 14 | 23 | 37 |
| - | 9 | 26 | 35 |
| Total | 23 | 49 | 72 |

Sensitivity = 0.61 (95% CI 0.45 – 0.77)

Specificity = 0.53 (95% CI 0.39 – 0.67)

LR + = 1.3

LR – = 0.9

### 5.2.2 Ultrasound compared with sinus radiography (III)

The multi-centre study included 150 patients with clinically suspected sinusitis, 105 women (70%) and 45 men (30%). The age range of the patients was from 18 to 75 years, and the mean was 39.7 years. The physicians performed sinus ultrasound on 148 patients, and 74 (50%) tested positive.

In the subgroup of 32 patients with radiological confirmation the sensitivity of ultrasound was 71% (95% CI 59 - 82%) and specificity was 91% (95% CI 85 - 98%) (Table 13) when the results were calculated per sinus. The results were better when calculated per patient:

sensitivity 92% (95% CI 83 - 100%) and specificity 95% (95% CI 87 - 100%)(Table 14). Positive likelihood ratios were 8.29 and 17.5, respectively.

Table 13. Comparison of ultrasound by primary care physician versus radiography: Sinuses as the unit of study (n=64)

| Ultrasound | Radiography + | Radiography - | Total |
|---|---|---|---|
| + | 12 | 4 | 16 |
| - | 5 | 43 | 48 |
| Total | 17 | 47 | 64 |

Sensitivity = 0.71(95% CI 0.59 – 0.82)

Specificity = 0.91 (95% CI 0.85 – 0.98)

LR + = 8.29

LR – = 0.32

Table 14. Comparison of ultrasound by a primary care physician versus radiography: Patients as the unit of study (n=32)

| Ultrasound | Radiography + | Radiography - | Total |
|---|---|---|---|
| + | 12 | 1 | 13 |
| - | 1 | 18 | 19 |
| Total | 13 | 19 | 32 |

Sensitivity = 0.92 (95% CI 0.83 – 1.00)

Specificity = 0.95 (95% CI 0.87 – 1.00)

LR + = 17.5

LR – = 0.08

### 5.2.3 Interpretation of ultrasound printouts (III)

Examinations of 129 patients were printed and analysed also by an ENT specialist (Matti Revonta). The interpretations of ultrasound examinations by the primary care physicians and the interpretations of the printouts by the specialist correlated moderately well (Table 15). The observed agreement was 81% and the Cohen's Kappa for agreement was 0.47. The specialist disagreed on sinusitis diagnosis in 35 cases. Of these, the reading of ultrasound printouts revealed 11 sinuses (31%) with a false positive A-mode echo peak at the distance of 3.5 cm or more caused by multiple reflections of the ultrasound between the probe and air in an aerated sinus.

Table 15. Agreement of ultrasound by a primary care physician and interpretation of ultrasound printouts by a specialist (Number of sinuses 251)

| Primary care physician | ENT specialist: Sinusitis | Specialist: No sinusitis |
|---|---|---|
| Sinusitis | 33 | 35 |
| No sinusitis | 12 | 171 |

Observed agreement 81%, Cohen's Kappa 0.47 (moderate agreement)

## *5.3. Ultrasound and the management of sinusitis patients (IV)*

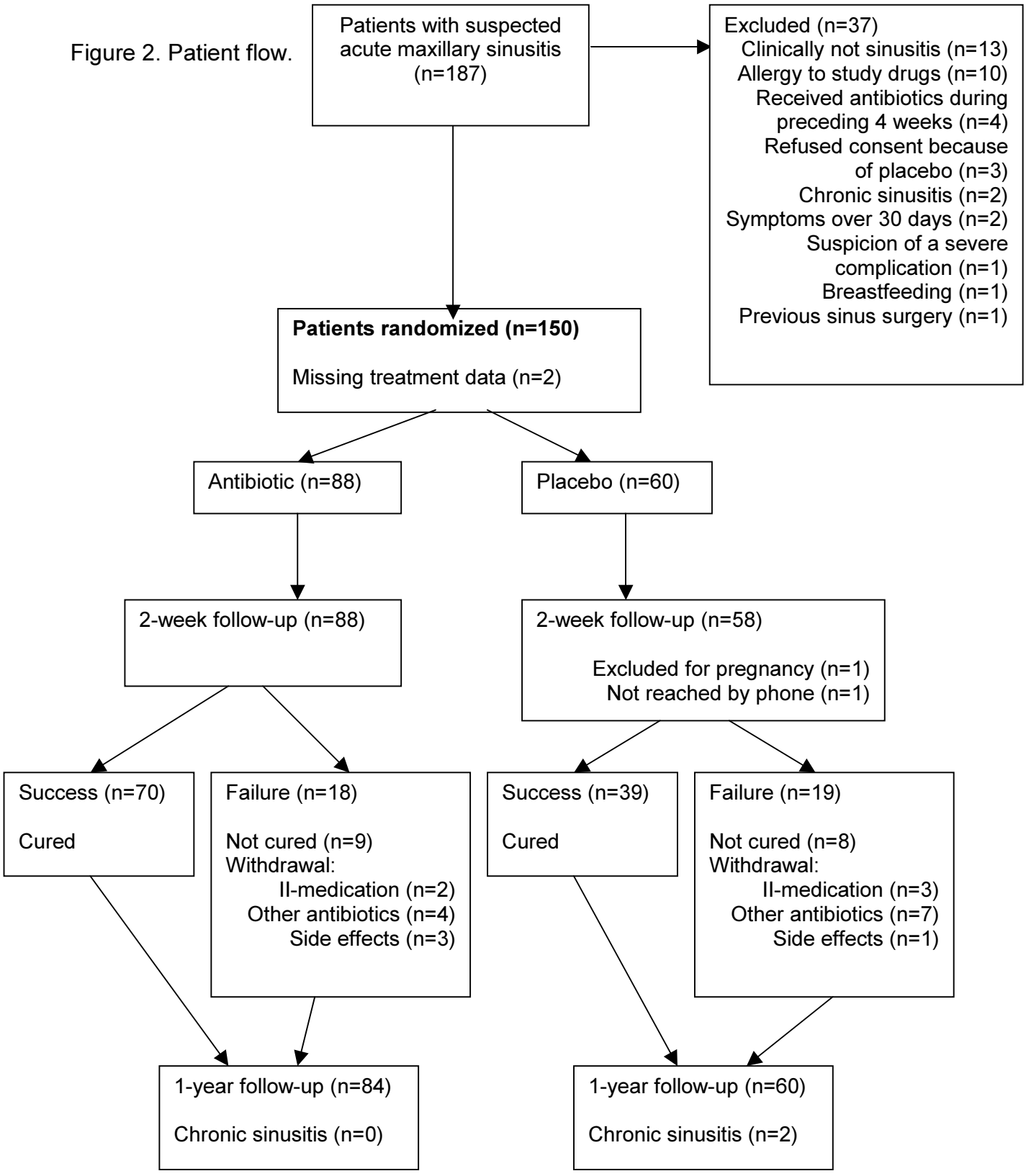
### 5.3.1 Main results

The patient flow in the study is presented in Figure 2. A total of 125 patients (83%) reported having had AMS before and 45 (30%) had experienced sinus puncture. Two weeks after consultation, 149 patients were interviewed by telephone, and 122 patients returned completed diaries by mail.

The physicians performed sinus ultrasound on 148 patients, and 74 (50%) tested positive. Fourteen patients (23%) had bilateral sinusitis. At Karstula health centre, 32 patients had sinus radiographies taken, and 13 (41%) had a radiologically diagnosed AMS.

The main outcome, recovery at the two-week follow up, was slightly but not significantly better in patients receiving active treatment, antibiotics (70/88, 80%), than in the placebo group (39/59 patients, 67%, $\chi^2$=3.33, DF=1, p=0.068). There were no differences between antibiotics (clinical success rates 18/23, 78% for amoxicillin, 26/33, 79% for doxycycline and 26/32, 81% for penicillin V).

Figure 2. Patient flow.



### 5.3.2 Subgroups of ultrasound positive and negative patients

Results split by ultrasound findings are presented in Table 16. Ultrasound positive and negative patients had similar symptom scores in the beginning of study (15.3, SD 4.3 and 15.4, SD 4.3, respectively). At the 2-week follow up patients with sinusitis on ultrasound examination had recovered better (symptom score 2.8, SD 3.2) than those without findings (symptom score 4.1, SD 3.8, p=0.03). In the placebo group, patients who had sinusitis on ultrasound started other antibiotics and withdrew from the study more often than those with no sinusitis on ultrasound (7/32, 22% versus 3/25, 12%, p=0.33) (Table 14).

Table 16. Main outcome split by status in ultrasound examination

| | Antibiotic | Placebo | Total |
|---|---|---|---|
| Ultrasound: Sinusitis (n=72) | (n=40) | (n=32) | |
| Success: Cured | 32 (80%) | 23 (72%) | 55 |
| Failure: | 8 | 9 | 17 |
| Not cured | 3 | 1 | |
| II medication | 2 | 1 | |
| Drop out: other | 1 | 6 | |
| antibiotic | 2 | 1 | |
| Drop out: side-effects | | | |
| Ultrasound: No sinusitis (n=72) | (n=47) | (n=25) | |
| Success: cured | 37 (79%) | 15 (60%) | 52 |
| Failure: | 10 | 10 | 20 |
| Not cured | 6 | 7 | |
| II medication | 0 | 2 | |
| Drop out: other | 3 | 1 | |
| antibiotic | | | |
| Drop out: side-effects | 1 | 0 | |
| Total | 87 | 57 | 144 |

### 5.3.3 Follow up

One-year follow up data was available for 144 patients, for 60 in the placebo arm and for 84 in the antibiotics group. Two patients in the placebo group developed a chronic sinusitis in follow up, and both of them had AMS in ultrasound examination. There were no differences in the number of cases with recurrent sinusitis in the study groups, but the patients who received antibiotics consulted slightly more often because of respiratory tract infections during the follow up year (32% versus 26%, p=0.42).

## *5.4 Costs of additional examinations for rhinosinusitis*

We assessed the costs resulting from additional testing in rhinosinusitis. Both market prices (private health services) and average true costs used in a Finnish health centre (Pekka Honkanen, personal communication and Heikkinen et al. 2001) are presented in Table 17.

Table 17. Market prices and average cost of additional examinations in sinusitis.

| | Market price | Average cost in health centre |
|---|---|---|
| Sinus ultrasound examination | 10 – 25€ | 0€ (considered part of clinical examination) |
| Sinus radiography, four views | 72€ | 28€ |
| Sinus radiography, one view | 65€ | 27€ |
| Bacteriologic culture | 37€ | 21€ |
| CRP | 12 – 25€ | 3€ |

When sinus ultrasound is introduced in a health centre, resources are needed not only for the equipment but also to teach the physicians to use the device (Table 18). The costs of a small group tutorial by a specialist can be estimated at 60€ per physician. The Sinuscan devices are not prone to technical problems, only the battery needs to be replaced approximately every three years (Manufacturers information). The additional yearly costs of sinus ultrasound per physician can hence be estimated at 178€ per year (Table 18). The primary care physician encounters approximately 100 – 200 patients with a acute rhinosinusitis in a year. Hence, the true additional cost of sinus ultrasound per examination can be estimated at 1 – 2 €.

Table 18. Estimated yearly costs related to sinus ultrasound use per physician

| Item | Cost |
|---|---|
| Education, 1.5 h tutorial | 60€ every sixth year |
| Ultrasound device | 752€ every sixth year |
| Service and repair (Includes a new battery) | 100€ every third year |

| | |
|---|---|
| Gel | 10€ every year<br><br>Estimated total cost per year 178€ |

## *5.5 Patient and physician views (V)*

Overall, 88% of patients (177/202) and 70% (245/348) of physicians responded to the survey after reminding. We conducted eight focus group interviews; the four patient groups included 22 and the four physician groups 20 participants. The focus group sessions lasted from 1 to 1.5 hours. In the survey, 145 patients (82%) reported that they had been diagnosed as having AMS on their last consultation and all but one had received a prescription for antibiotics. Three quarters of all survey patients had other diagnostic tests done besides clinical examination during their last visit, and some of them had several tests. The frequency of tests used on study patients is presented in Table 19.

Table 19. Diagnostic tests performed in addition to clinical examination to study patients at the last visit (some patients underwent several tests )

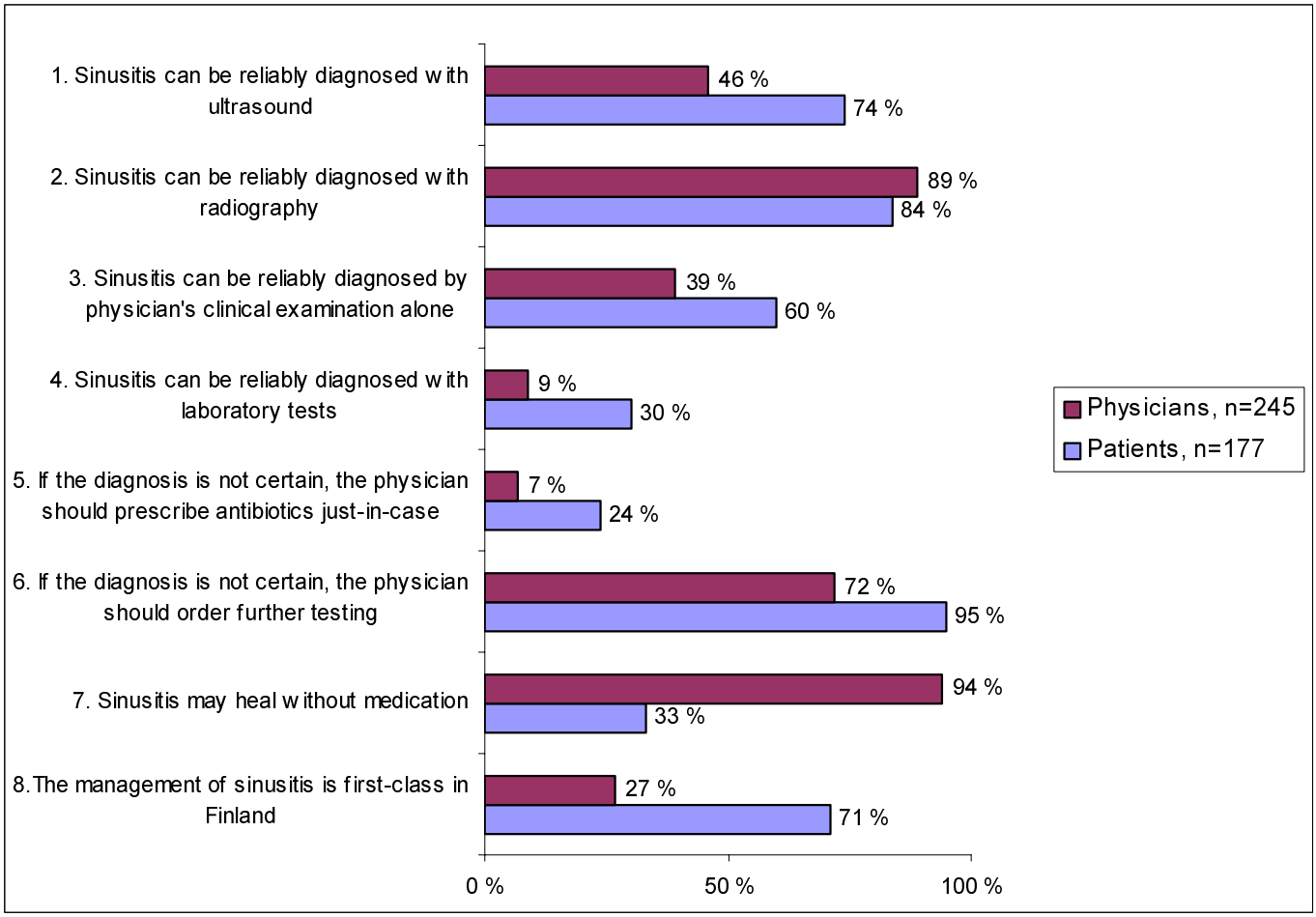
| Diagnostic method used | N =175 | % |
|---|---|---|
| Ultrasound | 103 | 58 |
| Radiography | 36 | 21 |
| Blood tests (CRP, leukocytes) | 13 | 7 |
| Sinus puncture | 17 | 10 |
| Clinical examination alone | 41 | 23 |

### 5.5.1 Management of sinusitis

The patients had less trust than the physicians in the natural healing process of AMS: 33% of patients as opposed to 95% of physicians agreed that AMS might heal without medication ($\chi^2$= 207, DF=4, p<0.0001) (Figure 3). In the focus groups the physicians described AMS as a difficult diagnosis and they sometimes faced the uncertainty with frustration. 'This sinusitis, the diagnosis is mainly the same nonsense as prolonged respiratory infections; we do not have the vainest idea what we are treating there. What is the meaning to see whether there is retention in sinus or not as we cannot know whether it is bacterial or viral, there is no guarantee at all…' (female, physician, 37 y.)

Patients had a better picture of the current treatment of AMS than the physicians. The statement 'the diagnosis and treatment of acute maxillary sinusitis are first-class in Finland' was agreed with by 71% of patients (126/177) and by 27 % of physicians (66/245) ($\chi^2$= 91, DF=4, p<0,0001) (Figure 3).

Figure 3. Percentage of patients and physicians who agreed with the survey statements on the management of sinusitis.




The patients in focus groups reported that they primarily wanted to know what was wrong with them. They wanted to be listened to in decisions about diagnostic and treatment choices. 'In my opinion, the most important thing is to have sinusitis diagnosed reliably. Then the patient should have right to decide whether to have a sinus puncture or not, and not just medication pushed first, and follow-up is important, too' (male, patient, 25 y.). The negative experiences included problems with communication, negligent attitudes or harsh comments from the physician. Some patients wondered why physicians prescribe antibiotics even though they have not been able to verify the diagnosis with imaging methods. 'It seems that it [the ultrasound] is like an addition, the physician may ask if the

patient wishes for it … but treatment with antibiotics is felt to be a matter of course anyway.' (female, patient, 43 y.).

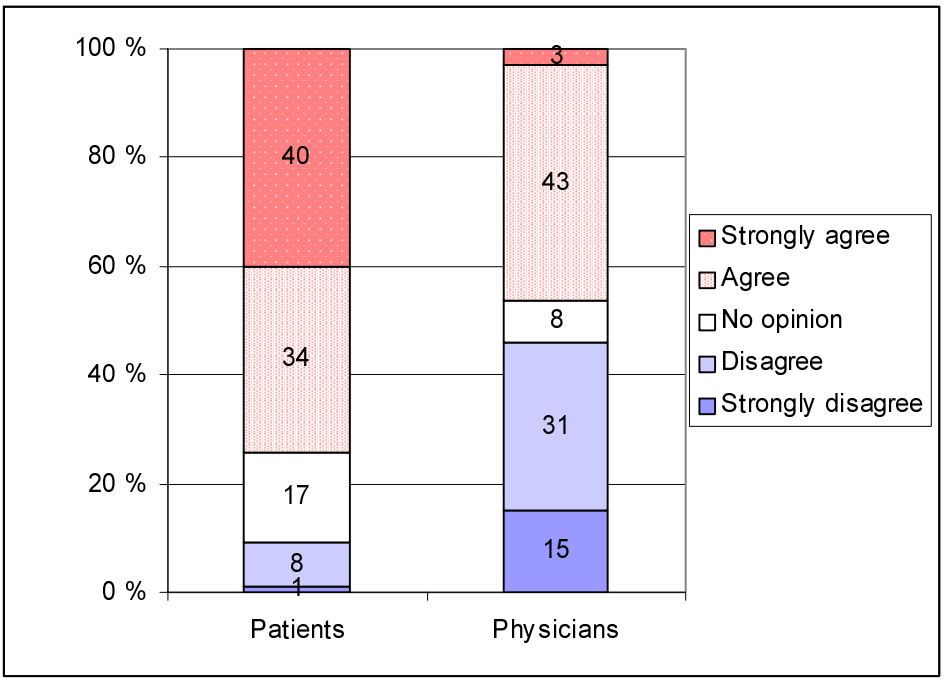
In the survey, 88% of the physicians agreed with the statement that too many antibiotics are prescribed for AMS in Finland. They did not approve of antibiotics prescribed just in case. 85% disagreed with the statement: 'If the diagnosis of AMS is uncertain, antibiotics should be prescribed to be on the safe side'. In the focus groups it was evident that this was the actual practice: the physicians prescribed antibiotics for security reasons. 'When you give a prescription of antibiotics to a probable sinusitis patient, you feel safe, you can sleep your nights in peace.' (male, physician, 45 y.)

### 5.5.2 Attitudes towards sinus ultrasound

Patients had better trust on the reliability of ultrasound than physicians (Figure 4). 74% of the patients compared with 46% of the physicians agreed that sinusitis could be diagnosed reliably by ultrasound. In the focus groups the patients saw ultrasound as a practical and comfortable method. They suggested that there should be more ultrasound devices available in health centres.

The physicians had divided attitudes, 46% agreed and 46% disagreed with the reliability of ultrasound (Figure 4). Conceptions of the accuracy of ultrasound varied and personal experience was very important. If ultrasound had once given contradictory results with sinus puncture, it was easily put aside. On the other hand, many physicians in the focus groups were active users of sinus ultrasound and they had good experiences of it.

Figure 4. 'Sinusitis can be diagnosed reliably by ultrasound'. Patient and physician answers to survey.




### 5.5.3 Changing practice

The patients' willingness to accept the results of the van Buchem study varied (Table 20). The older patients with a history of several AMS episodes could least accept the study results and a potential change in AMS treatment pattern. Younger patients and those with less experience of AMS regarded the news that antibiotics may not be needed for AMS as good news: they mentioned the cost savings and the importance of symptomatic medication. Physicians were more willing to accept the study results but they considered changing practice difficult and emphasized the need of both national and local guidelines and patient information to support the change (Table 20).

Table 20. The reactions of patients and physicians in the focus groups to the study (van Buchem et al. 1997) in which placebo was as effective as antibiotics for AMS.

| Patients | Physicians |
|---|---|
| 'Do I understand right, the placebo is no drug at all? This is hard to believe.' (female, 24 y.) | 'I don't think this Lancet paper is any surprise to any of us colleagues here' (male 40 y.) |
| 'It depends on the nasal sprays they had, perhaps they were effective then' (female, 42 y.) | 'There is great need for patient information. May I take this summary, copy and use it as a patient leaflet?' (male 46 y.) |
| 'You cannot get rid of it [AMS] with just thought' (male, 50 y.). 'Nor with chalk tablets…' (laughing, female, 49 y.) | 'Still, this is just one study, ' (female, 35 y.) |
| 'You may think that people have always had sinusitis and they used to recover without medication…on the other hand they may have died too, without medication…' (female, 55 y.) | 'It is hard to change practice. Not prescribing antibiotics would be a radical change.' (male, 45 y.) |
| 'Next time, I'll take a good look at myself and ask myself which placebo to take this time?' (female, 50 y.). | 'As a young physician you better do like the older colleagues do' (female, 24 y.) |

# 6. DISCUSSION

## *6.1 Accuracy of sinus ultrasound*

In our meta-analysis, the accuracy of sinus ultrasound was similar to that of radiography in the diagnosis of AMS. Sinus ultrasound was accurate if the aim was to detect fluid in the maxillary sinus as a sign of AMS. There was variability in the results between different

studies. This may be explained by different aims: ultrasound is not accurate in the diagnosis of mucosal swellings, and in patients with chronic sinusitis polypoid masses may resemble fluid in the sinuses (Vento et al. 1999). Another meta-analysis by Engels et al on diagnosing AMS produced similar figures but somewhat different conclusions: although unspecific, clinical examination was recommended (Engels et al. 2000). In the United States sinus ultrasound is a specialist examination not readily available to primary care physicians.

The accuracy of ultrasound depends greatly on the user. Specialists have achieved better results than primary care physicians. In the Nurmijärvi-Kajaani study (II) where the primary care physicians only had the manufacturer's written information, many false positive diagnoses were made. Because of imperfect examination techniques physicians may interpret normal anatomy as sinusitis.

The physicians in the multi-centre study learnt the correct pattern of ultrasound reading. It is probable that the small group tutorial had an effect on the physicians' ability to interpret the sinus ultrasound. The overall correlation of ultrasound interpretations by the specialist and the primary care physicians was good - of the 251 sinuses agreement was found in 204 (81%).

## *6.2 Clinical outcomes*

In our RCT, only half of primary care patients with a clinical suspicion of sinusitis had fluid in sinus ultrasound examination. If ultrasound would be used more widely in health centres, a large number of unnecessary antibiotic prescriptions for AMS could be avoided.

Antibiotics were slightly more effective than placebo for patients with sinusitis diagnosed by clinical criteria. Recovery was similar at two weeks; however, patients who received antibiotics recovered faster, having lower symptom scores on day 3. This finding is in line with the Cochrane review and another meta-analysis: antibiotics produce a statistically significant but small treatment effect in AMS [De Ferranti et al. 1998,Williams et al. 2000].

In our study refraining from giving antibiotics to the ultrasound-negative patients did not cause prolonged disease or complications. The two patients who developed chronic sinusitis were both ultrasound-positive and in the placebo group. No complications were seen in the ultrasound-negative patients in this material where severe cases were excluded.

The ultrasound-positive patients had a more severe pattern of disease and, if given placebo, they withdrew from study and started antibiotics during the two-week follow up more often than the ultrasound-negative patients. A problem is that because of unexpectedly low recruitment, the ultrasound subgroups were too small for definite conclusions.

## *6.3 Acceptability of sinus ultrasound*

The patients with rhinosinusitis did not merely wish for antibiotics but for a proper diagnosis and physician's explanations. They confronted the problem of AMS rather differently than the physicians. The patients did not know about the diagnostic uncertainty that suspected AMS may pose to the physician, instead they trusted the diagnostic methods. Some patients had a rather worried attitude towards AMS and its possible consequences: the stories of potential complications still live in the patients' mind. Very few patients thought that acute maxillary sinusitis could be a self-limiting disease as indicated by the latest research (De Ferranti et al. 1998).

In 1974 Argyris and Schön described two kinds of explanations that can be distinguished for behaviour: espoused theories that we believe we follow, and theories-in-use that actually explain what we do (Argyris and Schön 1974). Examples of espoused theory were evident in the physician survey: physicians presented views such as no antibiotics just in case for AMS, and that the management of AMS should be rational. The theory-in-use was revealed in the focus groups: the primary care physicians in Finland did not feel comfortable with the management of AMS. They felt forced to act opposite to what they believed to be correct: they kept on prescribing antibiotics for safety and because of the expectations of the patients even though they thought it was wrong.

Our study emphasizes the physician's role in communicating his findings and informing the patient. There was little consistency in the responses of the patients and the physicians in the survey to different aspects of the management of AMS, which reflects the lack of

communication. With modern empowered patients the physicians may need to turn their focus from curing infections to active listening and explaining [Charles et al. 2000].

The rhinosinusitis patients in the survey and focus groups had a positive attitude towards sinus ultrasound. They had high confidence in the accuracy of this method, and they valued the lack of radiation and the possibility of having the results immediately. Half of the physicians were opposed to sinus ultrasound, and the other half favoured it.

## *6.4 Costs*

A few attempts have been made to analyse the cost-effectiveness of sinusitis management [Balk et al. 2001,De Bock et al. 2001]. Because of differences in health care systems they cannot be generalized in Finland. In both analyses, ultrasound also was a secondary care investigation. Performing cost-effectiveness analysis for diagnostic techniques is complex [Sassi et al. 1997] and requires information of the utilities of different outcomes, the point of view of the patient and the physician [De Bock et al. 1999,Drummond 1987,Torrance 1987].

We only described the average additional costs sinus ultrasound produces, which are minor in a health centre budget. If sinus ultrasound could replace clinical work up, productivity might increase, especially in out-of-hours services. Performing and reporting ultrasound takes much less time than a proper clinical examination and reporting the findings in patient files. The productivity issue of sinus ultrasound should be evaluated in an empiric study.

## *6.5 Strengths and weaknesses of methods*

This set of studies was designed to form a comprehensive picture of sinus ultrasound in AMS management in primary care. As a basis a systematic review and meta-analysis was performed. In original studies both quantitative and qualitative approaches were used. The diagnostic studies were conducted in a patient population where the test is used, and verification bias was avoided by blinded comparisons (Ransohoff and Feinstein 1978). The empirical studies included a randomized controlled trial. Conducting a multi-centre RCT in primary care is challenging, and there are not many examples of such in Finnish primary care. Our RCT had a strong strategy: we combined diagnosis and treatment, the study was conducted in a real-life situation and the length of follow up was adequate.

A problem in the RCT was the slow rate of patient recruitment. Conducting underpowered studies should be avoided in all possible ways and adequate resources are a precondition (Halpern et al. 2002). The slow recruitment was a disappointment to us, and we tried to find out what the barriers had been. The first mentioned barrier was work pressure. Sinusitis is mostly treated during busy on-call hours, when filling study forms may be too much of a burden for the physician. Another problem was the placebo arm. Giving placebo to patients who normally would be treated with antibiotics was such a radical change of practice that the physicians might have needed more support from the researchers. Also, financial support was lacking: we did not remunerate the participating physicians for their work. Competing trials on other diseases with better benefits to physicians were meanwhile run by the pharmaceutical industry.

Randomized controlled trials are still uncommon in primary care settings. Primary care physicians face a great diversity of clinical problems and finding suitable study patients in an unselected population is complicated. Also, the motivation varies because the central assumptions of the evidence based medicine paradigm may not be shared by all primary care physicians [Tomlin et al. 1999]. Several studies have assessed the factors that facilitate primary care RCTs, and they include recruitment by a peer physician, assistance of a clinical research nurse, and motivation driven by the research group[De Wit et al. 2001,Sellors et al. 2002].

Lack of good reference standards makes studying the accuracy of ultrasound challenging in primary care settings. Radiography was the only feasible reference standard in our multi-centre study. Computed tomography is generally not available in primary care, and it also tends to produce false-positive findings [Gwaltney et al. 1994,Lindbaek et al. 1996c]. Sinus puncture is an accurate reference standard, but it is invasive and not ideal for primary care patients. In the Nurmijärvi-Kajaani study (II) patient recruitment was probably slow because of the invasive reference standard.

Radiography is not an error-free reference standard, and both false-negative and false-positive interpretations are possible. False-negative interpretations are even more likely when only one view is used. An imperfect reference standard reduces the estimated sensitivity and specificity of the test studied [Begg 1987]. The misclassifications arising from the imperfect reference standard can be corrected statistically [Staquet et al. 1981]. However, the size of our material did not allow making these corrections.

## *6.6 Concluding remarks*

Unnecessary prescribing of antibiotics for an upper respiratory tract infection has a long history [Hemminki et al. 1974] and remains the basic issue in the management of rhinosinusitis. In most countries the current clinical practice in AMS lies far from research evidence: AMS is diagnosed by diffuse clinical criteria and treated actively, often with broad-spectrum second-line antibiotics [Brooks et al. 2000,Klossek and Chidiac 2001,Low et al. 1997,Mainous and Hueston 1998]. To change this practice, a combination of several behavioural strategies would be needed [Bero et al. 1998,Oxman et al. 1995,Solomon et al. 1998]. Methods that have proved effective in changing practice include clinical protocols [Kinney 2002], medical audit [Melander et al. 1999], and reimbursement strategies [Friis et al. 1993].

An effective diagnostic strategy is the cornerstone in the management of rhinosinusitis. Diagnostic methods could be studied in randomized controlled trials [Cochrane 1972,Larsen et al. 1990]. An intriguing study design would be to randomize rhinosinusitis patients either to ultrasound or clinical examination, and treat them according to the result either with antimicrobial or symptomatic treatment. The criteria of clinical examination should be standardized, choosing the most specific clinical signs (maxillary toothache, purulent discharge). In this study the measured outcomes would be the number of AMS diagnosed, use of antibiotics in different study arms, and patient outcomes such as clinical cure and patient satisfaction. A validated instrument for clinical cure would also be required.

More research is needed to compare feasible strategies of AMS diagnosis in primary care to bridge the gap between current practice and the evidence. In proper use sinus ultrasound is accurate and practical and has no adverse effects. The findings in this thesis

suggest that sinus ultrasound may also decrease the prescribing of unnecessary antibiotics, and increase productivity and patient satisfaction. These topics warrant confirmation in further studies in primary care.

## 7. CONCLUSIONS

1., Sinus ultrasound has accuracy similar to that of sinus radiography in the diagnosis of AMS. Ultrasound is a highly user-dependent method. Sinus ultrasound is accurate in detecting fluid in maxillary sinuses but not in predicting cysts or mucosal thickening.

2. With practice and training, primary care physicians can achieve similar sensitivity and specificity in sinus ultrasound examination as specialists. Even a short tutorial improves primary care physicians' accuracy in. Training should emphasize the origins of possible false positive interpretations in sinus ultrasound.

3. Ultrasound positive rhinosinusitis patients seem to have a more severe pattern of disease than the ultrasound negative ones. Half of the patients with a clinical diagnosis of AMS have sinusitis in ultrasound examination. Use of sinus ultrasound reduces the number of unnecessary antibiotic prescriptions for rhinosinusitis in primary care.

4. Sinus ultrasound is less expensive than the other additional diagnostic options for patients with suspected AMS.

5. Most patients with acute rhinosinusitis primarily wish that the physician aimed at making a specific diagnosis. They respect the use of diagnostic imaging to achieve a reliable diagnosis. Very few patients are aware that acute rhinosinusitis can be a self-limiting disease and many fear potential complications.

6. Primary care physicians consider AMS as a difficult diagnosis. Physicians are not satisfied with the current management. They feel they are forced to prescribe unnecessary antibiotics for rhinosinusitis because of patient expectations and lack of good diagnostic device.

## ACKNOWLEDGEMENTS

References


1. Adelglass J, Jones TM, Ruoff G, Kahn JB, Wiesinger BA, Rielly-Gauvin K et al. A multicenter, investigator-blinded, randomized comparison of oral levofloxacin and oral clarithromycin in the treatment of acute bacterial sinusitis. Pharmacotherapy 18, 1255-63 (1998).
2. Antila J. Acute frontal sinusitis in adults. Sarja D. Osa 353. Turun yliopisto, Turku, (1999).
3. Argyris C,Schön D. Theory in practice. (Jossey-Bass., San Fransisco, 1974).
4. Atkins D,Larson EB. X-rays for sinusitis: a matter of which or when? J Gen Intern Med 7, 566 (1992).
5. Axelsson A,Brorson JE. The correlation between bacteriological findings in the nose and maxillary sinus in acute maxillary sinusitis. Laryngoscope 83, 2003-11 (1973).
6. Axelsson A, Chidekel N, Grebelius N,Jensen C. Treatment of acute maxillary sinusitis. A comparison of four different methods. Acta Otolaryngol 70, 71-6 (1970a).
7. Axelsson A, Chidekel N, Grebelius N, Jensen C,Sarne S. Treatment of acute maxillary sinusitis. II. A comparison of five further methods. Acta Otolaryngol 72, 148-54 (1971).
8. Axelsson A, Grebelius N, Chidekel N,Jensen C. The correlation between the radiological examination and the irrigation findings in maxillary sinusitis. Acta Otolaryngol 69, 302-6 (1970b).
9. Axelsson A,Runze U. Symptoms and signs of acute maxillary sinusitis. ORL 38, 298-308 (1976).

10. Bailey BJ. Landmark perspective: Abscess of the antrum. Jama 250, 400-4 (1983).
11. Balk EM, Zucker DR, Engels EA, Wong JB, Williams JW, Jr.,Lau J. Strategies for diagnosing and treating suspected acute bacterial sinusitis: a cost-effectiveness analysis. J Gen Intern Med 16, 701-11 (2001).
12. Barden LS, Dowell SF, Schwartz B,Lackey C. Current attitudes regarding use of antimicrobial agents: results from physician's and parents' focus group discussions. Clin Pediatr 37, 665-71 (1998).
13. Bauer WJ, Bockmeyer M,Mang WL. Endoskopisch kontrollierte Ultraschalldiagnostik der Kieeferhöhlen. Laryng Rhinol Otol 62, 443-5 (1983).
14. Begg CB. Biases in the assessment of diagnostic tests. Stat in Med 6, 411-23 (1987).
15. Benninger MS, Anon J,Mabry RL. The medical management of rhinosinusitis. Otolaryngol Head Neck Surg 117, S41-9 (1997).
16. Benninger MS, Sedory Holzer SE,Lau J. Diagnosis and treatment of uncomplicated acute bacterial rhinosinusitis: summary of the Agency for Health Care Policy and Research evidence-based report. Otolaryngol Head Neck Surg 122, 1-7 (2000).
17. Benninger MS,Senior BA. The development of the Rhinosinusitis Disability Index. Arch Otolaryngol Head Neck Surg 123, 1175-9 (1997).
18. Berg O, Bergstedt H, Carenfelt C, Lind MG,Perols O. Discrimination of purulent from nonpurulent maxillary sinusitis. Clinical and radiographic diagnosis. Ann Otol Rhinol Laryngol 90, 272-5 (1981).
19. Berg O,Carenfelt C. Analysis of symptoms and clinical signs in the maxillary sinus empyema. Acta Otolaryngol 105, 343-9 (1988).
20. Berg O,Carenfelt C. Etiological diagnosis in sinusitis: ultrasonography as clinical complement. Laryngoscope 95, 851-3 (1985).

21. Berg O, Carenfelt C,Kronvall G. Bacteriology of maxillary sinusitis in relation to character of inflammation and prior treatment. Scand J Infect Dis 20, 511-6 (1988).

22. Berg O, Carenfelt C, Rystedt G,Anggard A. Occurrence of asymptomatic sinusitis in common cold and other acute ENT-infections. Rhinology 24, 223-5 (1986).

23. Berger WE. Use of A-mode ultrasound for diagnosis of sinus disease in young children. Ann Allergy 56, 39-43 (1986).

24. Bero LA, Grilli R, Grimshaw JM, Harvey E, Oxman AD,Thomson MA. Closing the gap between research and practice: an overview of systematic reviews of interventions to promote the implementation of research findings. The Cochrane Effective Practice and Organization of Care Review Group. BMJ 317, 465-8 (1998).

25. Bertrand B, Jamart J, Marchal JL,Arendt C. Cetirizine and pseudoephedrine retard alone and in combination in the treatment of perennial allergic rhinitis: a double-blind multicentre study. Rhinology 34, 91-6 (1996).

26. Blevald NR. History of the treatment of maxillary sinusitis. J Laryngol Otol 71, 806-23 (1957).

27. Blomgren K, Hytonen M, Pellinen J, Relander M,Pitkaranta A. Diagnostic accuracy of acute maxillary sinusitis in adults in primary care. Scand J Prim Health Care 20, 40-4 (2002).

28. Brook I. Aerobic and anaerobic bacterial flora of normal maxillary sinuses. Laryngoscope 91, 372-6 (1981).

29. Brook I, Frazier EH,Foote PA. Microbiology of chronic maxillary sinusitis: comparison between specimens obtained by sinus endoscopy and by surgical drainage. J Med Microbiol 46, 430-2 (1997).

30. Brook I, Friedman EM, Rodriguez WJ,Controni G. Complications of sinusitis in children. Pediatrics 66, 568-72 (1980).

31. Brooks I, Gooch WM, 3rd, Jenkins SG, Pichichero ME, Reiner SA, Sher L et al. Medical management of acute bacterial sinusitis. Recommendations of a clinical advisory committee on pediatric and adult sinusitis. Ann Otol Rhinol Laryngol Suppl 182, 2-20 (2000).

32. Burke TF, Guertler AT,Timmons JH. Comparison of sinus x-rays with computed tomography scans in acute sinusitis. Acad Emerg Med 1, 235-9 (1994).

33. Calhoun KH,Hokanson JA. Multicenter comparison of clarithromycin and amoxicillin in the treatment of acute maxillary sinusitis. Arch Fam Med 2, 837-40 (1993).

34. Calhoun KH, Waggenspack GA, Simpson GA, Hokanson JA,Bailey BJ. CT evaluation of the paranasal sinuses in symptomatic and asymptomatic populations. Otolaryngol Head & Neck Surg 104, 477-81 (1991).

35. Camacho AE, Cobo R, Otte J, Spector SL, Lerner CJ, Garrison NA et al. Clinical comparison of cefuroxime axetil and amoxicillin/clavulanate in the treatment of patients with acute bacterial maxillary sinusitis. Am J Med 93, 271-6 (1992).

36. Charles C, Gafni A,Whelan T. How to improve communication between doctors and patients. Learning more about the decision making context is important. BMJ 320, 1220-1 (2000).

37. Cochrane AL. in Effectiveness and efficiency Random reflections on health services 35-44 (The Nuffield Trust, London, 1972).

38. Cochrane Methods Working Group on Systematic Review of Screening and Diagnostic Test. Recommended Methods. (Available at http://som.flinders.edu.au/cochrane/, 1997).

39. Cohen S, Doyle WJ, Skoner DP, Rabin BS,Gwaltney JM, Jr. Social ties and susceptibility to the common cold. JAMA 277, 1940-4 (1997).

40. Crater SE, Peters EJ, Phillips CD,Platts-Mills TA. Prospective analysis of CT of the sinuses in acute asthma. AJR Am J Roentgenol 173, 127-31 (1999).

41. de Bock GH, Dekker FW, Stolk J, Springer MP, Kievit J, van et al. Antimicrobial treatment in acute maxillary sinusitis: a meta- analysis. J Clin Epidemiol 50, 881-90 (1997).

42. de Bock GH, Reijneveld SA, van Houwelingen JC, Knottnerus JA,Kievit J. Multiattribute utility scores for predicting family physicians' decisions regarding sinusitis. Med Decis Making 19, 58-65 (1999).

43. de Bock GH, van Erkel AR, Springer MP,Kievit J. Antibiotic prescription for acute sinusitis in otherwise healthy adults. Clinical cure in relation to costs. Scand J Prim Health Care 19, 58-63 (2001).

44. de Ferranti SD, Ioannidis JP, Lau J, Anninger WV,Barza M. Are amoxycillin and folate inhibitors as effective as other antibiotics for acute sinusitis? A meta-analysis. BMJ 317, 632-7 (1998).

45. de Wit NJ, Quartero AO, Zuithoff AP,Numans ME. Participation and successful patient recruitment in primary care. J Fam Pract 50, 976 (2001).

46. Delbanco TL. Quality of care through the patients eyes. BMJ 313, 832-3 (1996).

47. Dessi P, Champsaur P, Paris J,Moulin G. [Imaging of the adult sinusitis: indications for using conventional techniques, CT scan and MRI]. Rev Laryngol Otol Rhinol (Bord) 120, 173-6 (1999).

48. Diagnosis and treatment of uncomplicated acute sinusitis in children. Evid Rep Technol Assess (Summ) Suppl 9, 1-3 (2000).

49. Dobson MJ, Fields J,Woodford T. A comparison of ultrasound and plain radiography in the diagnosis of maxillary sinusitis. Clinical Radiology 51, 170-2 (1996).

50. Dolan KD,Smoker WR. Paranasal sinus radiology, Part 4A: Maxillary sinuses. Head Neck Surg 5, 345-62 (1983).

51. 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 286, 3097-105 (2001).

52. Drettner B,Lindholm CE. The borderline between acute rhinitis and sinusitis. Acta Otolaryngol 64, 508-13 (1967).

53. Druce HM. Diagnosis of sinusitis in adults: History, physical examination, nasal cytology, echo and rhinoscope. J Allergy Clin Immunol 90, 436-41 (1992).

54. Druce HM. Emerging techniques in the diagnosis of sinusitis. Ann Allergy 66, 132-6 (1991).

55. Druce HM. The use of ultrasound as an imaging technique in the diagnosis of sinusitis. N Engl Reg Allergy Proc 9, 109-12 (1988).

56. Druce HM,Slavin RG. Sinusitis: a critical need for further study. J Allergy Clin Immunol 88, 675-7 (1991).

57. Drummond MF. Discussion: Torrances "utility approach to measuring health-related quality of life". J Chron Dis 40, 601-3 (1987).

58. Dubois J, Saint-Pierre C,Tremblay C. Efficacy of clarithromycin vs. amoxicillin/clavulanate in the treatment of acute maxillary sinusitis. Ear Nose Throat J 72, 804-10 (1993).

59. Durr DG, Desrosiers MY,Dassa C. Impact of rhinosinusitis in health care delivery: the Quebec experience. J Otolaryngol 30, 93-7 (2001).

60. Engels EA, Terrin N, Barza M,Lau J. Meta-analysis of diagnostic tests for acute sinusitis. J Clin Epidemiol 53, 852-62 (2000).

61. Evans FO, Sydnor JB, Moore WE, Moore GR, Manwaring JL, Brill AH et al. Sinusitis of the maxillary antrum. N Engl J Med 293, 735-9 (1975).

62. Evans KL. Diagnosis and management of sinusitis. BMJ 309, 1415-22 (1994).

63. Federspil P,Bamberg P. Sulphadiazine/trimethoprim once daily in maxillary sinusitis: a randomized double-blind comparison with sulphamethoxazole/trimethoprim B.I.D. J Int Med Res 9, 478-81 (1981).

64. Finkelstein JA, Davis RL, Dowell SF, Metlay JP, Soumerai SB, Rifas-Shiman SL et al. Reducing antibiotic use in children: a randomized trial in 12 practices. Pediatrics 108, 1-7 (2001).

65. Fitzpatrick R,Boulton M. Qualitative methods for assessing health care. Qual Health Care 3, 107-13 (1994).

66. Friis H, Bro F, Eriksen NR, Mabeck CE,Vejlsgaard R. The effect of reimbursement on the use of antibiotics. Scand J Prim Health Care 11, 247-51 (1993).

67. Gananca M,Trabulsi LR. The therapeutic effects of cyclacillin in acute sinusitis: in vitro and in vivo correlations in a placebo-controlled study. Curr Med Res Opin 1, 362-8 (1973).

68. Gehanno P, Barry B, Chauvin JP,Hazebroucq J. [Clarithromycin versus amoxicillin-clavulanic acid in the treatment of acute maxillary sinusitis in adults]. Pathol Biol 44, 293-7 (1996).

69. Gehanno P,Berche P. Sparfloxacin versus cefuroxime axetil in the treatment of acute purulent sinusitis. Sinusitis Study Group. J Antimicrob Chemother 37 Suppl A, 105-14 (1996).

70. Ghatasheh M,Smadi A. Ultrasonography versus radiography in the diagnosis of maxillary sinusitis. East Mediterr Health J 6, 1083-6 (2000).

71. Gleeson M. Diagnosing maxillary sinusitis. BMJ 305, 662-3 (1992).

72. Gordts F, Clement PA,Buisseret T. Prevalence of sinusitis signs in a non-ENT population. ORL J Otorhinolaryngol Relat Spec 58, 315-9 (1996).

73. Guggenmoos-Holzmann I. The meaning of kappa: probabilistic concepts of reliability and validity revisited. J Clin Epidemiol 49, 775-82 (1996).

74. Guillemot D, Carbon C, Vauzelle-Kervroedan F, Balkau B, Maison P, Bouvenot G et al. Inappropriateness and variability of antibiotic prescription among French office-based physicians. J Clin Epidemiol 51, 61-8 (1998).

75. Gwaltney JM, Jr. Acute community-acquired sinusitis. Clin Infect Dis 23, 1209-23 (1996).

76. Gwaltney JM, Jr., Jones JG,Kennedy DW. Medical management of sinusitis: educational goals and management guidelines. The International Conference on sinus Disease. Ann Otol Rhinol Laryngol Suppl 167, 22-30 (1995).

77. Gwaltney JM, Jr., Phillips CD, Miller RD,Riker DK. Computed tomographic study of the common cold. N Engl J Med 330, 25-30 (1994).

78. Gwaltney JM, Jr., Scheld WM, Sande MA,Sydnor A. The microbial etiology and antimicrobial therapy of adults with acute community-acquired sinusitis: a fifteen-year experience at the University of Virginia and review of other selected studies. J Allergy Clin Immunol 90, 457-61 (1992).

79. Gwaltney JM, Jr., Sydnor A, Jr.,Sande MA. Etiology and antimicrobial treatment of acute sinusitis. Ann Otol Rhinol Laryngol Suppl 90, 68-71 (1981).

80. Haapaniemi J. Comparison of ultrasound and X-ray maxillary sinus findings in school-aged children. Ear Nose Throat J 76, 102-6 (1997).

81. Haapaniemi J,Laurikainen E. Ultrasound and antral lavage in the examination of maxillary sinuses. Rhinology 39, 39-42 (2001).

82. Halpern SD, Karlawish JH,Berlin JA. The continuing unethical conduct of underpowered clinical trials. JAMA 288, 358-62 (2002).

83. Hansen JG, Schmidt H, Rosborg J,Lund E. Klinisk kriterium for sinuitis maxillaris acuta i almen praxis. Ugeskr Laeger 158, 3156-9 (1996).

84. Hansen JG, Schmidt H, Rosborg J,Lund E. Predicting acute maxillary sinusitis in a general practice population. BMJ 311, 233-6 (1995).

85. Hayward MW, Lyons K, Ennis WP,Rees J. Radiography of the paranasal sinuses - one or three views? Clin Radiol 41, 163-4 (1990).

86. Heikkinen K, Hujanen T,Rusama H. (Stakes, Helsinki, 2001).

87. Hemminki E, Forsman H,Hemminki K. Prescription of antimicrobial drugs by general practitioners. Infection 2, 203-6 (1974).

88. Herr RD. Acute sinusitis: diagnosis and treatment update. Am Fam Physician 44, 2055-62 (1991).

89. Hickner JM, Bartlett JG, Besser RE, Gonzales R, Hoffman JR,Sande MA. Principles of appropriate antibiotic use for acute rhinosinusitis in adults: background. Ann Emerg Med 37, 703-10 (2001).

90. Hilden J. The area under the ROC curve and its competitors. Med Decis Making 11, 95-101 (1991).

91. Holzapfel L, Chastang C, Demingeon G, Bohe J, Piralla B,Coupry A. A randomized study assessing the systematic search for maxillary sinusitis in nasotracheally mechanically ventilated patients. Influence of nosocomial maxillary sinusitis on the occurrence of ventilator-associated pneumonia. Am J Respir Crit Care Med 159, 695-701 (1999).

92. Hueston WJ, Eberlein C, Johnson D,Mainous AG, 3rd. Criteria used by clinicians to differentiate sinusitis from viral upper respiratory tract infection. J Fam Pract 46, 487-92 (1998).

93. Huovinen P,Cars O. Control of antimicrobial resistance: time for action. The essentials of control are already well known. BMJ 317, 613-4 (1998).

94. Hytonen M, Atula T,Pitkaranta A. Complications of acute sinusitis in children. Acta Otolaryngol Suppl 543, 154-7 (2000).

95. Ioannidis JP, Chew P,Lau J. Standardized retrieval of side effects data for meta-analysis of safety outcomes. A feasibility study in acute sinusitis. J Clin Epidemiol 55, 619-26 (2002).

96. Ioannidis JP, Contopoulos-Ioannidis DG, Chew P,Lau J. Meta-analysis of randomized controlled trials on the comparative efficacy and safety of azithromycin against other antibiotics for upper respiratory tract infections. J Antimicrob Chemother 48, 677-89 (2001).

97. Irwig L, Macaskill P, Glasziou P,Fahey M. Meta-analytic methods for diagnostic test accuracy. J Clin Epidemiol 48, 119-30 (1995).

98. Irwig L, Tosteson AN, Gatsonis C, Lau J, Colditz G, Chalmers TC et al. Guidelines for meta-analyses evaluating diagnostic tests. Ann Intern Med 120, 667-76 (1994).

99. Jackson RM,Rice DH. Acute bacterial sinusitis and diabetes mellitus. Otolaryngol Head Neck Surg 97, 469-73 (1987).

100. Jaeschke R, Guyatt G,Sackett DL. Users guides to the medical literature. III How to use an article about a diagnostic test. B. What are the results and will they help me in caring for my patients? JAMA 271, 703-7 (1994).

101. Jannert M, Andréasson L, Holmer N-G,Lorinc P. Ultrasonic examination of the paranasal sinuses. Acta Otolaryngol Suppl 389, 1-51 (1981).

102. Jefferson T, Demicheli V,Mugford M. Elementary economic evaluation in health care (BMJ Publishing Group, London, 1996).

103. Jensen C,von Sydow C. Radiography and ultrasonography in paranasal sinusitis. Acta Radiol 28, 31-4 (1987).

104. Jiang RS, Liang KL, Jang JW,Hsu CY. Bacteriology of endoscopically normal maxillary sinuses. J Laryngol Otol 113, 825-8 (1999).

105. Joki-Erkkilä VP, Penttilä M, Kääriäinen J,Rautiainen M. Local anesthesia with EMLA cream for maxillary sinus puncture. Ann Otol Rhinol Laryngol 111, 80-2 (2002).

106. Jones RL, Crowe P, Chavda SV,Pahor AL. The incidence of sinusitis in patients with multiple sclerosis. Rhinology 35, 118-9 (1997).

107. Jones RL, Violaris NS, Chavda SV,Pahor AL. Intracranial complications of sinusitis: the need for aggressive management. J Laryngol Otol 109, 1061-2 (1995).

108. Jousimies-Somer HR, Savolainen S,Ylikoski JS. Bacteriological findings of acute maxillary sinusitis in young adults. J Clin Microbiol 26, 1919-25 (1988).

109. Jousimies-Somer HR, Savolainen S,Ylikoski JS. Comparison of the nasal bacterial floras in two groups of healthy subjects and in patients with acute maxillary sinusitis. J Clin Microbiol 27, 2736-43 (1989).

110. Kaiser L, Lew D,Hirschel B. Effects of antibiotic treatment in the subset of common-cold patients who have bacteria in nasopharyngeal secretions. Lancet 347, 1507-10 (1996).

111. Kaliner M. Medical management of sinusitis. Am J Med Sci 316, 21-8 (1998a).

112. Kaliner M. Treatment of sinusitis in the next millennium. Allergy Asthma Proc 19, 181-4 (1998b).

113. Karantanas AH,Sandris V. Maxillary sinus inflammatory disease: ultrasound compared to computed tomography. Comput Med Imaging Graph 21, 233-41 (1997).

114. Karma P, Pukander J, Penttila M, Ylikoski J, Savolainen S, Olen L et al. The comparative efficacy and safety of clarithromycin and amoxycillin in the treatment of outpatients with acute maxillary sinusitis. J Antimicrob Chemother 27, 83-90 (1991).

115. Kay NJ, Setia RM,Stone J. Relevance of conventional radiography in indicating maxillary antral lavage. Ann Otol Rhinol Laryngol 93, 37-8 (1984).

116. Kearney B. Health technology assessment. J Qual Clin Pract 16, 131-43 (1996).

117. Kenny TJ, Duncavage J, Bracikowski J, Yildirim A, Murray JJ,Tanner SB. Prospective analysis of sinus symptoms and correlation with paranasal computed tomography scan. Otolaryngol Head Neck Surg 125, 40-3 (2001).

118. Kern EB. Sinusitis. J Allergy Clin Immunol 73, 25-31 (1984).

119. Kinney WC. Rhinosinusitis treatment protocol: changing provider habits in primary care. Otolaryngol Head Neck Surg 126, 614-22 (2002).

120. Klossek J-M,Chidiac C. Current approaches to community-acquired acute maxillary rhinosinusitis or sinusitis in France and literature review. Rhinology Suppl 17, 1-38 (2001).

121. Klossek JM, Dubreuil L, Richet H, Richet B, Sedallian A,Beutter P. Bacteriology of the adult middle meatus. J Laryngol Otol 110, 847-9 (1996).

122. Kumlien J. [Diagnosis of sinusitis]. Lakartidningen 90, 3057-8 (1993).

123. Kunnamo I. [Clinical application of technology in acute medical practice]. Duodecim 112, 537-45 (1996).

124. Kuusela T, Kurri J,Sirola R. Ultraschall in der Sinusitis-Diagnostik bei Rekruten - Vergleich der Befunde der Punktion, Ultraschall- und Röntgenuntersuchung. Wehrmed Mschr Heft 11, 461-4 (1983).

125. Kuusela T, Kurri J,Sirola R. [Ultrasound in diagnosing acute maxillary sinusitis in consricpt soldiers - a comparison of puncture, ultrasound and radiography]. Ann Med Milit Fenn 57, 138-41 (1982).

126. Laine K, Maatta T, Varonen H,Makela M. Diagnosing acute maxillary sinusitis in primary care: a comparison of ultrasound, clinical examination and radiography. Rhinology 36, 2-6 (1998).

127. Lang J. Clinical Anatomy of the Nose, Nasal Cavity and Paranasal Sinuses (Thieme Medical Publishers, New York, 1989).

128. Larsen ML, Horder M,Mogensen EF. Effect of long-term monitoring of glycosylated hemoglobin levels in insulin-dependent diabetes mellitus. N Engl J Med 323, 1021-5 (1990).

129. Lasko B, Lau CY, Saint-Pierre C, Reddington JL, Martel A,Anstey RJ. Efficacy and safety of oral levofloxacin compared with clarithromycin in the treatment of acute sinusitis in adults: a multicentre, double-blind, randomized study. The Canadian Sinusitis Study Group. J Int Med Res 26, 281-91 (1998).

130. Lichtenstein D, Biderman P, Meziere G,Gepner A. The "sinusogram", a real-time ultrasound sign of maxillary sinusitis. Intensive Care Med 24, 1057-61 (1998).

131. Lindbaek M,Hjortdahl P. The clinical diagnosis of acute purulent sinusitis in general practice--a review. Br J Gen Pract 52, 491-5 (2002).

132. Lindbaek M,Hjortdahl P. [Sinusitis in general practice--a diagnostic challenge]. Tidsskrift for Den Norske Laegeforening 113, 700-3 (1993).

133. Lindbaek M, Hjortdahl P,Holth V. Acute sinusitis in adults in Norwegian general practice. Eur J Gen Pract 3, 7-11 (1997).

134. Lindbaek M, Hjortdahl P,Johnsen UL-H. Randomised, double blind, placebo controlled trial of penicillin V and amoxycillin in treatment of acute sinusitis infections in adults. BMJ 313, 325-8 (1996a).

135. Lindbaek M, Hjortdahl P,Johnsen UL-H. Use of symptoms, signs, and blood tests to diagnose acute sinus infections in primary care: comparison with computed tomography. Fam Med 28, 183-8 (1996b).

136. Lindbaek M, Johnsen UL, Kaastad E, Dolvik S, Moll P, Laerum E et al. CT findings in general practice patients with suspected acute sinusitis. Acta Radiologica 37, 708-13 (1996c).

137. Lindbaek M, Kaastad E, Dolvik S, Johnsen U, Laerum E,Hjortdahl P. Antibiotic treatment of patients with mucosal thickening in the paranasal sinuses, and validation of cut-off points in sinus CT. Rhinology 36, 7-11 (1998).

138. Lindbaek M, Melby KK, Schoyen R,Hjortdahl P. Bacteriological findings in nasopharynx specimens from patients with a clinical diagnosis of acute sinusitis. Scand J Prim Health Care 19, 126-30 (2001).

139. Littenberg B,Moses LE. Estimating diagnostic accuracy from multiple conflicting reports: a new meta-analytic method. Med Decis Making 13, 313-21 (1993).

140. Low DE, Desrosiers M, McSherry J, Garber G, Williams JW, Jr., Remy H et al. A practical guide for the diagnosis and treatment of acute sinusitis. CMAJ 156 Suppl 6, S1-14 (1997).

141. Lucchin F, Minicuci N, Ravasi MA, Cordella L, Palu M, Cetoli M et al. Comparison of A-mode ultrasound and computed tomography: detection of secretion in maxillary and frontal sinuses in ventilated patients. Intensive Care Med 22, 1265-8 (1996).

142. Macfarlane J, Holmes W, Macfarlane R,Britten N. Influence of patients' expectations on antibiotic management of acute lower respiratory tract illness in general practice: questionnaire study. BMJ 315, 1211-4 (1997).

143. Mafee MF. Imaging methods for sinusitis. JAMA 269, 2608 (1993).

144. Mainous AG, 3rd,Hueston WJ. The cost of antibiotics in treating upper respiratory tract infections in a medicaid population. Arch Fam Med 7, 45-9 (1998).

145. Malm L. Pharmacological background to decongesting and anti-inflammatory treatment of rhinitis and sinusitis. Acta Otolaryngol Suppl 515, 53-6 (1994).

146. Mann W. [Diagnostics in infectious sinus diseases]. Laryngol Rhinol Otol (Stuttg) 59, 1-5 (1980).

147. Mann W. Die Ultraschalldiagnostik der Nasannebenhöhlen und ihre Anwendung in der Freiburger HNO-Klinik. Arch Otorhinolaryngol 211, 145-7 (1975).

148. Mann W. [Echography of the paranasal sinuses using A- and B-Scan]. Laryngol Rhinol Otol (Stuttg) 55, 48-53 (1976).

149. Mann W, Beck C,Apostolidis T. Liability of ultrasound in maxillary sinus disease. Arch Otorhinolaryngol 215, 67-74 (1977).

150. Mann W, Schumann K,Kafer U. [Comparative x-ray and ultrasound examination in infantile sinusitis]. Klin Padiatr 188, 67-72 (1976).

151. Marra A,Brigham D. Streptococcus pneumoniae causes experimental meningitis following intranasal and otitis media infections via a nonhematogenous route. Infect Immun 69, 7318-25 (2001).

152. McNeill RA. Comparison of the findings on transillumination, x-ray and lavage of the maxillary sinus. J Laryngol Otol, 1009-13 (1962).

153. Melander E, Bjorgell A, Bjorgell P, Ovhed I,Molstad S. Medical audit changes physicians' prescribing of antibiotics for respiratory tract infections. Scand J Prim Health Care 17, 180-4 (1999).

154. 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 106, 630-7 (2000).

155. Meltzer EO, Orgel HA, Backhaus JW, Busse WW, Druce HM, Metzger WJ et al. Intranasal flunisolide spray as an adjunct to oral antibiotic therapy for sinusitis. J Allergy Clin Immunol 92, 812-23 (1993).

156. Morgan DL. Succesful Focus Groups (Sage Publications, Newbury Park, 1993).

157. Moses LE, Shapiro D,Littenberg B. Combining independent studies of a diagnostic test into a summary ROC curve: data-analytical approaches and some additional considerations. Stat in Med 12, 1293-316 (1993).

158. Mäkelä M,Leinonen K. Diagnosis of maxillary sinusitis in Finnish primary care. Scand J Prim Health Care 14, 29-35 (1996).

159. Nord CE. Efficacy of penicillin treatment in purulent maxillary sinusitis. A European multicenter trial. Infection 16, 209-14 (1988).

160. Norrelund N. [Treatment of sinusitis in general practice. A controlled investigation of pivampicillin (Pondocillin)]. Ugeskr Laeger 140, 2792-5 (1978).

161. Oppenheimer RW. Sinusitis. How to recognize and treat it. Postgrad Med 91, 281-6, 9-92 (1992).

162. Oxman AD, Thomson MA, Davis DA,Haynes RB. No magic bullets: a systematic review of 102 trials of interventions to improve professional practice. CMAJ 153, 1423-31 (1995).

163. Pediatrics. AAo. Clinical practice guideline: management of sinusitis. Pediatrics 108, 798-808 (2001).

164. Penttila M, Rautiainen M, Pukander J,Kataja M. Functional vs. radical maxillary surgery. Failures after functional endoscopic sinus surgery. Acta Oto-Laryngologica - Supplement 529, 173-6 (1997).

165. Penttilä M, Savolainen S, Kiukaanniemi H, Forsblom B,Jousimies-Somer H. Bacterial findings in acute maxillary sinusitis - European study. Acta Otolaryngol Suppl 529, 165-8 (1997).

166. Pessey JJ, Reitz C,Los F. [Acute rhinosinusitis in the adult: national survey of general practice management]. Rev Laryngol Otol Rhinol (Bord) 121, 237-41 (2000).

167. Petitti DB. Meta-Analysis, Decision Analysis, and Cost-Effectiveness Analysis (Oxford University Press, New York, 1994).

168. Pfister R, Lutolf M, Schapowal A, Glatte B, Schmitz M,Menz G. Screening for sinus disease in patients with asthma: a computed tomography-controlled comparison of A-mode ultrasonography and standard radiography. J Allergy Clin Immunol 94, 804-9 (1994).

169. Pfleiderer AG, Drake-Lee AB,Lowe D. Ultrasound of the sinuses: a worthwhile procedure? A comparison of ultrasound and radiography in predicting the findings of proof puncture on the maxillary sinuses. Clin Otolaryngol 9, 335-9 (1984).

170. Piccirillo JF, Mager DE, Frisse ME, Brophy RH,Goggin A. Impact of first-line vs second-line antibiotics for the treatment of acute uncomplicated sinusitis. JAMA 286, 1849-56 (2001).

171. Pichichero ME. Short course antibiotic therapy for respiratory infections: a review of the evidence. Pediatr Infect Dis J 19, 929-37 (2000).

172. Pichichero ME,Cohen R. Shortened course of antibiotic therapy for acute otitis media, sinusitis and tonsillopharyngitis. Pediatr Infect Dis J 16, 680-95 (1997).

173. Pitkäranta A, Arruda E, Malmberg H,Hayden FG. Detection of rhinovirus in sinus brushings of patients with acute community-acquired sinusitis by reverse transcription-PCR. J Clin Microbiol 35, 1791-3 (1997).

174. Pitkäranta A, Atula T, Lindahl P, Saxen H,Malmberg H. Unilateral blindness in a child with acute sinusitis. Rhinology 38, 43-4 (2000).

175. Pitkäranta A, Starck M, Savolainen S, Pöyry T, Suomalainen I, Hyypiä T et al. Rhinovirus RNA in the maxillary sinus epithelium of adult patients with acute sinusitis. Clin Infect Dis 33, 909-11 (2001).

176. Pocock SJ. Clinical trials: a practical approach (John Wiley & Sons, Chichester, 1990).

177. Poole MD. A focus on acute sinusitis in adults: changes in disease management. Am J Med 106, 38S-52S (1999).

178. Pope C,Mays N. Reaching the parts other methods cannot reach; an introduction to qualitative methods in health and health services research. BMJ 311, 42-5 (1995).

179. Puhakka T, Heikkinen T, Makela MJ, Alanen A, Kallio T, Korsoff L et al. Validity of ultrasonography in diagnosis of acute maxillary sinusitis. Arch Otolaryngol Head Neck Surg 126, 1482-6 (2000).

180. Puhakka T, Makela MJ, Alanen A, Kallio T, Korsoff L, Arstila P et al. Sinusitis in the common cold. J Allergy Clin Immunol 102, 403-8 (1998).

181. Quick CA,Payne E. Complicated acute sinusitis. Laryngoscope 82, 1248-63 (1972).

182. Ransohoff DF,Feinstein AR. Problems of spectrum and bias in evaluating the efficacy of diagnostic tests. N Engl J Med 299, 926-30 (1978).

183. Rantanen T,Arvilommi H. Double-blind trial of doxicycline in acute maxillary sinusitis. A clinical and bacteriological study. Acta Otolaryngol 76, 58-62 (1973).

184. Rautakorpi UM, Klaukka T, Honkanen P, Makela M, Nikkarinen T, Palva E et al. Antibiotic use by indication: a basis for active antibiotic policy in the community. Scand J Infect Dis 33, 920-6 (2001).

185. 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 103, 408-14 (1999).

186. [Recommended treatment of acute sinusitis. Finnish Otolaryngological Association]. Duodecim 115, 2147-53 (1999).

187. Reilly JS, Hotaling AJ, Chiponis D,Wald ER. Use of ultrasound in detection of sinus disease in children. Int J Pediatr Otorhinolaryngol 17, 225-30 (1989).

188. Revonta M. Ultrasound in the diagnosis of maxillary and frontal sinusitis. Acta Otolaryngol Suppl 370, 1-55 (1980).

189. Revonta M,Suonpaa J. Diagnosis of subacute maxillary sinusitis in children. J Laryngol Otol 95, 133-40 (1981).

190. Revonta M, Suonpaa J,Meurman OH. [Ultrasound testing in the diagnosis and management of maxillary sinusitis in children (author's transl)]. Hno 28, 91-6 (1980).

191. Richtsmeier WJ. Medical and surgical management of sinusitis in adults. Ann Otol Rhinol Laryngol Suppl 155, 46-50 (1992).

192. Roberts DN, Hampal S, East CA,Lloyd GA. The diagnosis of inflammatory sinonasal disease. J Laryngol Otol 109, 27-30 (1995).

193. Rohr AS, Spector SL, Siegel SC, Katz RM,Rachelefsky GS. Correlation between A-mode ultrasound and radiography in the diagnosis of maxillary sinusitis. J Allergy Clin Immunol 78, 58-61 (1986).

194. Rombaux P, Bertrand B,Eloy P. Sinusitis in the immunocompromised host. Acta Otorhinolaryngol Belg 51, 305-13 (1997).

195. Roth RP, Cantekin EI, Bluestone CD, Welch RM,Cho YW. Nasal decongestant activity of pseudoephedrine. Ann Otol Rhinol Laryngol 86, 235-42 (1977).

196. Sackett DL, Haynes RB, Guyatt GH,Tugwell P. Clinical Epidemiology: A Basic Science for Clinical Medicine (Little, Brown and Company, Boston, 1991).

197. Sassi F, McKee M,Roberts JA. Economic evaluation of diagnostic technology. Methodological challenges and viable solutions. Int J Technol Assess Health Care 13, 613-30 (1997).

198. Savolainen S. Allergy in patients with acute maxillary sinusitis. Allergy 44, 116-22 (1989).

199. Savolainen S, Jousimies-Somer H, Karjalainen J,Ylikoski J. Do simple laboratory tests help in etiologic diagnosis in acute maxillary sinusitis? Acta Otolaryngol Suppl 529, 144-7 (1997a).

200. Savolainen S, Pietola M, Kiukaanniemi H, Lappalainen E, Salminen M,Mikkonen P. An ultrasound device in the diagnosis of acute maxillary sinusitis. Acta Otolaryngol Suppl 529, 148-52 (1997b).

201. Savolainen S, Ylikoski J,Jousimies-Somer H. The bacterial flora of the nasal cavity in healthy young men. Rhinology 24, 249-55 (1986).

202. Segesten K. Qualitative methods--an alternative road to knowledge. Scand J Prim Health Care 15, 161-2 (1997).

203. Sellors J, Cosby R, Trim K, Kaczorowski J, Howard M, Hardcastle L et al. Recruiting family physicians and patients for a clinical trial: lessons learned. Fam Pract 19, 99-104 (2002).

204. Settipane RA. Complications of allergic rhinitis. Allergy Asthma Proc 20, 209-13 (1999).

205. Shapiro GG, Furukawa CT, Pierson WE, Gilbertson E,Bierman CW. Blinded comparison of maxillary sinus radiography and ultrasound for diagnosis of sinusitis. J Allergy Clin Immunol 77, 59-64 (1986a).

206. Shapiro GG, Furukawa CT, Pierson WE, Gilbertson E,Bierman CW. Blinded comparison of maxillary sinus radiography and ultrasound for diagnosis of sinusitis. J Allergy Clin Immunol 77, 59-64 (1986b).

207. Shapiro GG,Rachelefsky GS. Introduction and definition of sinusitis. J Allergy Clin Immunol 90, 417-8 (1992).

208. Sher LD, McAdoo MA, Bettis RB, Turner MA, Li NF,Pierce PF. A multicenter, randomized, investigator-blinded study of 5- and 10-day gatifloxacin versus 10-day amoxicillin/clavulanate in patients with acute bacterial sinusitis. Clin Ther 24, 269-81 (2002).

209. Sixma HJ, Kerssens JJ, Campen CV,Peters L. Quality of care from the patients' perspective: from theoretical concept to a new measuring instrument. Health Expect 1, 82-95 (1998).

210. Slavin RG. Sinusitis in adults. J Allergy Clin Immunol 81, 1028-32 (1988).

211. Solomon DH, Hashimoto H, Daltroy L,Liang MH. Techniques to improve physicians' use of diagnostic tests: a new conceptual framework. JAMA 280, 2020-7 (1998).

212. Sorri M, Hartikainen-Sorri AL,Karja J. Rhinitis during pregnancy. Rhinology 18, 83-6 (1980).

213. Sorri M, Peltomaki E,Jokinen K. Bacampicillin in acute maxillary sinusitis: concentration in sinus secretion and clinical effect. A randomized, double-blind study of two dosage regimens. Scand J Infect Dis 13, 277-80 (1981).

214. Stalman W, van Essen GA, Gubbels JW,de Melker RA. Difficulties in diagnosing acute sinusitis in a Dutch group practice. Eur J Gen Pract 3, 12-5 (1997a).

215. Stalman W, van Essen GA, van der Graaf Y,de Melker RA. The end of antibiotic treatment in adults with acute sinusitis-like complaints in general practice? A placebo-controlled double-blind randomized doxycycline trial. Br J Gen Pract 47, 794-9 (1997b).

216. Stalman W, van Essen GA, van der Graaf Y,de Melker RA. Maxillary sinusitis in adults: an evaluation of placebo-controlled double-blind trials. Fam Pract 14, 124-9 (1997c).

217. Staquet M, Rozencweig M, Lee YJ,Muggia FM. Methodology for the assessment of new dichotomous diagnostic tests. J Chronic Dis 34, 599-610 (1981).

218. Steffensen FH, Schonheyder HC,Sorensen HT. High prescribers of antibiotics among general practitioners--relation to prescribing habits of other drugs and use of microbiological diagnostics. Scand J Infect Dis 29, 409-13 (1997).

219. Su WY, Liu C, Hung SY,Tsai WF. Bacteriological study in chronic maxillary sinusitis. Laryngoscope 93, 931-4 (1983).

220. Suonpää J,Revonta M. Diagnosis of frontal sinusitis: one-dimensional ultrasonography versus radiography. J Laryngol Otol 103, 765-7 (1989).

221. Swift AC,Gill GV. Serious unexpected sinus infection discovered by CT scanning for presumed neurological disease. Postgrad Med J 70, 203-6 (1994).

222. Tarp B, Fiirgaard B, Christensen T, Jensen JJ,Black FT. The prevalence and significance of incidental paranasal sinus abnormalities on MRI. Rhinology 38, 33-8 (2000).

223. Tiedjen KU, Becker E, Heimann KD, Knorz S,Hildmann H. [Value of B-image ultrasound in diagnosis of paranasal sinus diseases in comparison with computerized tomography]. Laryngorhinootologie 77, 541-6 (1998).

224. Tomlin Z, Humphrey C,Rogers S. General practitioners' perceptions of effective health care. BMJ 318, 1532-5 (1999).

225. Torrance GW. Utility approach to measuring health related quality of life. J Chron Dis 40, 593-600 (1987).

226. Unsworth L,Walley T. Trends in primary care antibiotic prescribing in England 1994-1998. Pharmacoepidemiol Drug Saf 10, 309-14 (2001).

227. Urdal K,Berdal P. The microbial flora in 81 cases of maxillary sinusitis. Acta otolaryngol 37, 20-5 (1949).

228. van Buchem FL, Knottnerus JA, Schrijnemaekers VJJ,Peeters MF. Primary-care-based randomised placebo-controlled trial of antibiotic treatment in acute maxillary sinusitis. Lancet 349, 683-7 (1997).

229. van Buchem L, Peeters M, Beaumont J,Knottnerus JA. Acute maxillary sinusitis in general practice: The relation between clinical picture and objective findings. Eur J Gen Pract 1, 155-60 (1995).

230. Waters CA,Waldron CW. Roentgenology of accessory nasal sinuses describing a modification of the occipitofrontal position. Am J Roentgenol 2, 633-9 (1915).

231. Vento SI, Ertama LO, Hytonen ML,Malmberg CH. A-mode ultrasound in the diagnosis of chronic polypous sinusitis. Acta Otolaryngol 119, 916-20 (1999).

232. Williams Jr JW, Aguilar C, Makela M, Cornell J, Holleman DR, Chiquette E et al. Antibiotics for acute maxillary sinusitis. Cochrane Database Syst Rev 2, CD000243 (2000).

233. Williams JW, Jr., Holleman DR, Jr., Samsa GP,Simel DL. Randomized controlled trial of 3 vs 10 days of trimethoprim/sulfamethoxazole for acute maxillary sinusitis. JAMA 273, 1015-21 (1995).

234. Williams JW, Jr., Roberts L, Jr., Distell B,Simel DL. Diagnosing sinusitis by X-ray: is a single Waters view adequate? J Gen Intern Med 7, 481-5 (1992a).

235. Williams JW,Simel DL. Does this patient have sinusitis? JAMA 270, 1242-6 (1993).

236. Williams JW, Simel DL, Roberts L,Samsa GP. Clinical evaluation for sinusitis. Making the diagnosis by history and physical examination. Ann Intern Med 117, 705-10 (1992b).

237. Wittek G,Beuthan J. [Infrared diaphanoscopy (IRD)--a choice diagnostic procedure? Preliminary results of the clinical testing]. Kinderarztl Prax 58, 581-5 (1990).

238. von Sydow C, Axelsson A,Jensen C. Acute maxillary sinusitis--a comparison between 27 different treatment modes. Rhinology 20, 223-9 (1982).

239. Ylikoski J, Savolainen S,Jousimies-Somer H. The bacteriology of acute maxillary sinusitis. ORL J Otorhinolaryngol Relat Spec 51, 175-81 (1989).

240. Zinreich J. Imaging of inflammatory sinus disease. Otolaryngol Clin North Am 26, 535-47 (1993).