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Anthroposophic vs. conventional therapy of acute respiratory & ear infections: a prospective outcomes study

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Abbreviations

±	Standard Deviation
95-%-CI	95% confidence interval
AE	Adverse Events
A-doctors	Anthroposophic physicians
A-group	Anthroposophy Group
A-patients	Anthroposophy Group patients
ADR	Adverse Drug Reactions
AOM	Acute otitis media
AM	Anthroposophic medicine
ATC-Index	Anatomical Therapeutic Chemical Index
C-doctors	Conventional physicians
C-group	Conventional Group
C-patients	Conventional Group patients
GCP	Good Clinical Practice
ICD-9	International Classification of Diseases, 9th Edition
LOCF	Last Observation Carried Forward
NE-A-patients	Screened, not enrolled A-patients fulfilling all eligibility criteria
n. s.	Not statistically significant
OR	Odds Ratio
RTI	Respiratory tract infections
SAE	Serious Adverse Events
SDV	Source Data Verification

Summary

Context

Acute respiratory and ear symptoms are very common in primary care. In conventional medical practice these symptoms are frequently treated with antibiotics; in anthroposophic medicine, antibiotics are only prescribed if strongly needed.

Objective.

To compare anthroposophic treatment to conventional treatment of acute respiratory and ear symptoms in primary care: clinical outcome, medication use and safety, patient satisfaction.

Design

Prospective, comparative, non-randomised, real-world outcomes study

Setting

29 primary care practices in Austria, Germany, Netherlands, UK, USA

Participants and interventions

1016 outpatients aged ≥ 1 month, consulting an anthroposophic (A-patients: n = 715) or conventional physician (C-patients: n = 301) with acute onset (≤ 7 days) of sore throat, ear pain, sinus pain, runny nose or cough, treated according to the physician's discretion.

Outcome measures

Primary outcome: Response rate (complete recovery or major improvement) at Day 14. Secondary outcomes: First improvement ≤ 24 hours and ≤ 3 days; response at Day 7; complete recovery at Days 7 and 14; antibiotic prescription; patient satisfaction with therapy; patients' choice of therapy again for chief complaint; adverse drug reactions. Multiple logistic regression analysis was used to adjust for country, gender, age, chief complaint, duration of chief complaint, previous episode of chief complaint within last year, and baseline symptom severity.

Results

First improvement within 24 hours occurred in 30.9% (221/715) of A-patients and 16.6% (50/301) of C-patients ($p < 0.0001$), improvement within 3 days in 73.1% and 57.1% ($p < 0.0001$). Response rate at Day 7 was 77.1% in A-group and 66.1% in C-group ($p = 0.0004$), at Day 14 (primary outcome) 89.7% and 84.4% ($p = 0.0198$). Complete recovery rates at Day 7 were 30.5% and 23.3% ($p < 0.0001$), at Day 14: 64.2% and 49.5% ($p < 0.0001$).

Adjusted odds ratios (A- vs. C-) favoured the A-group for improvement within 24 hours: 1.54 (95%-CI: 1.03-2.31); improvement within 3 days: 1.61 (1.16-2.22); Day 7 response: 1.50 (1.07-2.11); Day 14 response: 1.29 (0.82-2.00); Day 7 recovery: 1.05 (0.72-1.54); Day 14

recovery: 1.35 (0.98-1.86); patient satisfaction: 1.39 (0.98-1.95); and patients' choice of therapy again: 3.54 (2.13-5.19).

During the study 5.5% of A-patients and 33.6% of C-patients were prescribed antibiotics ($p < 0.0001$). Anthroposophic medicines were prescribed to all A-patients (median 3, range 1-9 medicines per patient) and no C-patient. Adverse drug reactions were reported in 2.7% of A-patients and 6.0% of C-patients ($p = 0.0157$).

Conclusion

In this prospective outcome study, unselected outpatients with acute respiratory and ear symptoms were treated in anthroposophic and conventional primary care settings. Compared to conventional treatment, anthroposophic treatment had more favourable outcomes, lower antibiotic prescription rates, less adverse drug reactions, and higher patient satisfaction.

Zusammenfassung: Anthroposophische vs. konventionelle Therapie bei akuten Ohr- und Atemwegsinfekten: eine prospektive Outcomes-Studie

Hintergrund

Akute Atemwegs- und Ohrenbeschwerden sind sehr häufig in der hausärztlichen Praxis. In konventionellen „schulmedizinischen“ Praxen werden solche Symptome häufig mit Antibiotika behandelt, in der anthroposophischen Medizin werden Antibiotika jedoch nur bei dringendem Bedarf verschrieben.

Fragestellung

Vergleich von anthroposophischer und schulmedizinischer Behandlung akuter Atemwegs- und Ohrenbeschwerden in der hausärztlichen Praxis hinsichtlich Krankheitsverlauf, Arzneimittelverbrauch und –sicherheit sowie Patientenzufriedenheit.

Design

Prospektive vergleichende, nicht-randomisierte, GCP-konforme Outcomes-Studie unter den Bedingungen der therapeutischen Alltagsrealität.

Setting

29 Hausarztpraxen in Deutschland, Großbritannien, Niederlande, Österreich, USA.

Teilnehmer und Behandlung

1016 Patienten im Alter ≥ 1 Monat, die einen anthroposophischen (A-Gruppe, n = 715) oder schulmedizinischen Arzt (S-Gruppe, n = 301) wegen akuten (≤7 Tage) Beschwerden aufsuchen: Husten, Laufen der Nase, Hals-, Nebenhöhlen- oder Ohrenschmerzen. Behandlung nach Ermessen des Arztes.

Zielparameter

Primärer Zielparameter: Responsrate (beschwerdefrei oder deutlich gebessert) nach 14 Tagen. Sekundäre Zielparameter: Erste Besserung innerhalb 24 Stunden bzw. 3 Tage, Responsrate nach 7 Tagen, Beschwerdefreiheit nach 7 und 14 Tagen, Antibiotika-Verschreibungsrate, Patientenzufriedenheit mit der Therapie, Patientenentscheidung für die gleiche Therapie in der Zukunft, Unerwünschte Arzneimittelwirkungen. Multiple logistische Regressionsanalyse wurde verwendet, um für mögliche Confounder zu adjustieren (Land, Geschlecht, Alter, Hauptbeschwerde, Dauer der Hauptbeschwerde, früheres Auftreten der Hauptbeschwerde im letzten Jahr, Schweregrad der Krankheitssymptomatik bei Studienaufnahme).

Ergebnisse

Eine Besserung trat innerhalb von 24 Stunden bei 30,9% (221/715 Patienten) in der A-Gruppe und 16,6% (50/301) in der S-Gruppe auf ($p < 0,0001$), eine Besserung innerhalb von 3 Tagen bei 73,1% bzw. 57,1% ($p < 0,0001$). Die Responsrate betrug nach 7 Tagen 77,1% in der A-Gruppe und 66,1% in der S-Gruppe ($p = 0,0004$), nach 14 Tagen (Hauptzielparameter) 89,7% bzw. 84,4% ($p = 0,0198$). Die Anteile beschwerdefreier Patienten betrugen nach 7 Tagen 30,5% bzw. 23,3% ($p < 0,0001$), nach 14 Tagen 64,2% bzw. 49,5% ($p < 0,0001$). Adjustierte Odds Ratios (A-Gruppe vs. S-Gruppe) zeigten eine Überlegenheit der A-Gruppe hinsichtlich Besserung innerhalb von 24 Stunden: 1,54 (95%-CI: 1,03-2,31); Besserung innerhalb von 3 Tagen: 1,61 (1,16-2,22); Respons nach 7 Tagen: 1,50 (1,07-2,11); Respons nach 14 Tagen: 1,29 (0,82-2,00); Beschwerdefreiheit nach 7 Tagen: 1,05 (0,72-1,54), Beschwerdefreiheit nach 14 Tagen: 1,35 (0,98-1,86); Patientenzufriedenheit: 1,39 (0,98-1,95) und Patientenentscheidung für die gleiche Therapie: 3,54 (2,13-5,19).

Während der Studie wurden 5,5% der Patienten der A-Gruppe und 33,6% der S-Gruppe Antibiotika verschrieben ($p < 0,0001$). Anthroposophische Arzneimittel wurden allen Patienten der A-Gruppe (im Median 3, zwischen 1 und 9 Arzneimittel pro Patient) und keinem der S-Gruppe verschrieben. Unerwünschte Arzneimittelwirkungen wurden von 2,7% der Patienten der A-Gruppe und 6,0% der S-Gruppe berichtet ($p = 0,0157$).

Schlussfolgerung

In dieser prospektiven Outcomes-Studie wurden unselektierte Patienten mit akuten Atemwegs- oder Ohrenbeschwerden in anthroposophischen bzw. schulmedizinischen Hauarztpraxen behandelt. Im Vergleich zur schulmedizinischen Behandlung erzielte die anthroposophische Behandlung günstigere Krankheitsverläufe, niedrigere Antibiotika-Verschreibungsraten und weniger Arzneimittelnebenwirkungen bei höherer Patientenzufriedenheit.

Introduction

Acute respiratory tract and ear infections

Acute respiratory tract infections (RTI) are the most common illnesses experienced by people of all ages worldwide (69). In primary care settings, symptoms like cough, sore throat and earache are among the most common reasons for patient consultations (19), particularly in the winter season. In a representative German primary care sample of children aged 0-10 years (n = 2,854) seen in January to March 2001, three-fourths of all office visits were due to acute RTI (bronchitis, common cold, nonspecific upper RTI, tonsillitis) and acute otitis media (AOM) (109).

Although mostly self-limiting within 1-2 weeks (22;38;67;82;101), the total health burden of RTI due to symptoms, school and work absence is formidable. In the WHO Global Burden of Disease Study, RTI contributed to 8.5% of all Disability Adjusted Life Years worldwide (70).

Antibiotic use in acute respiratory tract and ear infections

Most patients consulting a doctor with an acute respiratory or ear infection will be prescribed an antibiotic (29;46;57;72;74;100). This practice is not well-supported by research evidence. Cochrane Reviews of randomised trials in acute otitis media (32), acute sinusitis (106), sore throat / tonsillitis (22), common cold (8), and acute bronchitis (88) have found only small or negligible short-time effects of antibiotics, comparable to their potential for side effects. Since suppurative and non-suppurative complications of RTI are rare in most Western society settings (76;82), large numbers of patients must be treated unnecessarily with antibiotics to prevent them (22). These considerations, and the acknowledgment of antimicrobial resistance as a major threat to public health (108) have led to widespread concern to reduce antibiotic prescription rates in RTI and AOM (23;30;33;41;65). At present, UK (4;85), Dutch (7) and German (10) guidelines do not support routine use of antibiotics in AOM, and UK (2;84) and Dutch (20) guidelines even argue against routine antibiotic treatment of Group A Streptococcus pharyngitis. In acute sinusitis, US and German guidelines recommend antibiotics only in severe or persistent symptoms (> 7 days in adults, > 10-14 days in children) (5;10;40;49;91). Antibiotics are generally not recommended as routine treatment of acute bronchitis (3;10;34;89) or nonspecific upper RTI / common cold (10;35;83;90).

Anthroposophic medicine in acute respiratory tract and ear infections

Anthroposophic medicine (AM) is a system of medicine founded in the 1920s by Rudolf Steiner and Ita Wegman (26;95). AM is provided by medical doctors as an extension of their conventional medical practice, in most European countries, the Americas, some African and Asian countries, as well as in Australia and New Zealand. AM aims to stimulate the patient's salutogenetic, self-healing capacities (81). AM treatment of RTI and AOM rely on an array of AM medications (mostly herbal or homeopathic), supported by external herbal and hydrotherapeutic applications for symptomatic relief. Antibiotics are only given if strongly needed, and fever is not routinely suppressed with conventional analgesics (26;48;55;87;92-

94). Currently, all AM medications used for RTI and AOM are produced by the pharmaceutical companies Weleda AG, Switzerland (www.weleda.com) and WALA-Heilmittel, Germany (www.wala.de), and subsidiary companies.

The clinical documentation of AM therapy of acute RTI and AOM is restricted to case reports (104), retrospective (28) and prospective single-arm cohort studies (16;27;47;62;68;99). Two consecutive case series of AOM (16) and pharyngitis (47), each carried out by individual primary care doctors over a 10-year period, suggest that low antibiotic prescription rates (1.5% of AOM cases, 7.5% in "follicular angina") are possible in AM therapy without increased complication rates.

This study

This study is the first prospective, controlled study of AM therapy in acute respiratory or ear infections. It was designed as a (a) real-world (b) outcomes study (c) comparing two therapy settings (anthroposophic vs. conventional physicians). Thus, the following applies:

a) There were no restrictions on patient self-selection into either of the two settings or on the doctors' treatment of their patients. We did not aim at having comparable groups at baseline, but adjusted outcomes for baseline confounders.
b) Eligibility criteria were not a narrow set of diagnostic criteria, but patients' symptoms (21).
c) The study was not restricted to patients treated with specific anthroposophic or conventional medicines, but compared anthroposophic and conventional treatment as global therapy packages, including physician-patient interactions.

In the light of the considerable overlap between symptoms, signs and diagnoses of respiratory and ear infections, this first large-scale evaluation included patients with symptoms referring to the ear, nose, paranasal sinuses, pharynx, larynx, and bronchi. To assess a variety of settings, patients were recruited in 29 different medical practices in five countries.

Objectives

The objective of this study was to compare anthroposophic treatment to conventional treatment of acute respiratory and ear symptoms in primary care with respect to clinical outcome, medication use and safety, and patient satisfaction.

Methods

Study design

This is an international, multi-centre, prospective, real-world study assessing outcomes of patients seeing anthroposophic physicians, compared to the outcomes of patients seeing conventional physicians.

Setting and participating physicians

Setting

The study was conducted in primary care outpatient medical practices in five countries: Austria, Germany, The Netherlands, United Kingdom, United States.

Participating physicians

Licensed physicians with primary care outpatient practice and at least five years in medical practice were invited to participate.

- Anthroposophic physicians (A-doctors) recruiting Anthroposophy Group (A-group) patients: physicians certified by the anthroposophic physicians' association of their respective country (www.anthromed.at, www.anthroposophischeaerzte.de, www.nvaa.nl, www.anthroposophy.org.uk/main/medicine, www.paam.net) with at least five years of practical experience in AM, prescribing AM medicines regularly (at least 75% of all prescriptions) for patients with acute pharyngitis, tonsillitis, rhinitis, sinusitis, bronchitis and otitis.
- Conventional physicians (C-doctors) recruiting Conventional Group (C-group) patients: physicians not prescribing anthroposophic medicines for patients with these diagnoses.

Anthroposophic doctors were recruited through anthroposophic physicians' associations, conventional doctors were recruited through HomInt research network.

Patient recruitment

Inclusion criteria

- Outpatients consulting a primary care physician because of acute onset (≤ 7 days) of runny nose, sore throat, ear pain, sinus pain or cough (chief complaint).
- Age ≥ 1 month. (In The Netherlands the lower age limit was 4 years as requested by the Independent Review Board.)
- Written informed consent to study participation obtained from patient or legal guardian.

Exclusion criteria

- Dementia, schizophrenia, psychosis, spinal cord injury, stroke, renal failure, severe hepatic disease
- Immunosuppressive treatment, chemotherapy or radiation treatment for cancer
- Recent history of alcohol or drug abuse
- Incompetence, or incapability of understanding the nature, meaning and consequences of the trial
- Previous participation in this study

Study interventions

Patients were treated according to the best medical practice known to the physician. There were no treatment restrictions placed on the participating physicians or patients.

Primary study hypothesis

The primary study hypothesis was that the response rate (proportion of patients with treatment outcome = complete recovery or major improvement) by Day 14 was not lower after AM treatment than after conventional treatment.

Statistical plan

The study was designed to confirm non-inferiority of anthroposophic treatment in comparison to conventional treatment regarding the primary outcome response rate at day 14, i. e. to demonstrate that anthroposophic treatment is not less effective than conventional treatment. The predefined equivalence region was 5%. In case of superiority of anthroposophic treatment it is feasible to calculate the p-value associated with a test of superiority and to evaluate whether this is sufficiently small to reject convincingly the hypothesis of no difference (97).

Financial issues

Physicians were paid an economical compensation corresponding to € 25 per included patients. Patients received no remuneration for study participation.

Data collection

An overview of study items and their documentation is given in Table 1. At the initial patient contact leading to study enrolment (Day 0), the physician collected written informed consent and documented baseline data. In addition, the patient or legal guardian documented demographics and quality of life. On Day 7, Day 14, and Day 28, follow-up interviews with patients (legal guardians) were conducted by an independent Contract Research Organisation. However, for patients with a treatment outcome response of “complete recovery” at the Day 7 or Day 14 follow-up interview, no further follow-up interviews were performed. Thus, the duration of the trial for each individual patient was 7, 14 or 28 days. In case of patients being unavailable on the telephone, altogether three attempts within two days were made to reach the patient.

Patients' Day 0 documentation was by a self-report questionnaire. Doctors’ Day 0 documentation and the follow-up interviews with patients were documented using a remote data entry system provided on the internet. Patient responses were not made available to their doctors.

Data collection: overview				
Patient contacts	**Day 0**	**Day 7**	**Day 14**	**Day 28**
Doctor's documentation				
Inclusion / exclusion criteria	X			
Informed consent	X			
Chief complaint	X			
Severity of complaint-related symptoms	X			
Concomitant medical problems & medications	X			
Primary treatment prescribed	X			
Adjunctive therapies prescribed	X			
Consultation details: type, length, follow-up recommendation	X			
Serious Adverse Events		X		
Patient's documentation				
Demographic data	X			
Severity of complaint-related symptoms		X	X	X
Time until occurrence of first improvement		X	X	X
Treatment outcome		X	X	X
Patient satisfaction, patients' choice of treatment and doctor again		X	X	X
Quality of life (SF-12 Health Survey / KINDL)	X	X	X	X
Use of therapy for chief complaint and concomitant medication		X	X	X
Adverse Events		X	X	X

Table 1 Overview of data collection.

Outcome measures

Baseline data of enrolled patients

- Demographics: date of birth, gender, weight, height, race/ethnicity, smoking, number of persons in household
- Chief complaint: runny nose, sore throat, ear pain, sinus pain or cough
- Duration of chief complaint: 0 to ≤ 24h, > 24h to ≤ 48h, > 2 days to ≤ 3 days, > 3 days to ≤ 5 days, > 5 days to ≤ 7 days
- Previous episode of chief complaint within last 12 months: yes/no; if yes: How often: 1-2 times, 3-4 times, 5-6 times, > 6 times
- Doctor's diagnosis of chief complaint
- Doctor's confidence in diagnosis of chief complaint: numeric scale from 0 (= none) to 10 (= total)
- Reason for confidence in diagnosis: clinical symptoms, clinical investigation of chief complaint (nose check / tonsil check / ear check / lung check), other
- Patient's and doctor's preference for treatment of chief complaint: No preference, preference for anthroposophic treatment (anthroposophic group only), preference for conventional treatment, other

- Patient's willingness to be randomised if treatment is part of a clinical trial: yes/no. If no: Reason for unwillingness to be randomized: patient has a treatment preference, patient does not want to be randomized, patient perceived risk of at least one treatment option, other
- Patient freedom to choose the doctor: yes/no
- Patient previous experience with the study doctor: yes/no
- Patient previous experience with anthroposophic medicine (in anthroposophic group only)
- Payment source: self-payment, third party (private), government, other
- Patient willingness to pay for the treatment he/she will receive, regardless of payments arrangements: willing to pay the entire costs, willing to pay some of the costs, not willing to pay any portion of the costs
- Total annual household income: categories corresponding to: less than < 15,000 €; 15,000-29,999 €; 30,000-44,999 €; 45,000-59,.999 €; 60,000-74,999 €; 75,000 or more
- Patient confidence in the doctor's professional skills: not at all, slightly, moderately, quite a bit, extremely
- Patient confidence that the doctor will solve his/her medical problem: yes/no
- Concomitant medical problems: diagnosis (1 to 8 possible)
- Medication use for concomitant medical problems (1 to 8 medicines possible): name, indication, dose, medication form, start date, stop date or ongoing
- Follow-up contact recommendations at study entry: appointment, telephone consultation, no recommendation
- Consultation type at study entry: office visit, telephone consultation only, home visit
- Consultation length: < 5 min., > 5 to ≤ 15 min, > 15 to ≤ 30 min, > 30 to ≤ 60 min

<u>Screening data on not enrolled patients with one of the chief complaints</u>

- Date of birth, gender, patient initials
- Chief complaint: runny nose, sore throat, ear pain, sinus pain or cough
- Severity of chief complaint: 0 = not present, 1 = mild, 2 = moderate, 3 = severe, 4 = very severe
- Reason for non-inclusion
- Screening date
- Therapy prescribed or measure taken

<u>Prescribed therapies at baseline</u>

- Primary therapy prescribed at study entry: a) anthroposophic medicines: any medication produced by Wala or Weleda, 1 to 2 remedies possible, b) conventional medicines: any non-anthroposophic medication, only 1 remedy possible;
- Adjunctive therapies prescribed at study entry: c) anthroposophic medicines, d) homeopathic medicines, e) herbal medicines, f) conventional medicines = not anthroposophic, homeopathic or herbal, g) external non-medication applications, h) steam,

i) nasal lavage, j) saline lavage, k) gargle, l) ear oil, m) diet, n) enema, o) acupuncture, p) other adjunctive therapy.

Items a), g), m), and n) were only documented in the A-group.

For items a) and b): name, dose, medication form, dosing frequency, number of days prescribed, doctor's confidence in prescription: numeric scale from 0 (= none) to 10 (= total).

For items c), d), and e): 1 to 3 remedies possible, for each remedy: name, dose, medication form, dosing frequency, number of days prescribed.

For each remedy of items a) and c): manufacturer.

For item g): name, dosing frequency, number of days prescribed.

Outcomes collected at baseline and follow-up

- Severity of chief complaint: 0 = not present, 1 = mild, 2 = moderate, 3 = severe, 4 = very severe
- Symptom Score: mean severity (0 = not present, 1 = mild, 2 = moderate, 3 = severe, 4 = very severe) of complaint-related symptoms, according to chief complaint:
  - Chief complaint runny nose: runny nose, sneezing, itchy nose, nasal congestion, loss of smell, post-nasal drip, itchy eyes, red / watery eyes
  - Chief complaint sore throat: sore throat, difficulty swallowing, lump in throat, swollen glands, fever
  - Chief complaint ear pain: ear pain, feeling of 'plugged ear', discharge from ear, hearing loss, fever
  - Chief complaint sinus pain: sinus pain, headache, post-nasal drip, purulent discharge, fever
  - Chief complaint cough: cough, expiratory wheezing, sputum expectoration, pain with coughing/breathing, shortness of breath, fever

  Fever was graded: 0 = < 37.5°C, 1 = 37.5°C to < 38.5°C, 2 = 38.5°C to < 39.5°C, 3 = 39.5°C to <40.5, 4 = ≥ 40.5°C
- Health-related quality of life:
  - KINDL® Parents' Questionnaire for patients from > 1 month to < 8 years (14;78;79)
  - KINDL® Children's Questionnaire for patients from ≥ 8 to < 16 years
  - SF-12® Health Survey for patients > 16 years (31;105)

Follow-up outcomes

- Time to first improvement: number of hours or days
- Treatment outcome ("How would you rate the outcome of your treatment?"): complete recovery, major improvement, slight to moderate improvement, no change, deterioration
- Time to total recovery: number of hours or days
- Follow-up contact with doctor: office visit, home visit, telephone consultation, no follow-up contact
- Change in medication for chief complaint or for concomitant medical problems
- Medication taken as prescribed since the initial contact? (yes/no)

- Adverse Events (AE), Serious Adverse Events (An Adverse Event was assessed as serious if the necessary action due to the adverse event was "admit to hospital" or if the outcome of the adverse event was "patient alive, but with permanent health damage" or "patient died").
  - Name of AE
  - Intensity of AE: mild (no impairment of the normal daily activities), moderate (impairment of the normal daily activities), severe (complete impairment of the normal daily activities)
  - Relationship of AE with study medication: probable, possible, improbable, unable to evaluate, no relationship
  - Other causes if no relationship: concomitant illness, concomitant medication, other
  - Necessary actions against AE: none, dose reduction of study medication, withdrawal of study medication, admit to hospital, therapeutic counteractions, change of concomitant medications, others
  - Outcome of AE: AE subsided, AE still being treated, uncertain – AE still under observation, patient lost to follow-up, patient alive but with permanent health damage
- Patient satisfaction with the treatment: very satisfied, satisfied, neutral, dissatisfied, very dissatisfied
- Patient satisfaction with the doctor: very satisfied, satisfied, neutral, dissatisfied, very dissatisfied
- "Would you choose this therapy again for your problem?" (yes/no)
- "Would you choose this health care provider again for your problem?" (yes/no)

Quality Assurance

Quality assurance of data entry

The remote data entry system used (ClinWeb®) was constructed to check each entry of the investigator concerning completeness and consistency. The system notifies the investigator of the entry of implausible data into the system or when he fails to enter important data. In addition, warning messages for data violating the protocol are displayed. After entry of data into the remote data entry system, the data are automatically encrypted and transferred by the investigator via the internet to the central study database. The remote data entry system records all data values with date and time of entry into the database in the audit trail. The altering of a value in the system is stored together with the identity of the person who stored the data into the database. It is not possible to modify the audit trail.

To prevent an illegal access to the database, the remote data entry system offers password identification. Each user of the system has a unique password provided in a sealed envelope. The system stores all data values entered into the database with the number identifying the study centre, and connection to the password of the user entering the data.

Study monitoring

Monitoring of the study was performed adherent to the GCP-Guidelines. At each study centre, monitoring visits took place at least twice during the course of the trial. During this visit Source Data Verification (SDV) was carried out by direct comparison with the original

patient files, or by counter-checking the documents in the presence of the investigator physician.

For the following items SDV of 100% of the study data was performed: initials, date of birth, gender, inclusion criteria, chief complaint, exclusion criteria, inclusion of patient, informed consent, name, duration of chief complaint, complaint-related symptoms, diagnosis, primary treatment, adjunctive therapies, study withdrawal during initial consultation, changes in concomitant medication, Adverse Events. For the following items SDV of ≥ 20% of the study data was performed: concomitant medical problem, concomitant medication.

Data preparation and analysis

Data preparation

Data collection, follow-up telephone interviews, electronic query generation and the preparation of the database for analysis were performed by the Institute for Numerical Statistics GmbH (now: Omnicare Clinical Research GmbH & Co. KG), Cologne, Germany. Diagnoses were coded according to the International Classification of Diseases, 9th Edition (ICD-9). All medications were coded according to WHO Drug Dictionary. In addition, all anthroposophic medications were coded according to Wala and Weleda medication lists. Anthroposophical medications with identical name and dosage form but different decimal potencies were grouped together, medications with identical name but different dosage form were separately coded. In cases where more than one anthroposophic medication had been entered into a preparation name field or where an anthroposophic medication had been incorrectly documented as a herbal medication or external application, this medication was reallocated as “adjunctive therapy, anthroposophic medicine”. Adverse Events were coded according to WHO Adverse Reaction Terminology. For this study report, all Adverse Events with a probable or possible causal relationship with study medication – according to the patient follow-up responses – were classified as Adverse Drug Reactions without further evaluation of the causal relationship.

Data analysis

Patients fulfilling all inclusion and no exclusion criteria and with evaluable data for at least one scheduled follow-up interview (Day 7, Day 14, or Day 28) were included in the analysis. For patients with treatment outcome “complete recovery” on Day 7 or Day 14 the study participation was terminated and their follow-up data from this study day were used for the analysis of subsequent Study Days (Last Observation Carried Forward principle, LOCF). Follow-up data missing for other reasons were also replaced by data from previous follow-ups when available (LOCF). For Symptom Score, SF-12 Summary Score and KINDL Summary Score, however, only available follow-up data were analysed.

Data analysis followed the intention-to-treat principle, including patients non-compliant with study prescriptions. Data were analysed by ClinResearch GmbH, Cologne, Germany (univariate, bivariate and multivariate statistical methods using SAS 8.2®) and IFAEMM e. V., Freiburg, Germany (supplementary univariate and bivariate analyses using SPSS 11.0® and StatXact 5.0.3®). Bivariate comparisons were performed using the two-tailed Fisher’s exact

test for dichotomous data and the two-tailed Mann-Whitney U-test for rank ordered data. Median differences with 95% confidence intervals were estimated with the method of Hodges and Lehmann (42). Pre-post effect sizes were calculated as Standardized Response Mean ($Mean_{pre\text{-}post}$ / $SD_{pre\text{-}post}$) (56). Major follow-up outcomes were dichotomised (antibacterial prescription throughout the study, time to first improvement ≤ 24 hours, time to first improvement ≤ 3 days, response rate on Day 7, Day 14 and Day 28, complete recovery rate on Day 7, Day 14 and Day 28, patient satisfaction with treatment = very satisfied at all evaluable follow-ups, patients' choice of therapy again for chief complaint = yes at all evaluable follow-ups, adverse drug reaction throughout the study) and analysed in subgroups pertaining to seven predefined variables: country (A, D, NL, UK, US), gender, age (< 2 years, 2-5 years, 6-17 years, 18-34 years, 35-64 years, ≥ 65 years), chief complaint (runny nose, sore throat, ear pain, sinus pain, cough), duration of chief complaint (0 to ≤ 24 hours, 24 to ≤ 48 hours, 2 to ≤ 7 days), previous episode of chief complaint within last 12 months (yes/no), and Symptom Score on Day 0 (0 to < 1, 1 to < 2, 2 to < 3, 3 to 4). Unadjusted odds ratios, with 95% confidence intervals were determined for the total sample and the above-mentioned subgroups. For all major outcomes except antibacterial prescription and adverse drug reactions, multiple logistic regression analysis was conducted to adjust for potentially confounding factors affecting the outcomes (country, gender, age, chief complaint, duration of chief complaint, chief complaint episode within last 12 months, Symptom Score at Day 0). Criteria for statistical significance were $p < 0.05$ and (where applicable), 95%-CI not including 0.

Adherence to regulations

Ethics Committee approvals

The study was approved by the following institutions:

- Germany: the Ethics Committees of Landesärztekammer Thüringen, Landesärztekammer Hessen, Ärztekammer Berlin, Landesärztekammer Baden-Württemberg, Ärztekammer Westphalen-Lippe, Westfälische Wilhelms-Universität Münster, Freiburger Ethik-Kommission International
- The Netherlands: Independent Review Board, Amsterdam
- United Kingdom: The Southampton & S. W. Hants Joint Research Ethics Committee, (The United Bristol Healthcare NHS Trust Research Committee and The Grampian Research Ethics Committee considered the study an audit not requiring formal approval)
- United States: The Institutional Review Board of the Los Angeles College of Chiropractic

In Austria, the study was registered as an „Anwendungsbeobachtung", not requiring formal approval.

Legal requirements

The study was conducted according to the Declaration of Helsinki, the Good Clinical Practice (GCP) guidelines and the legal requirements in the participating countries. Written informed consent was obtained from all patients before study entry.

Results

Participating doctors

43 doctors (27 anthroposophic + 16 conventional) consented to participate, 37 doctors (26 anthroposophic + 11 conventional) enrolled patients. 36 physicians (26 anthroposophic and 10 conventional) had evaluable patients, these physicians were located in Austria (3 anthroposophic + 3 conventional physicians), Germany (7+3), The Netherlands (6+2), United Kingdom (2+2) and the USA (8+0), in altogether 29 different primary care practices (21 anthroposophic + 8 conventional) in 23 different municipalities (17 municipalities with anthroposophic practices + 3 with conventional + 3 with anthroposophic and conventional practices).

The anthroposophic doctors had median 15.5 years (range 6.0-40.0) years medical practice, thereof median 13.5 years (range 6.0-40.0) practicing anthroposophic medicine. Corresponding information was not obtained from the conventional doctors. Six (17%) anthroposophic doctors and two (20%) conventional doctors were women.

Patient recruitment and follow-up

Overview

From 21 April 1999 to 30 March 2000 a total of 1171 patients were enrolled. 1016 patients were evaluable (data from at least one follow-up interview): 715 in the Anthroposophy Group (A-group) and 301 in the Conventional group (C-group). 155 patients had no evaluable follow-up data and were excluded from the analysis (Figure 1).

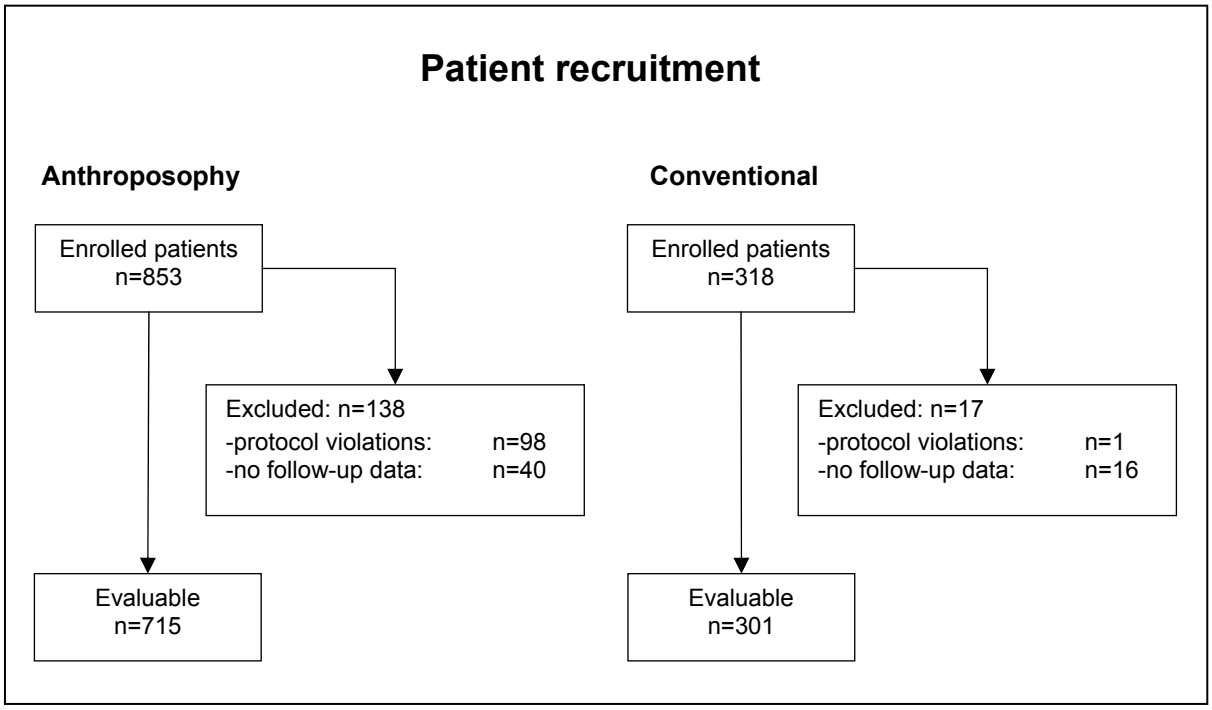


Figure 1 Patient recruitment

Evaluable patients: Availability of baseline and follow-up data

Doctors' Day 0 documentation was available for all patients. For administrative reasons, patients' Day 0 self-report questionnaires were unavailable for 141 (19.7%) of 715 A-patients and 37 (12.3%) of 301 C-patients ($p = 0.0049$).

For the 1016 evaluable patients, altogether 2152 follow-up interviews were scheduled on Day 7-28, for 219 (10.2%) interviews data are missing. Reasons were:

- patient unreachable on the phone: 116 interviews, 53% of missing interviews, 5.4% of all scheduled interviews,
- other practical or technical reasons, e. g. remote data entry system failure, follow-up script unavailable to interviewer: 95 interviews, 43.4% of missing interviews, 4.4% of scheduled interviews,.
- patient refusal to participate: 8 interviews (1 interview on Day 14 in the A-group, 2+2+3 interviews on Days 7+14+28 with 5 C-patients), 3.7% of missing interviews, 0.4% of scheduled interviews.

The proportion of missing data for each follow-up interview (Figure 2) did not differ significantly between the A-group and C-group.

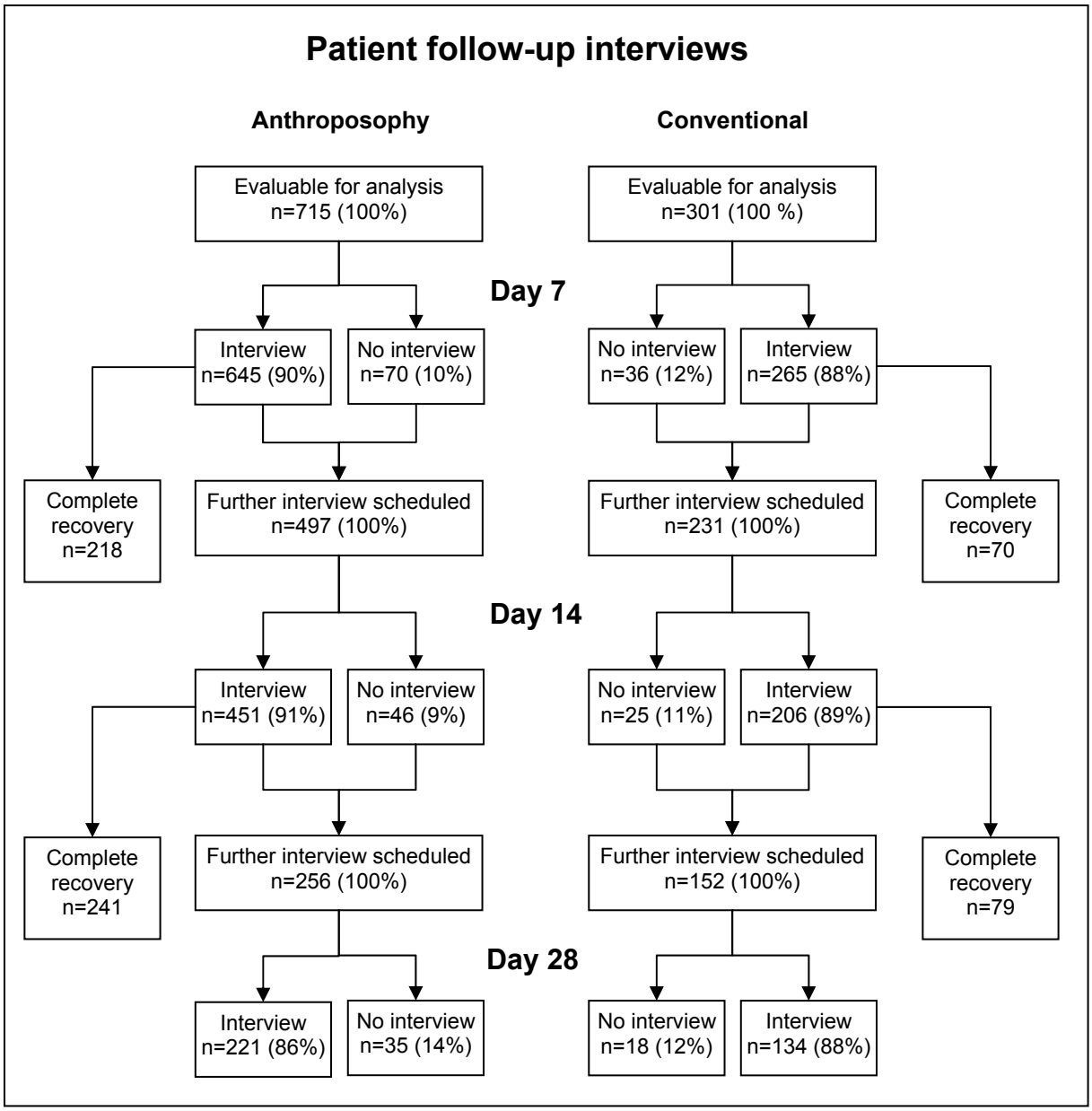


Figure 2 Patient follow-up telephone interviews. Evaluable for analysis = patients with at least one follow-up interview.

Screened, not enrolled patients

Screening data were available from 19 out of A-26 doctors. These 19 A-doctors had enrolled 679 (95.0%) of the 715 A-patients. No screening data were available from C-doctors. In the A-group 878 patients were screened but not enrolled. 461 of screened and not enrolled A-patients fulfilled all study inclusion and no study exclusion criteria (NE-A-patients): reasons for non-inclusion were: doctor's lack of time (68.1%, n = 314/461), practical or technical obstacles (12.1%, n = 56), ongoing therapy for chief complaint (2.0%, n = 9), special diagnoses (5.6%, n = 26), other reasons or not specified (12.1%, n = 56). The NE-A-patients (n = 461) did not differ from the enrolled and evaluable A-patients (n = 715) with respect to gender, severity of chief complaint and the proportion of patients with a chief complaint of sinus pain or cough. Compared to the evaluable A-patients, the NE-A-patients were median 1.13 years younger (95%-CI: 0.38-1.95, p = 0.0036) and had significantly less

frequent chief complaints of runny nose (4.0% = 18/455 vs. 6.9% = 49/715) and sore throat (17.6% = 80/455 vs. 26.3% = 188/715) and significantly more frequent a chief complaint of ear pain (27.7% = 126/461 vs. 20.0% = 143/715). 13 (2.8%) of 461 NE-A-patients and 6 (0.8%) of 715 evaluable patients were prescribed antibacterial agents (p = 0.0153).

Patient exclusions

The quality control of the follow-up data revealed that one telephone interviewer had not performed interviews according to the protocol (protocol violations). This interviewer, who had been responsible for all follow-up interviews with US patients, was replaced on 13 Feb 2000, and all US follow-up data until that date (99 patients) were excluded from the analysis.

56 patients (A-group: n = 40, C-group: n = 16) were excluded because no follow-up telephone interviews had been performed. 49 of these 56 patients were lost to follow-up due to technical or practical reasons, 7 patients (A-group: 5/40 patients, C-group: 2/16) refused to participate in the follow-up interviews.

In the 155 excluded patients, 2 Adverse Events were recorded, one Serious Adverse Event in the C-group (acute hospitalization due to pneumonia; cause: investigational medication; outcome: patient alive, but with permanent health damage) and one not serious in the A-group (exanthema + viral infection). In the A-group, evaluable patients had significantly higher, i. e. worse baseline Symptom Score than excluded patients (mean 1.3 ± 0.7 vs. 1.0 ± 0.6, p < 0.0001), whereas baseline Symptom Score did not differ significantly between evaluable and excluded C-patients (1.2 ± 0.6 vs. 1.3 ± 0.4, p = 0.4205).

Number of patients recruited per doctor

A-doctors recruited median 11 patients (i. q. r. 6-41, mean 28 ±28 patients), C-doctors recruited median 25 patients (i. q. r. 15-33, mean 30 ±25 patients) each. 13 A-doctors and 9 C-doctors recruited at least 10 patients each (Figure 3), altogether these 22 doctors recruited 645 (90.2%) of the 715 A-patients and 299 (99.3%) of the 301 C-patients.

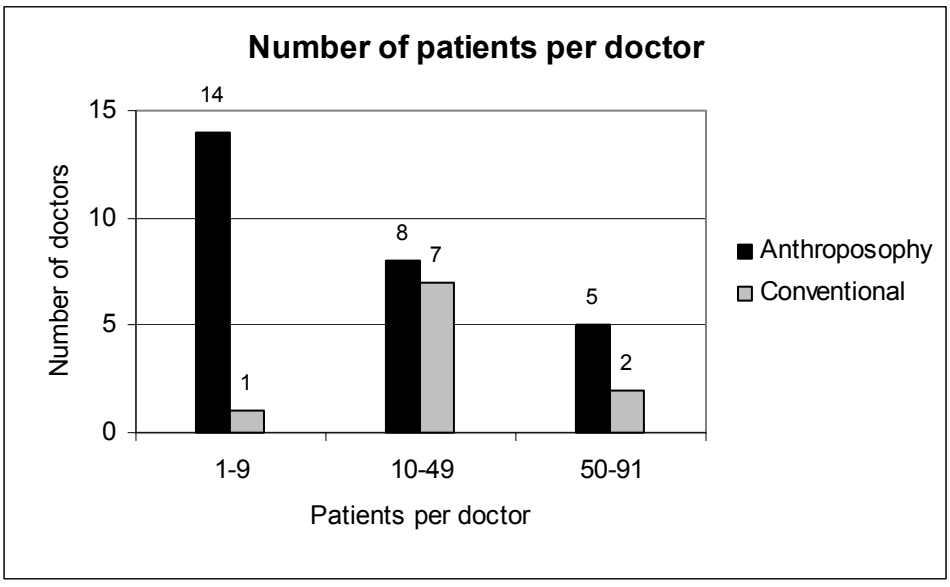


Figure 3 Number of patients recruited per doctor, Anthroposophy Group: n = 26 doctors, Conventional Group: n = 10 doctors.

Baseline characteristics

Demographics

In the A-group the proportions of patients from Germany and the USA were significantly higher and the proportion of patients from the UK was significantly lower than in the C-group (Figure 4).

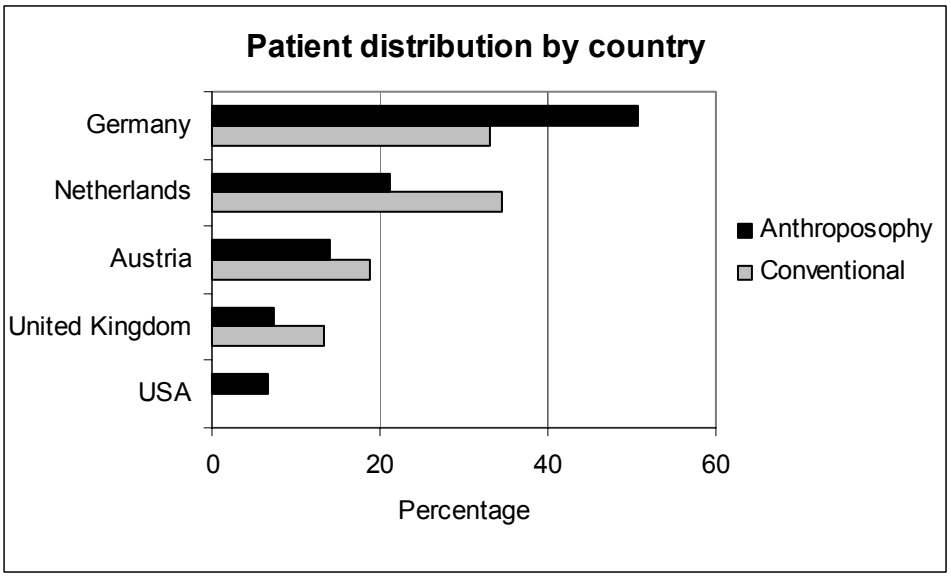


Figure 4 Patient distribution by country, Anthroposophy Group: n = 715, Conventional Group: n = 301.

The two groups did not differ significantly with respect to gender (females: 53.4% in A-group and 59.8% in C-group), body mass index in adults and in children, proportion of smokers, and the total number of persons in household. Median (interquartile range) age was 6.0 years (3.0-28.0) in the A-group and 32.0 years (10.0-42.0) in the C-group, with a relative over-representation of children up till the age of 11 years in the A-group (Figure 5).

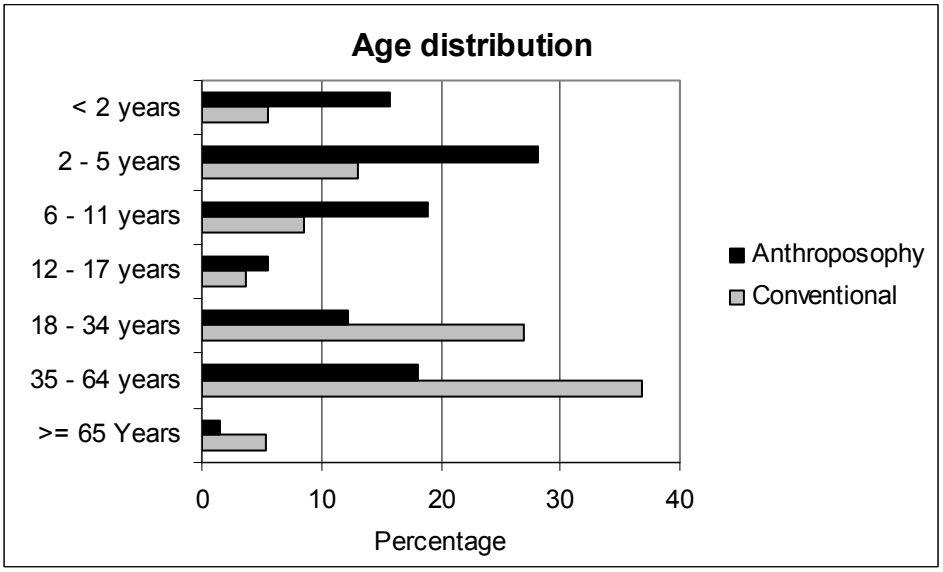


Figure 5 Age distribution, Anthroposophy Group: n = 715, Conventional Group: n = 301

The relative over-representation of children aged 11 years or less in the A-group was present in all chief complaint subgroups (Figure 6). There were considerable age differences between the chief complaint subgroups, especially between the ear pain (predominantly children) and sinus pain groups (predominantly adults).

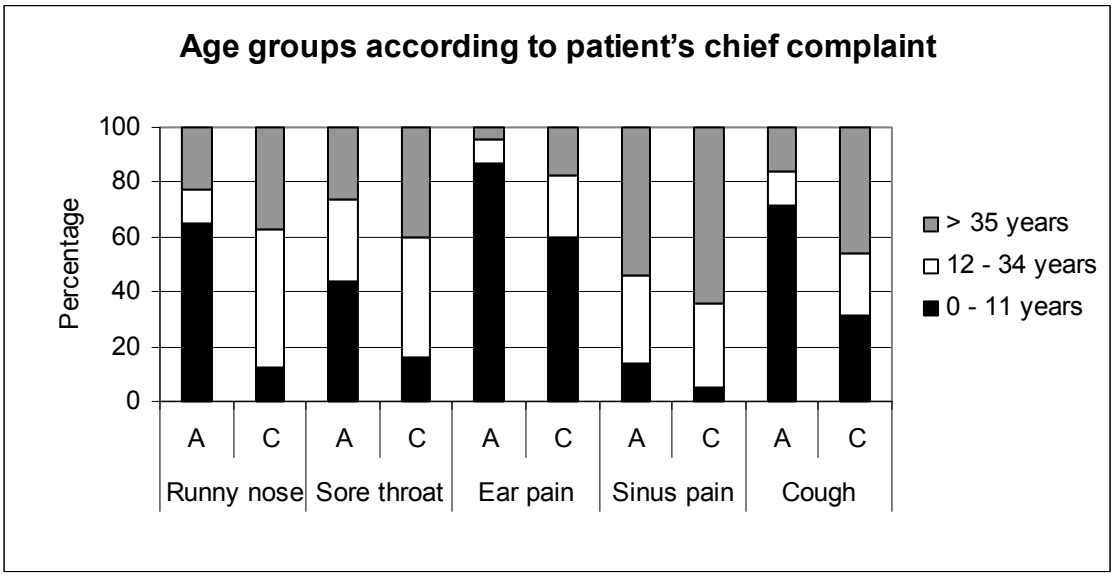


Figure 6 Age distribution according to patient's chief complaint. A: Anthroposophy Group, C: Conventional Group. Percentages refer to the number of A-group and C-group patients with each Chief Complaint.

The annual household income did not differ significantly between the groups, but the A-group had a much higher proportion of self-pay patients than the C-group (20.1% vs. 0.8%) and also a higher proportion of patients willing to pay the entire costs of the treatment (30.8% vs. 12.5%) (Table 2).

Baseline characteristics: Economic issues					
	Anthroposophy		Conventional		
Total annual household income	**N**	**%**	**N**	**%**	**Mann-Whitney U-test**
< 15,000 €	75	21.5%	31	20.7%	
15,000-29,999 €	95	27.2%	42	28.0%	
30,000-44,999 €	88	25.2%	45	30.0%	p = 0.5856
45,000-59,999 €	47	13.5%	22	14.7%	
60,000-74,999 €	28	8.0%	7	4.7%	
≥ 75,000 €	16	4.6%	3	2.0%	
Sum respondents	349	100.0%	150	100.0%	
Further economic issues	**Proportion of patients**	**%**	**Proportion of patients**	**%**	**Fisher's exact test**
Self-pay patients	113/562	20.1%	2/258	0.8%	p < 0.0001
Willing to pay the entire treatment costs	168/545	30.8%	32/257	12.5%	p < 0.0001

Table 2 Total annual household income, proportion of self-pay patients and patients willing to pay the entire treatment costs. Percentage of respondents.

Chief complaint

A chief complaint of sinus pain was significantly more frequent in the C-group (56 out of 301 patients) than in the A-group (50/715) ($p < 0.0001$). The frequency of the other chief complaints did not differ significantly between the groups (Figure 7).

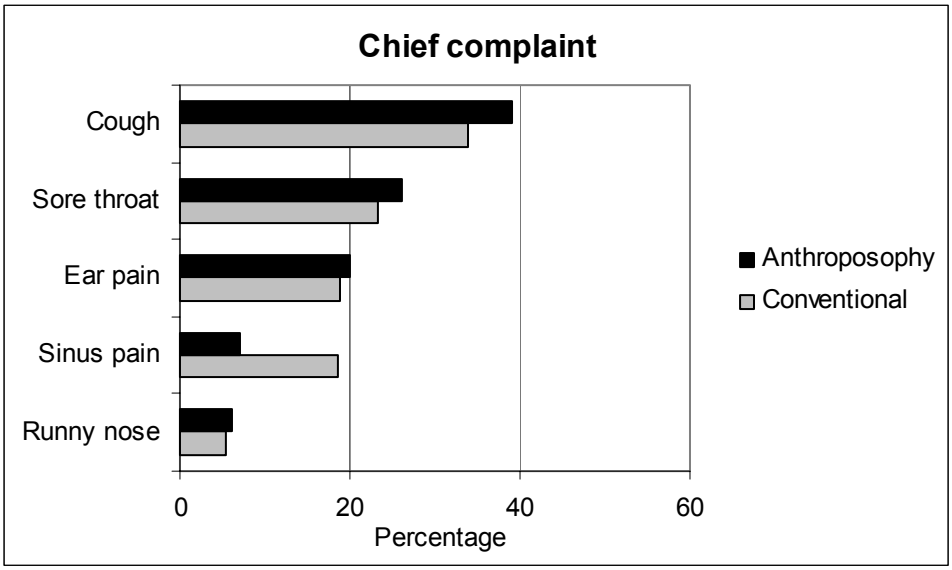


Figure 7 Chief complaint, Anthroposophy Group: n = 715, Conventional Group: n = 301

The onset of the chief complaint was more recent in the A-group than in the C-group ($p = 0.0043$) (Figure 8).

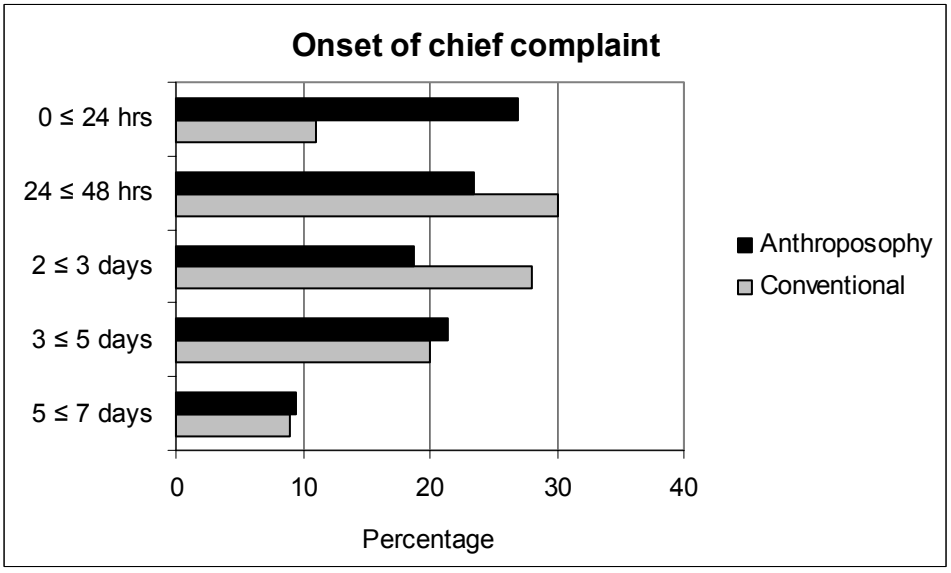


Figure 8 Duration of chief complaint from onset until the Day 0 consultation, Anthroposophy Group: n = 715, Conventional Group: n = 301

Most patients had a chief complaint of moderate to severe severity (Figure 9). The proportion of patients with a chief complaint of very severe severity was higher in the A-group than in the C-group ($p < 0.0001$).

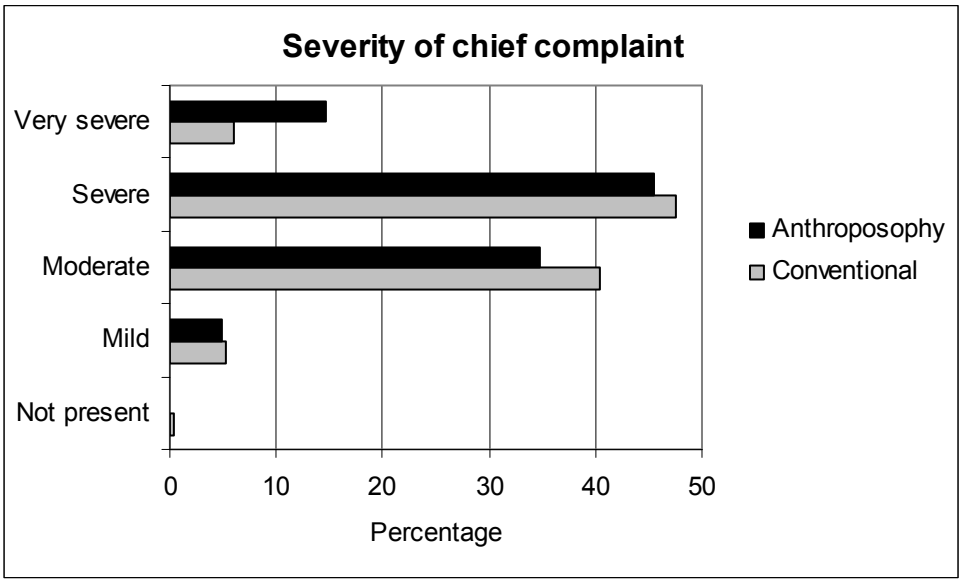


Figure 9 Baseline severity of chief complaint, percentage of responses. Anthroposophy Group: n = 715, Conventional Group: n = 301

Mean baseline severity of chief complaint was similar in the two groups, also within each chief complaint subgroup (Figure 10), except for patients with a chief complaint of ear pain, with a mean severity (0-4) of 2.9 ± 0.8 in the A-group (n = 143) and 2.3 ± 0.8 in the C-group (n = 57), $p < 0.0001$, estimated median difference: 1.00 (95%-CI: 0.00-1.00). The proportion of patients with severe or very severe ear pain was higher in the A-group (69.2%; 99/143 patients) than in the C-group (43.9%; 25/57) ($p = 0.0012$).

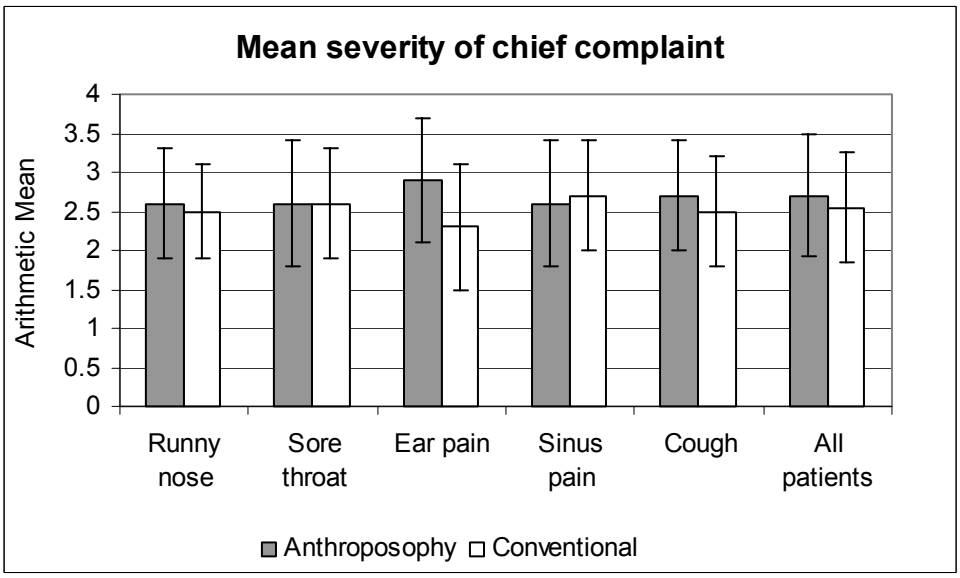


Figure 10 Mean (standard deviation) baseline severity of chief complaint. 0 = not present, 1 = mild, 2 = moderate, 3 = severe, 4 = very severe. All patients: n = 714 (Anthroposophy Group), n = 300 (Conventional Group).

A previous episode of the chief complaint within the last 12 months was reported in a significantly higher proportion of A-patients than C-patients (Figure 11).

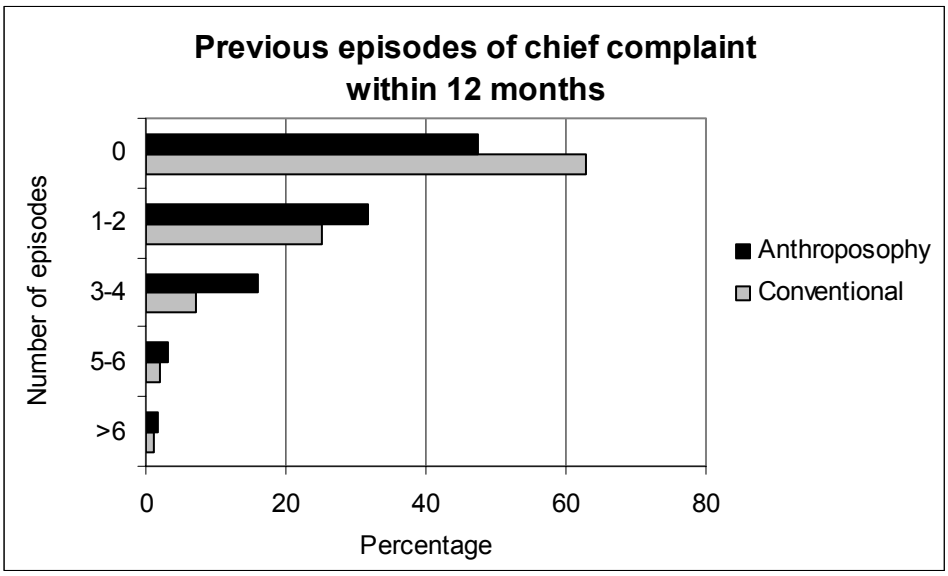


Figure 11 Number of episodes of chief complaint within the last 12 months. Anthroposophy Group: n = 714, Conventional Group: n = 298

The proportions of patients with an episode of the chief complaint within the last 12 months was higher in the A-group among patients with a chief complaint of runny nose, sore throat, ear pain and cough, and higher in the C-group among patients with a chief complaint of sinus pain. These subgroup differences were significant for three of the five subgroup comparisons (Table 3).

Episode of the chief complaint within the last 12 months					
Chief complaint	Anthroposophy		Conventional		Fisher's exact test
	Proportion of patients	%	Proportion of patients	%	
Runny nose	32/49	65.3%	4/16	25.0%	p = 0.0082
Sore throat	78/188	41.5%	18/69	26.1%	p = 0.0288
Ear pain	77/143	53.8%	22/57	38.6%	n. s.
Sinus pain	18/50	36.0%	29/56	51.8%	n. s.
Cough	171/284	60.2%	38/102	37.3%	p = 0.0001
All patients	376/714	52.7%	111/300	37.0%	p < 0.0001

Table 3 Patients with a previous episode of the chief complaint within the last 12 months. Subgroup analysis for chief complaint.

Of the more commonly occurring chief complaint diagnoses, a diagnosis of pharyngitis/tonsillitis or bronchitis was significantly more frequent and a diagnosis of sinusitis was less frequent in the A-group. Otherwise the distribution of diagnoses differed little between the groups (Table 4).

Diagnosis of chief complaint					
Diagnosis	**Anthroposophy N=715**		**Conventional N=301**		**Fisher's exact test**
	N	**%**	**N**	**%**	
Pharyngitis or tonsillitis	185	25.9%	60	19.9%	p = 0.0449
Bronchitis	138	19.3%	42	14.0%	p = 0.0475
Otitis media	123	17.2%	39	13.0%	n. s.
Laryngitis or tracheitis	108	15.1%	43	14.3%	n. s.
Rhinitis / common cold	81	11.3%	32	10.6%	n. s.
Sinusitis	53	7.4%	59	19.6%	p < 0.0001
Acute URI unspecified	22	3.1%	16	5.3%	n. s.
Eustachian tube disease	11	1.5%	8	2.7%	n. s.
Viral infection unspecified	11	1.5%	0	0.0%	p = 0.0401
Asthma, obstructive bronchitis	8	1.1%	2	0.7%	n. s.

Table 4 Diagnosis of chief complaint. Multiple responses possible. Percentages of patients in the A-group and C-group. Diagnoses occurring in at least 1% of patients in A-group or C-group listed.

Doctors' confidence in their diagnosis (0-10) was similarly high in the A-group (mean 9.1 ±1.1) and C-group (9.0 ±1.2). In 53 (7.4%) of A-715 and in 53 (17.6%) of 301 C-patients this confidence was based on clinical symptoms alone ($p < 0.0001$), in all other patients a nose check, tonsil check, lung check, ear check or another investigation had been performed. In the chief complaint subgroups, this difference was significant for sore throat: Diagnosis was based on symptoms alone in 6.4% (12/188) of A-patients and 31.4% (22/70) of C-patients ($p < 0.0001$).

Complaint-related symptoms, quality of life, concomitant medical problems

At baseline, the two groups did not differ significantly with respect to baseline Symptom Score, the presence of severe or very severe pain (sore throat, ear pain, sinus pain, pain on coughing), fever ≥ 39.5°C (Figure 12), SF-12 Summary Score, KINDL Summary Score, and the presence of or medication use for concomitant medical problems (Table 5). No patients were using anti-bacterial agents, one C-patient and no A-patient was using systemic corticosteroids at study entry.

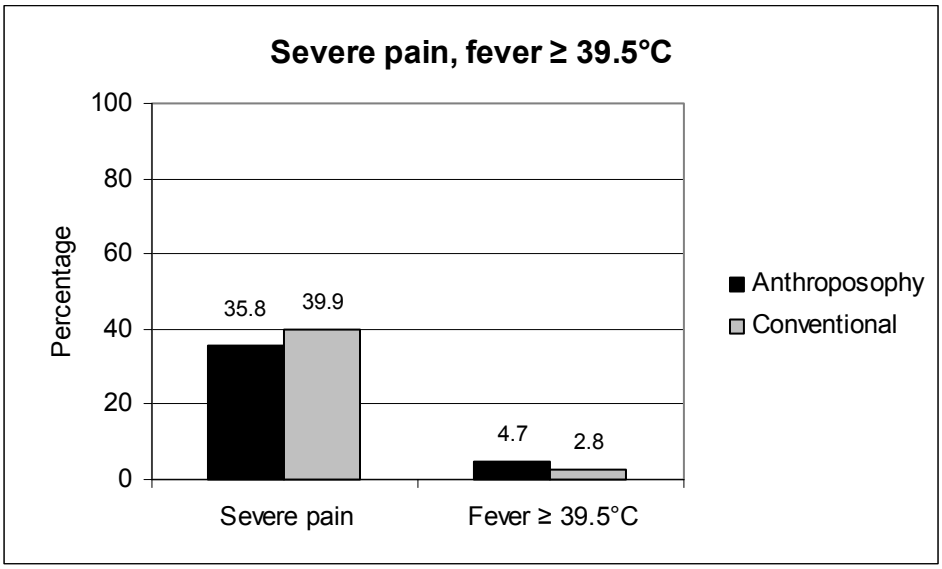


Figure 12 Percentage of patients with baseline pain (sore throat, ear pain, sinus pain, pain on coughing) severity: severe or very severe, percentage of patients with fever ≥ 39.5°C at baseline. Patients with chief complaint sore throat, ear pain, sinus pain, or cough. Anthroposophy Group: n = 666, Conventional Group: n = 283.

Baseline characteristics: concomitant medical problems					
	Anthroposophy N=715		Conventional N=301		
	N	%	N	%	Fisher's exact test
Concomitant medical problem present	226	31.6%	97	32.2%	n. s.
ICD-9 classification of concomitant medical problem*					
-Diseases of the respiratory system	65	9.1%	30	10.0%	n. s.
-Endocrine, nutritional and metabolic diseases, immunity disorders	35	4.9%	16	5.3%	n. s.
-Diseases of the nervous system and sense organs	30	4.2%	6	2.0%	n. s.
-Symptoms, signs, and ill-defined conditions	29	4.1%	14	4.7%	n. s.
-Diseases of the circulatory system	14	2.0%	17	5.6%	p = 0.0041
Any medication use for concomitant medical problem	128	17.9%	62	20.6%	n. s.
Main medication groups**					
-Anti-asthmatics	12	1.7%	10	3.3%	
-Cough and cold preparations	1	0.1%	7	2.3%	

Table 5 Concomitant medical problems at baseline. *ICD-9 groups present in ≥ 5% of the patients of the Anthroposophy Group or Conventional Group listed. ** Medication groups (coding according to Drug Dictionary) used by ≥ 2% of the patients in the Anthroposophy Group or Conventional Group listed.

Previous experience with doctor, confidence in doctor, consultation type and length

The proportions of patients previously treated by the doctor and the proportions of patients with an office visit leading to study inclusion were similarly high in both groups. In the A-group a higher proportion of patients had freedom to choose the study doctor (Table 6).

Baseline characteristics: Patient-doctor aspects					
	Anthroposophy N=715		Conventional N=301		
	Proportion of patients	%	Proportion of patients	%	Fisher's exact test
Patients with previous experience with this doctor	507/566	89.6%	236/260	90.8%	n. s.
Patients with previous experience with anthroposophic medicine	498/567	87.8%	Not asked		
Patients confident that the doctor will solve his/her medical problem	556/560	99.3%	258/262	98.5%	n. s.
Consultation type: office visit	682/715	97.3%	284/301	94.4%	n. s.
Freedom to choose this doctor: yes	525/573	91.6%	203/250	78.1%	p < 0.0001

Table 6 Baseline characteristics: Patient-doctor aspects

Nearly all patients in both groups were confident that the doctor would solve their medical problem (Table 6). Patients' confidence in their doctor's professional skills was significantly higher in the A-group than in the C-group (p < 0.0001) (Figure 13).

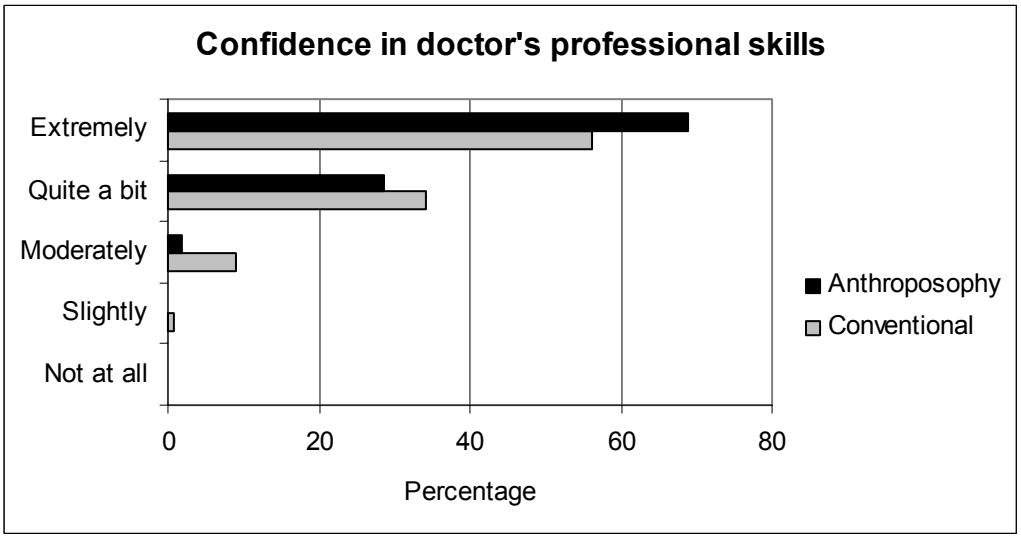


Figure 13 Patients' confidence in their doctor's professional skills. Percentage of respondents. Anthroposophy: Group n = 563. Conventional Group: n = 264.

The consultation length was significantly longer in the A-group than in the C-group ($p < 0.0001$) (Figure 14).

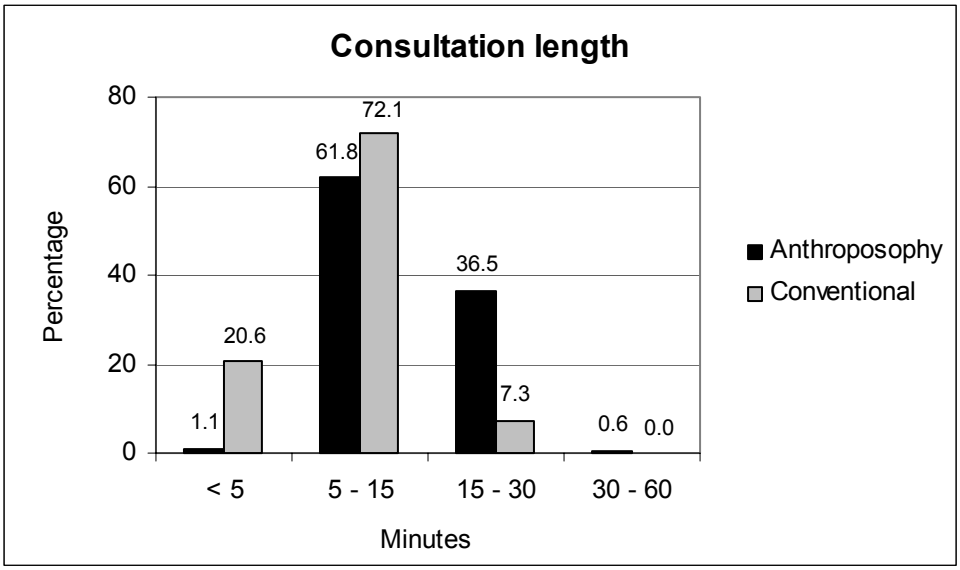


Figure 14 Total length of consultation on Day 0, Anthroposophy Group: n = 715, Conventional Group: n = 301

Patients' and doctors' therapy preferences for the chief complaint, willingness to be randomised

In the A-group 676 (94.5%) of 714 patients had a preference for anthroposophic treatment of their chief complaint, 25 (3.5%) had no preference, five (0.7%) had a preference for conventional treatment and eight (1.1%) patients had another preference. In the C-group 200 (66.7%) of 300 patients had a preference of conventional treatment, 97 (32.3%) had no therapy preference and three (1.0%) patients had another preference.

For 709 (99.3%) of 714 A-patients, their doctor's preference was an anthroposophic treatment for their chief complaint, for four (0.6%) A-patients, the doctor had no preference and for one (0.1%) A-patient the doctor had a preference for conventional treatment. For 286 (95.3%) of 300 C-patients, their doctor's preference was a conventional treatment, for nine (3.0%) C-patients the doctor had no preference, and for five (1.7%) C-patients the doctor had another preference.

96.8% (691/714) of A-patients and 65.0% (195/300) of C-patients were not willing to be randomised if their treatment would be part of a clinical trial ($p < 0.0001$). The most frequent reason for patients refusing randomisation was a treatment preference: 645 (93.3%) of 691 refusals in the A-group and 164 (84.1%) of 195 refusals in the C-group.

Interventions

Primary and adjunctive therapy prescribed on Day 0: main groups

On Day 0, all A-patients and 97% of C-patients were prescribed medicines (Table 7).

Therapy prescribed on Day 0					
Therapy	**Anthroposophy N = 715**		**Conventional N = 301**		**Fisher's exact test**
	N	%	N	%	
Anthroposophic medicines	715	100.0%	0	0.0%	p < 0.0001
Homeopathic medicines	96	13.4%	0	0.0%	p < 0.0001
Herbal medicines	80	11.2%	10	3.3%	p < 0.0001
Conventional medicines = not anthroposophic. homeopathic or herbal	72	10.1%	292	97.0%	p < 0.0001
No medicines	0	0.0%	9	3.0%	p < 0.0001

Table 7 Therapy prescribed on Day 0. Number of patients with prescribed medicine. Multiple responses possible.

Medication was prescribed to be taken for mean 6.3 days ±3.0 in the A-group and 4.6 days ±2.5 in the C-group (estimated median difference: 1.00 days, 95-%-CI: 1.00-2.00 days, p < 0.0001). Doctors mean confidence (0-10) in their prescription was 8.8 ±1.1 in the A-group and 8.0 ±1.7 in the C-group (p < 0.0001, estimated difference: 1.00 points, 95%-CI: 0.00-1.00).

In the A-group, 61 (8.5%) patients were recommended external non-medication applications, 35 (4.9%) patients were recommended steam, 34 (4.8%) nasal lavage, 24 (3.4%) saline lavage, 13 (1.8%) gargle, nine (1.3%) ear oil, four (0.4%) diet, one (0.1%) enema and 59 (8.3%) patients were recommended some other adjunctive therapy. In the C-group one (0.3%) patient was recommended ear oil, one (0.3%) gargle, and one (0.3%) patient had another adjunctive therapy. No patients were recommended steam, nasal lavage, or saline lavage. Diet, enema, and external applications were not documented in the C-group.

Anthroposophic medicine use in the A-group

On Day 0 the A-patients were prescribed average three anthroposophic medicines per patient as primary or adjunctive therapies. 18% of A-patients had at least one further prescription of anthroposophic medicines during the follow-up period (Table 8).

Number of anthroposophic medicines per patient						
Period	**Patients with medicine**		**Number of medicines per patient**			
	N	**%**	**Mean**	**±**	**Mini-mum**	**Maxi-mum**
Taken at study entry for concomitant medical problems	75	10.5%	0.18	0.62	0	7
Prescribed on Day 0 for chief complaint	715	100.0%	2.99	1.48	1	9
Prescribed Day 1-28 for any condition	131	18.3%	0.33	0.87	0	8

Table 8 Number of anthroposophic medicines per patient: taken at study entry and prescribed during the study. Anthroposophy Group (n = 715)

On Day 0, the 715 A-patients were prescribed altogether 222 different anthroposophic remedies, 153 different remedies were prescribed as primary therapy. Throughout the study, altogether 265 different anthroposophic remedies were prescribed. The most frequently prescribed medicines are listed in Table 9.

Most frequently prescribed anthroposophic remedies in A-group, n = 715						
Primary therapy on Day 0	**N**	**%**		**Any prescription Day 0-28**	**N**	**%**
1. Erysidoron® 1 Dilution	91	12.7%		1. Plantago Bronchialbalsam	122	17.1%
2. Zinnober comp. Trituration	91	12.7%		2. Erysidoron® 1 Dilution	100	14.0%
3. Pneumodoron 1 Dilution	65	9.1%		3. Zinnober comp. Trit.	97	13.6%
4. Pyrit / Zinnober Tabletten	56	7.8%		4. Pyrit / Zinnober Tabletten	72	10.1%
5. Plantago Bronchialbalsam	55	7.7%		5. Pneumodoron 1 Dilution	71	9.9%
6. Bolus Eucalypti comp. Trituration	50	7.0%		6. Bolus Eucalypti comp. Trituration	59	8.3%
7. Echinacea Mund- und Rachenspray	39	5.5%		7. Weleda Fichtennadel-Bademilch	53	7.4%
8. Levisticum Rh D.. Dilution	36	5.0%		8. Berdonia Nasenspray	50	7.0%
9. Hepar Sulfuris D.. Trituration	33	4.6%		9. Echinacea Mund- und Rachenspray	49	6.9%
10. Bryonia / Spongia comp. Dilution	30	4.2%		10. Hepar Sulfuris D.. Trituration	49	6.9%
11. Berdonia Nasenspray	27	3.8%		11. Sticta D.. Dilution	49	6.9%
12. Weleda Hustenelixier	25	3.5%		12. Aconit Ohrentropfen	46	6.4%
13. Kalium carbonicum D.. Dilution	23	3.2%		13. Chamomilla comp. Supp.	44	6.2%
14. Apis/Belladonna cum Mercurio Globuli	22	3.1%		14. Infludo® Dilution	40	5.6%
15. Sticta D.. Dilution	22	3.1%		15. Levisticum Rh D.. Dilution	40	5.6%
16. Meteoreisen / Phosphor / Quarz Globuli	21	2.9%		16. Quarz 1% 10 ml Ohrentropfen	35	4.9%
17. Infludo® Dilution	20	2.8%		17. Weleda Hustenelixier	35	4.9%
18. Plantago Hustensaft	20	2.8%		18. Kalium carbonicum D.. Dilution	34	4.8%
19. Ferrum phosphoricum comp. Globuli	19	2.7%		19. Capsicum annuum D.. Dilution	33	4.6%
20. Echinacea comp. Dilution	19	2.7%		20. Nasenbalsam für Kinder	33	4.6%
21-153 Other remedies	550			21-265 Other remedies	1235	
Total number of prescriptions	1314			Total number of prescriptions	2346	

Table 9 20 most frequently prescribed anthroposophic remedies as primary therapy at Day 0, and any prescription Day 0-28, German names. N: Number of patients with prescription. %: Percentage of all patients. Multiple responses possible, sum of percentages does not equal 100%. Anthroposophy Group, n = 715 patients. D..: Remedy exists in several decimal potencies grouped together.

The most common dosage forms of the prescribed anthroposophic medicines were liquids (35% of prescriptions), pillules (11%), and powder (11%). Further details are listed in Table 10 and in the Appendix.

Anthroposophic medicines: Dosage Forms					
Dosage Form	Primary therapy Day 0			Any prescription Day 0-28	
	N	%		N	%
1. Liquid	526	38.6%		830	35.1%
2. Pillules	174	12.8%		263	11.1%
3. Powder	201	14.7%		259	11.0%
4. Ointment	89	6.5%		205	8.7%
5. Ampoule	77	5.6%		137	5.8%
6. Tablets	75	5.5%		110	4.7%
7. Ear drops	24	1.8%		88	3.7%
8. Syrup	55	4.0%		82	3.5%
9. Suppositories	28	2.1%		55	2.3%
10. Bath preparations	0	0.0%		53	2.2%
11. Nose spray	27	2.0%		51	2.2%
12. Mouth spray	39	2.9%		49	2.1%
13. Bath oil	6	0.4%		47	2.0%
14. Oil	9	0.7%		35	1.5%
15. Cream	2	0.1%		33	1.4%
Other	31	2.3%		68	2.9%
Total	1363	100.0%		2365	100.0%

Table 10 15 most common dosage forms of prescribed anthroposophic medicines as primary therapy at Day 0, and any prescription Day 0-28. N: Number of prescriptions. %: Percentage of prescriptions. Anthroposophy Group (n = 715 patients)

Most common ATC groups prescribed Day 0, Day 1-28, Day 0-28

At Day 0, antibiotics (ATC-Index J01 Antibacterial Agents) were prescribed to 80 (26.6%) of 301 C-patients and six (0.8%) A-patients ($p < 0.0001$). Also analgesics, anti-inflammatory agents and antihistamines were prescribed significantly more often in the C-group than in the A-group (Figure 15). During the follow-up period these differences increased (Figure 16). Throughout the study, 101 (33.6%) C-patients and 39 (5.5%) in the A-group were prescribed antibacterial agents ($p < 0.0001$) (Figure 16).

The proportions of patients prescribed nasal or cough and cold preparations did not differ significantly between the two groups throughout the study, except a larger proportion of C-patients being prescribed cough and cold preparations on Day 1-28 ($p = 0.0348$). About half of the cough and cold preparations and one-fourth of the nasal preparations prescribed in the A-group were anthroposophic medicines.

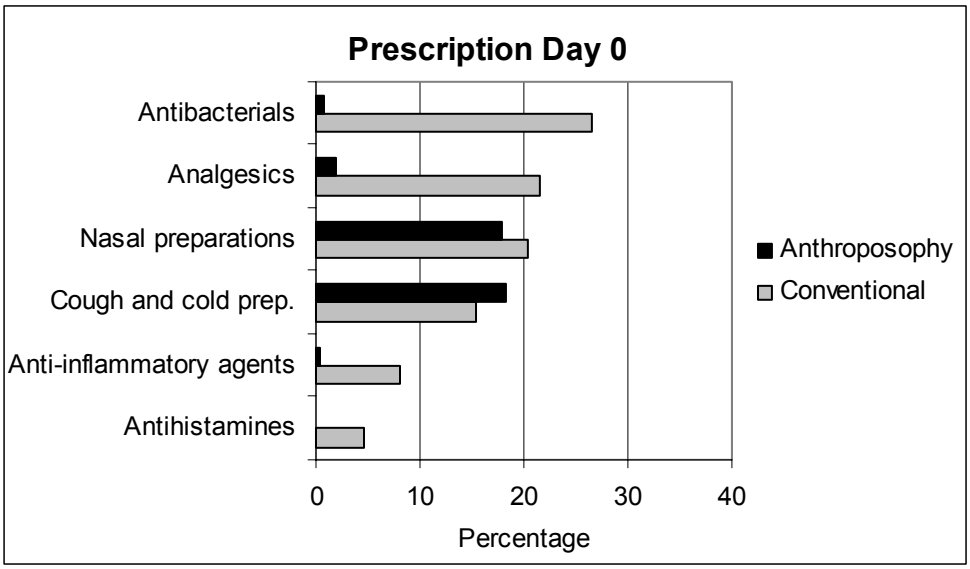


Figure 15 Prescription Day 0: Six most common ATC groups (except V03 All Other Therapeutic Products). Percentage of patients with prescribed medicine. Anthroposophy Group: n = 715, Conventional Group: n = 301

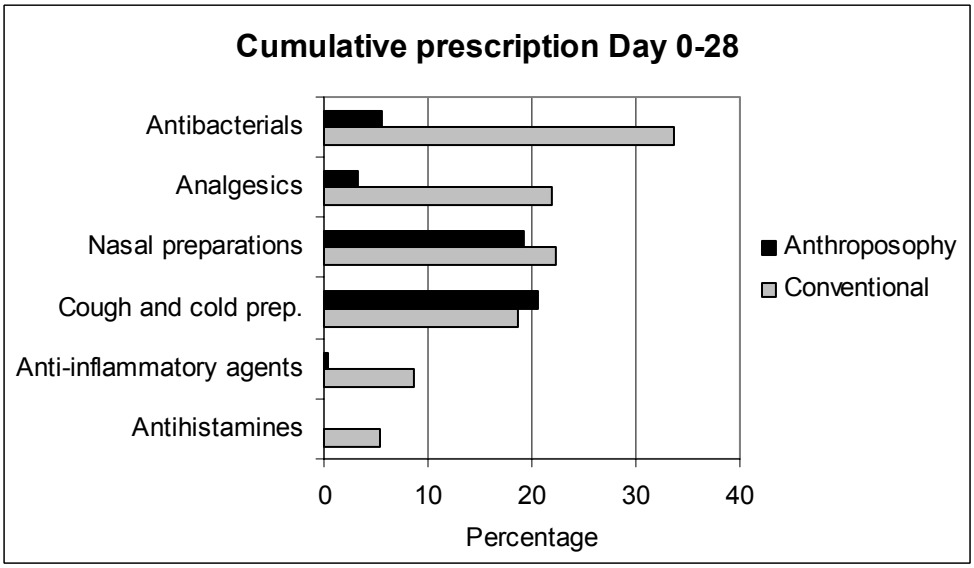
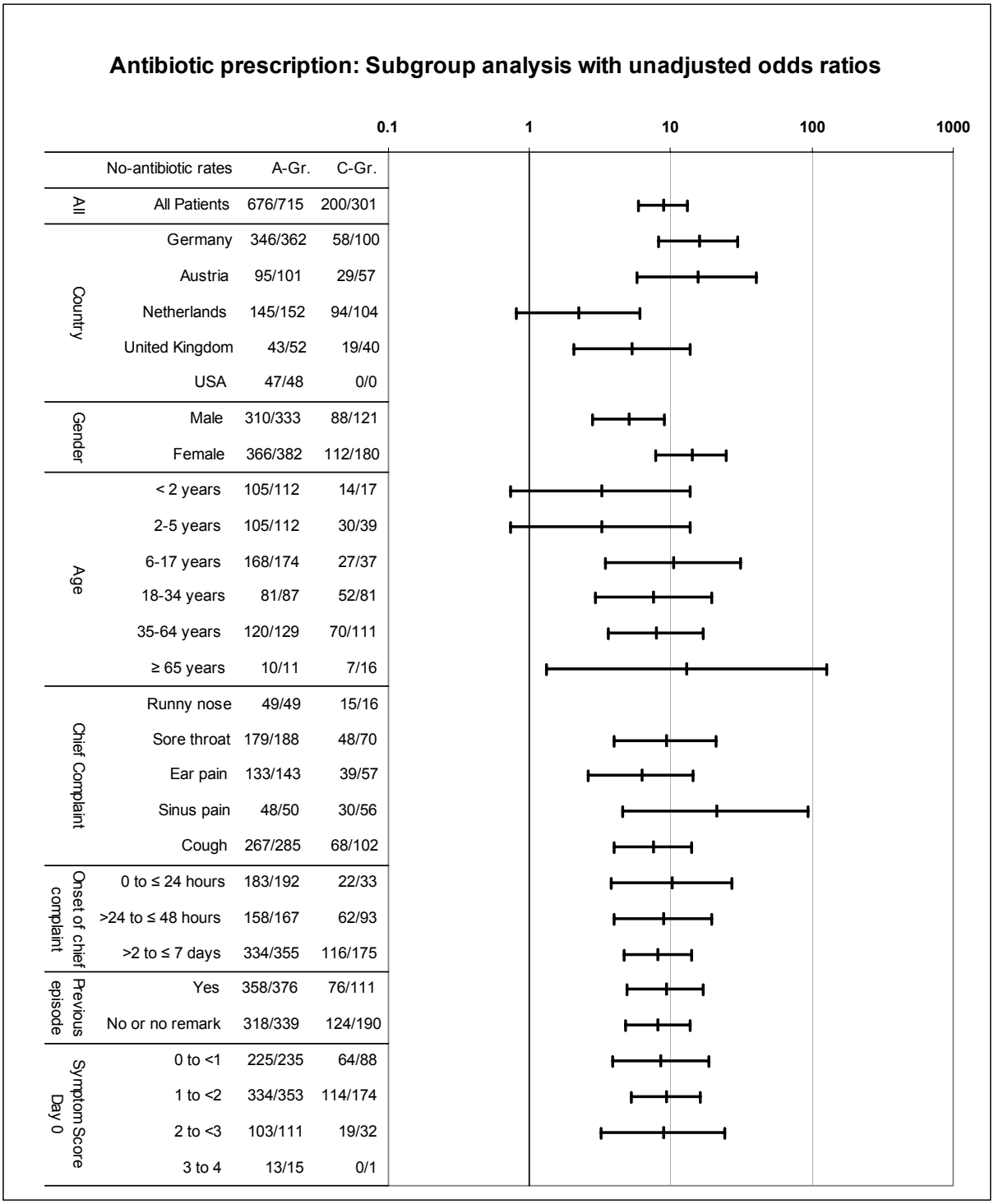


Figure 16 Prescription Day 0 to Day 28: Six most common ATC-groups (except V03 All Other Therapeutic Products). Percentage of patients with prescribed medicine. Anthroposophy Group: n = 715, Conventional Group: n = 301

The proportion of patients prescribed antibacterial agents on Day 0 to Day 28 was lower in the A-group than in the C-group in all subgroups analysed (Figure 18).



	No-antibiotic rates	A-Gr.	C-Gr.
All	All Patients	676/715	200/301
Country	Germany	346/362	58/100
	Austria	95/101	29/57
	Netherlands	145/152	94/104
	United Kingdom	43/52	19/40
	USA	47/48	0/0
Gender	Male	310/333	88/121
	Female	366/382	112/180
Age	< 2 years	105/112	14/17
	2-5 years	105/112	30/39
	6-17 years	168/174	27/37
	18-34 years	81/87	52/81
	35-64 years	120/129	70/111
	≥ 65 years	10/11	7/16
Chief Complaint	Runny nose	49/49	15/16
	Sore throat	179/188	48/70
	Ear pain	133/143	39/57
	Sinus pain	48/50	30/56
	Cough	267/285	68/102
Onset of chief complaint	0 to ≤ 24 hours	183/192	22/33
	>24 to ≤ 48 hours	158/167	62/93
	>2 to ≤ 7 days	334/355	116/175
Previous episode	Yes	358/376	76/111
	No or no remark	318/339	124/190
Symptom Score Day 0	0 to <1	225/235	64/88
	1 to <2	334/353	114/174
	2 to <3	103/111	19/32
	3 to 4	13/15	0/1

Figure 17 Unadjusted oodds ratios (95%-CI) for “no prescription of antibiotics” (ATC-Index J01 Antibacterial Agents for Systemic Use) in Anthroposophy Group (n = 715) vs. Conventional Group (n = 301), in whole sample and subgroups. No-antibiotic rates: number of patients without a prescription of antibiotics from Day 0 to Day 28 / number of patients. Odds ratio > 1 indicates lower percentage of patients prescribed antibiotics in Anthroposophy Group.

Follow-up contact with doctor, medication intake

Although a follow-up contact was recommended three times more often by A-doctors than by C-doctors, the proportion of patients reporting a follow-up contact with their physician did not differ significantly between the two groups at any follow-up. A similarly high proportion of patients in both groups reported being compliant with study medication prescription (Table 11).

Follow-up contact with doctor, medication intake					
	Anthroposophy N=715		Conventional N=301		Fisher's exact test
Patients with follow-up recommendations at study entry	368	51.5%	49	16.3%	p < 0.0001
Patients reporting follow-up contact with study doctor					
0-7 days	233	32.6%	92	30.6%	n. s.
0-14 days	301	42.1%	122	40.5%	n. s.
0-28 days	336	47.0%	135	44.9%	n. s.
Patient reporting medication intake as prescribed at all follow-ups	641	89.7%	262	87.0%	n. s.

Table 11 Follow-up recommendations, follow-up contact with doctor, medication intake as prescribed

Patient outcomes

Treatment outcome: overview and chief complaint subgroups

Primary outcome – response rate (complete or major improvement) after 14 days was 89.7% (641/715) in A-patients and 84.4% (254/301) in C-patients (Figure 18). The one-sided test confirmed non-inferiority of anthroposophic treatment ($p < 0.00001$); thus, a test for superiority was performed. The test for difference between the two treatments demonstrated a significant difference in favour of anthroposophic treatment ($p = 0.0198$).

The response rate (proportion of patients with complete recovery or major improvement) on Day 7 was significantly higher in the A-group (77.1%; 551/715 patients) than in the C-group (66.1%; 199/301) ($p = 0.0004$). Day 28 response rate did not differ significantly between the groups.

At all follow-ups, the proportion of patients completely recovered was significantly higher in the A-group than in the C-group. (Figure 18).

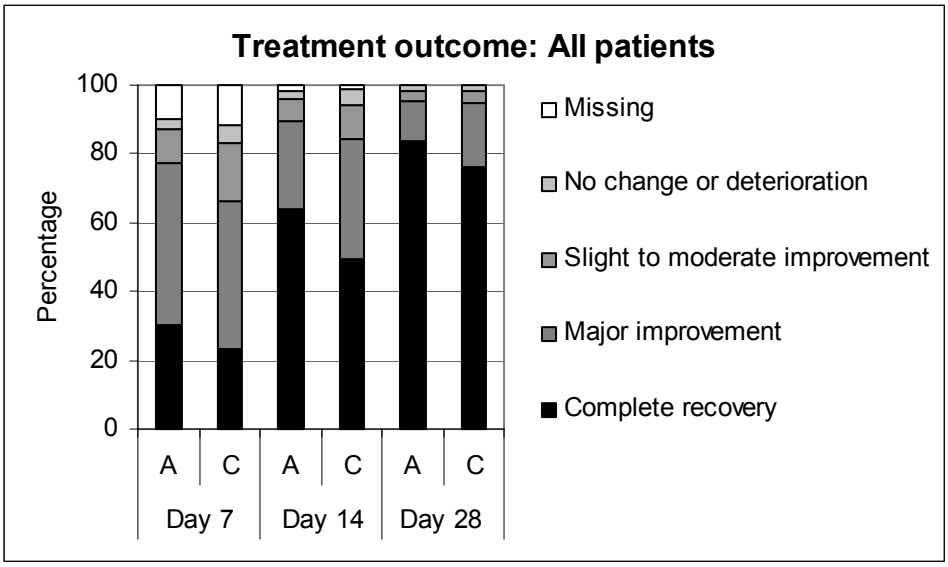


Figure 18 Treatment outcome at Day 7, Day 14 and Day 28. Last observation carried forward. Percentage of patients at Day 28. A: Anthroposophy Group: n = 715, C: Conventional Group: n = 301.

In the chief complaint runny nose subgroup response rates were similar at all follow-ups. The complete recovery rate was higher in the A-group than in the C-group on Day 7 and Day 14 (Figure 19). With small sample sizes, especially in the C-group (n = 16), these differences were not significant.

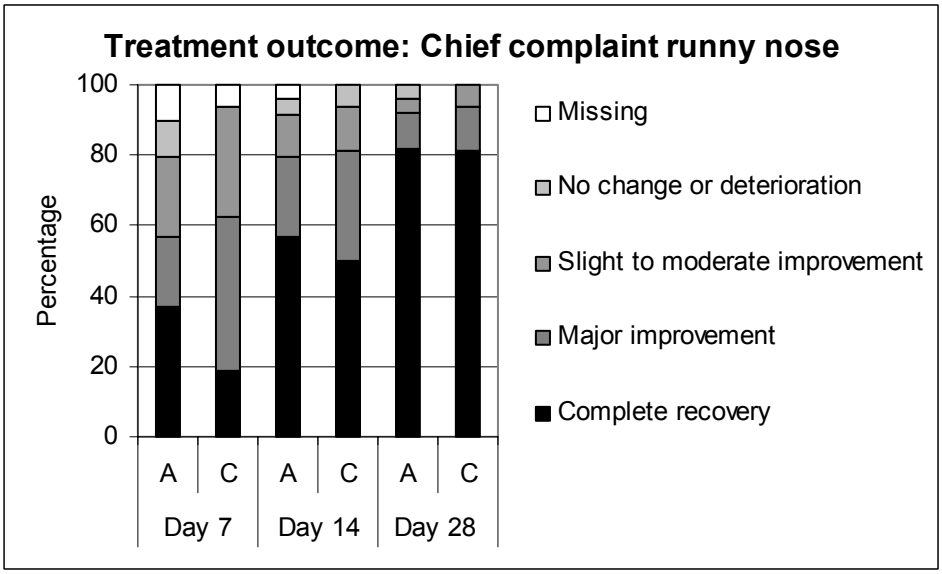


Figure 19 Treatment outcome at Day 7, Day 14 and Day 28. Last observation carried forward. Percentage of patients with chief complaint runny nose at Day 28. A: Anthroposophy Group: n = 49, C: Conventional Group: n = 16.

In the chief complaint sore throat subgroup response rates were similar at all follow-ups. The complete recovery rates were higher in the A-group on Day 14 ($p = 0.1242$) and Day 28 ($p = 0.0390$) (Figure 20).

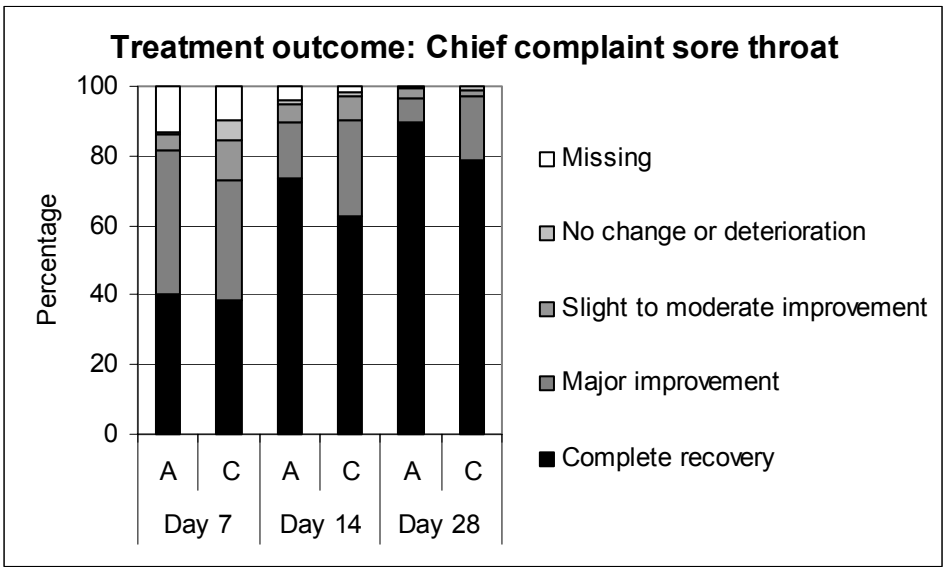


Figure 20 Treatment outcome at Day 7, Day 14 and Day 28. Last observation carried forward. Percentage of patients with chief complaint sore throat at Day 28. A: Anthroposophy Group: n = 188, C: Conventional Group: n = 70

In the chief complaint ear pain subgroup response rates were higher in the A-group on Day 7 ($p = 0.0001$) and Day 28 ($p = 0.0180$). Complete recovery rates were higher in the A-group at all follow-ups, but the differences were not statistically significant (Figure 21).

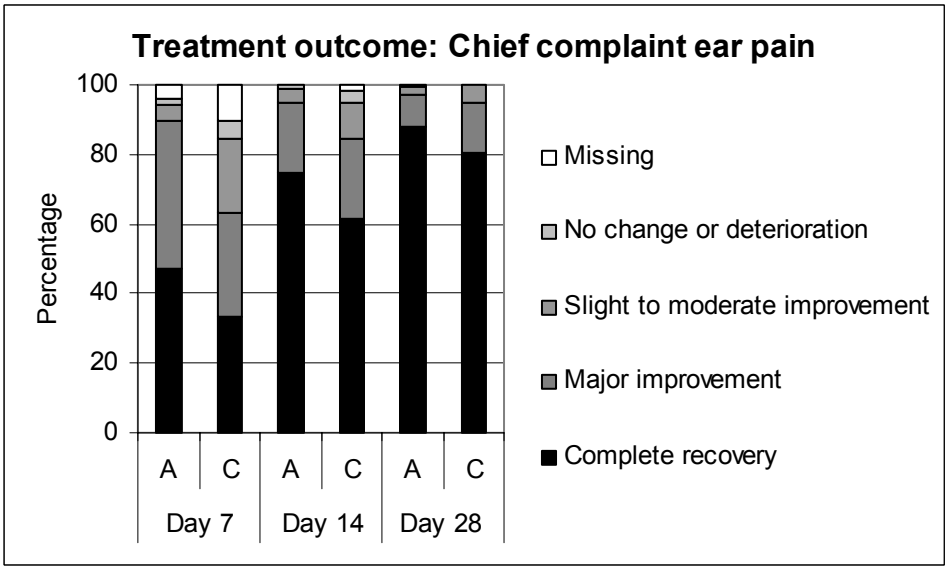


Figure 21 Treatment outcome at Day 7, Day 14 and Day 28. Last observation carried forward. Percentage of patients with chief complaint sore throat at Day 28. A: Anthroposophy Group: n = 143, C: Conventional Group: n = 57

In the chief complaint sinus pain subgroup with altogether 106 patients, response rates were slightly higher in the A-group at all follow-ups, but these differences were not statistically significant. Complete recovery rates were similar at all follow-ups (Figure 22). Notably, Day 7 complete recovery rates were lower in this subgroup (and in the chief complaint cough subgroup, see below) than in the preceding chief complaint subgroups.

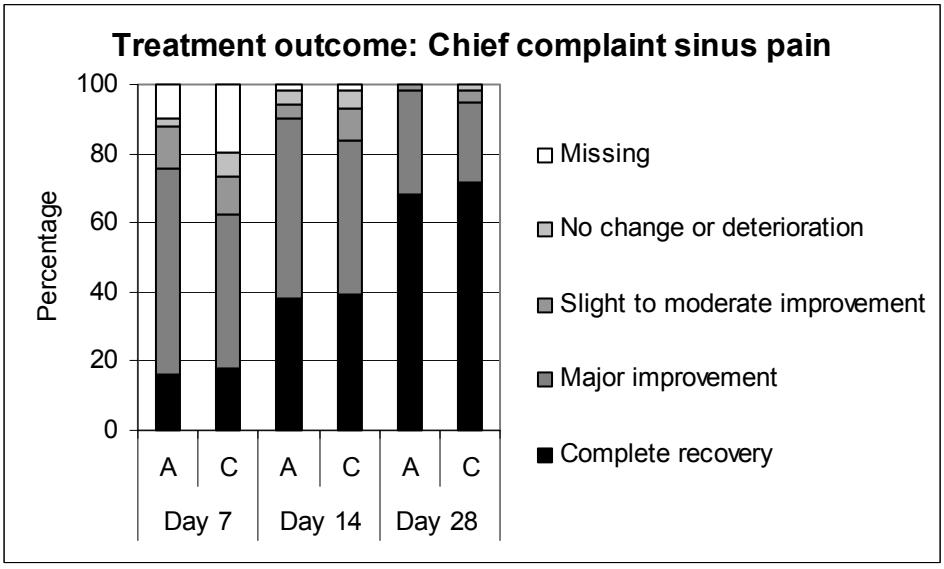


Figure 22 Treatment outcome at Day 7, Day 14 and Day 28. Last observation carried forward. Percentage of patients with chief complaint sinus pain at Day 28. A: Anthroposophy Group: n = 50, C: Conventional Group: n = 56

In the chief complaint cough subgroup, response rates were slightly higher in the A-group at Day 7 and Day 14, but these differences were not statistically significant (Figure 23). Complete recovery rates were also slightly higher in the A-group at all follow-ups, on Day 14 this difference was statistically significant (p = 0.0017).

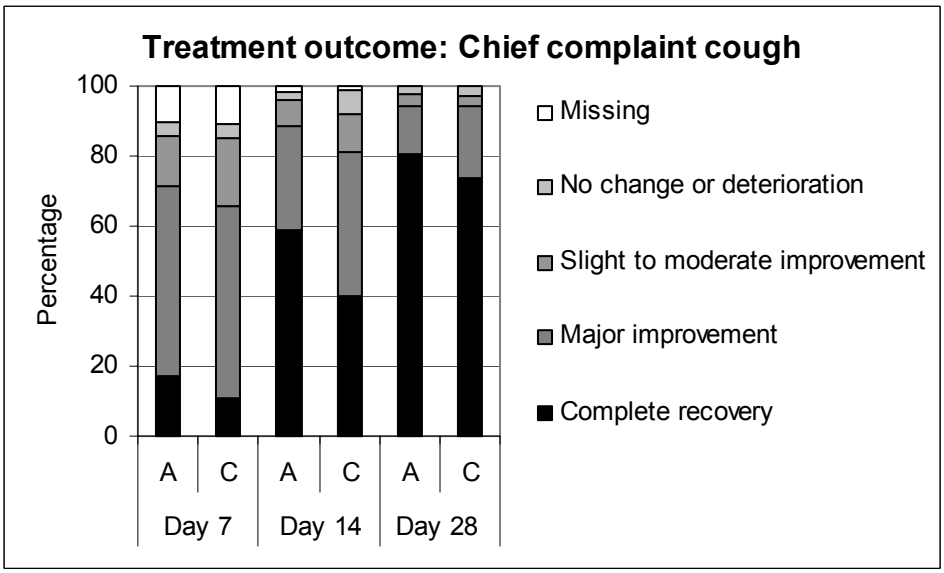


Figure 23 Treatment outcome at Day 7, Day 14 and Day 28. Last observation carried forward. Percentage of patients with Chief complaint cough at Day 28. A: Anthroposophy Group: n = 285, C: Conventional Group: n = 102

Treatment outcome: Subgroup analysis with odds ratios

The proportion of patients with a response (complete recovery or major improvement) by Day 7 was 551 (77.1%) of 715 A-patients and 199 (66.1%) of 301 C-patients, resulting in an OR (A-group vs. C-group) for a response by Day 7 of 1.72 (95%-CI: 1.28-2.31), favouring the A-group. The A-group was favoured in all analysed subgroups except among patients aged 35-64 years, and patients with a chief complaint of runny nose (Figure 24).

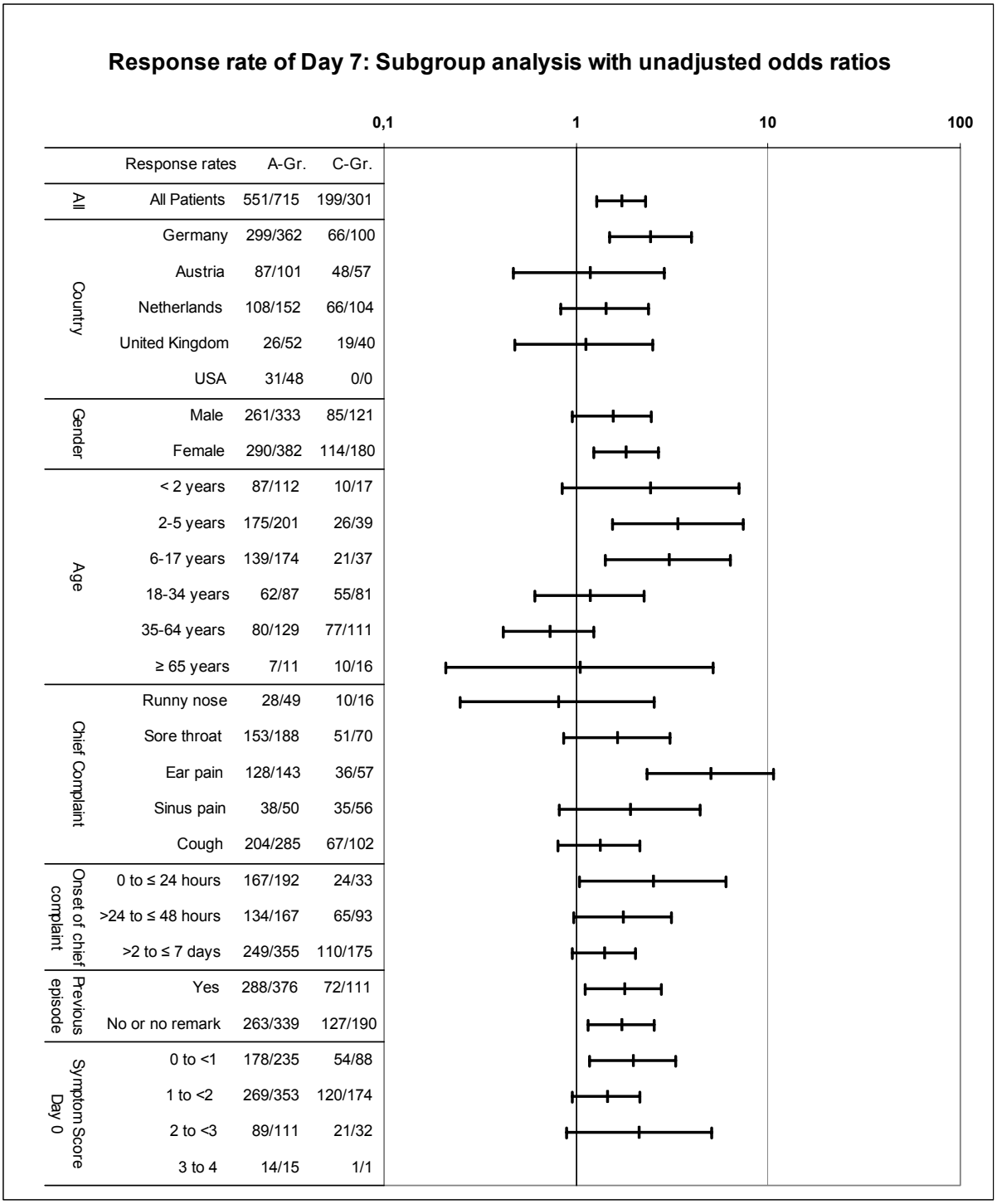


Figure 24 Unadjusted odds ratios (95%-CI) for response (treatment outcome = complete recovery or major improvement) by Day 7 in Anthroposophy Group (n = 715) vs. Conventional Group (n = 301), in whole sample and subgroups. Previous episode: Previous episode of chief complaint within the last 12 months. Response rates: number of patients with complete recovery or major improvement by Day 7 / number of patients. Odds ratio > 1 indicates higher response rate in Anthroposophy Group.

After multiple logistic regression analysis, adjusting for all predefined covariates (Figure 25), the OR for response by Day 7 was 1.50 (95%-CI: 1.07-2.11), favouring the A-group.

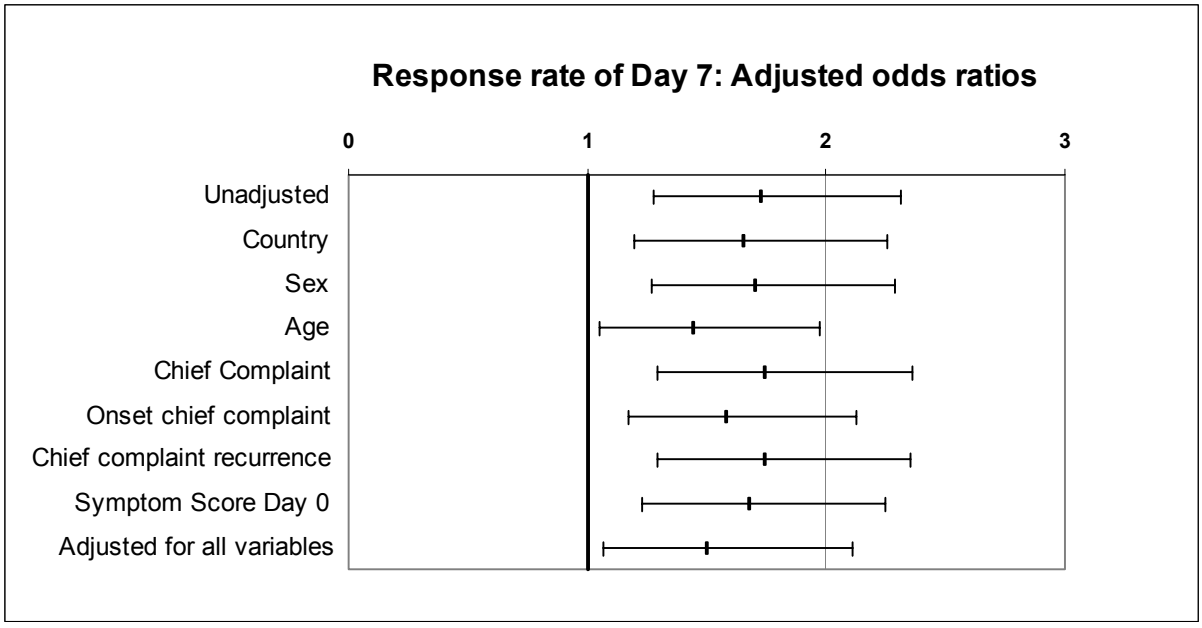


Figure 25 Adjusted odds ratios (95%-CI) for response rate (Treatment outcome: complete recovery or major improvement) by Day 7 in Anthroposophy Group (n = 715) vs. Conventional Group (n = 301): adjusting for country, gender, age, chief complaint, duration of chief complaint, chief complaint episode within the last 12 months, and Symptom Score at day 0 respectively, combined adjustment for all these variables using multiple logistic regression analysis. Odds ratio > 1 indicates higher response rate in Anthroposophy Group.

The proportion of patients with a response (complete recovery or major improvement) by Day 14 was 641 (89.7%) of 715 A-patients and 254 (84.4%) of 301 C-patients, resulting in an OR (A-group vs. C-group) for a response by Day 14 of 1.60 (95%-CI: 1.08-2.38), favouring the A-group. The A-group was favoured in all analysed subgroups except among patients from Austria, patients aged 18-34 years, and patients with a chief complaint of runny nose or sore throat (Figure 26).

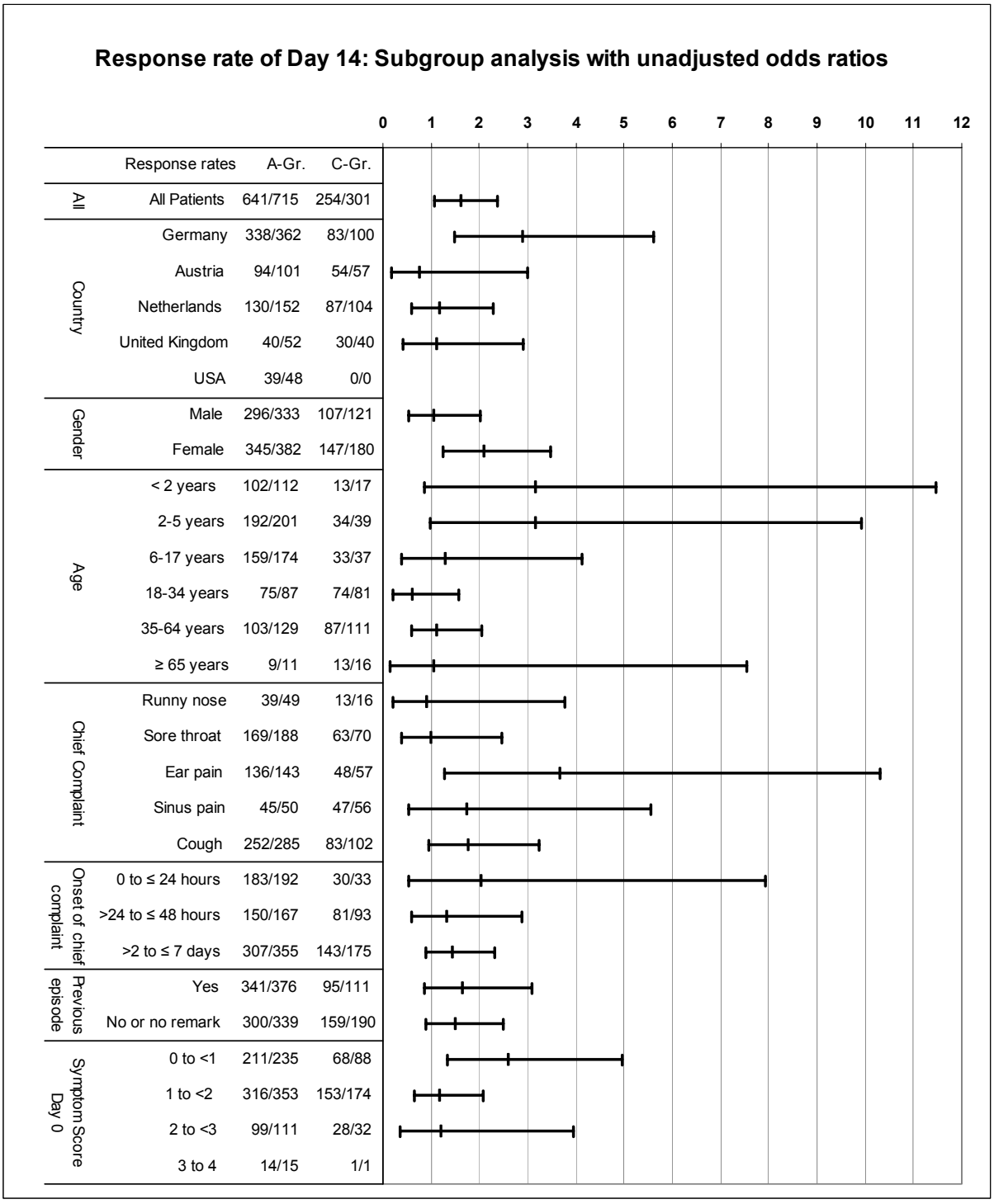


Figure 26 Unadjusted odds ratios (95%-CI) for response (treatment outcome = complete recovery or major improvement) by Day 14 in Anthroposophy Group (n = 715) vs. Conventional Group (n = 301), in whole sample and subgroups. Previous episode: Previous episode of chief complaint within the last 12 months. Response rates: number of patients with complete recovery or major improvement by Day 14 / number of patients. Odds ratio > 1 indicates higher response rate in Anthroposophy Group.

After multiple logistic regression analysis, adjusting for all prescribed covariates (Figure 27), the OR for response by Day 14 was 1.29 (95%-CI:0.82-2.00), favouring the A-group.

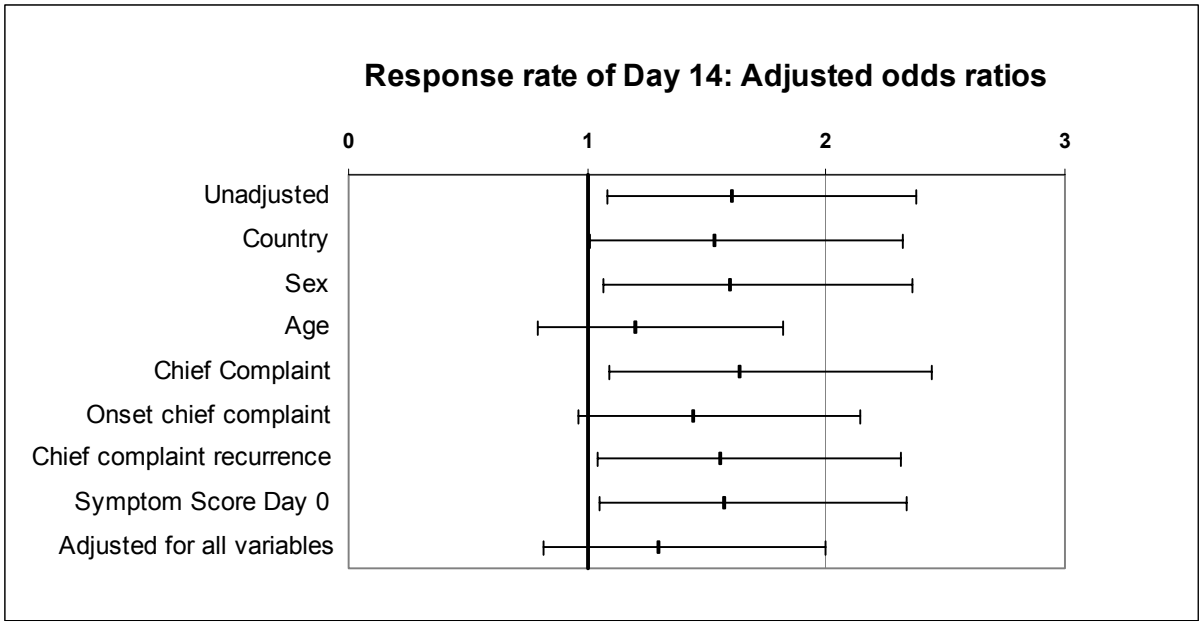


Figure 27 Adjusted odds ratios (95%-CI) for cumulative response rate (Treatment outcome: complete recovery or major improvement) by Day 14 in Anthroposophy Group (n = 715) vs. Conventional Group (n = 301): adjusting for country, gender, age, chief complaint, duration of chief complaint, chief complaint episode within the last 12 months, and Symptom Score at day 0 respectively, combined adjustment for all these variables using multiple logistic regression analysis. Odds ratio > 1 indicates higher response rate in Anthroposophy Group.

The proportion of patients with a response (complete recovery or major improvement) by Day 28 was similarly high in the A-group (95.4%) and the C-group (95.0%), resulting in an OR (A-group vs. C-group) for a response by Day 28 of 1.08 (95%-CI: 0.58-2.03) favouring the A-group. The A-group was favoured in 12 subgroups and the C-groups was favoured in 13 analysed subgroups (Figure 28).

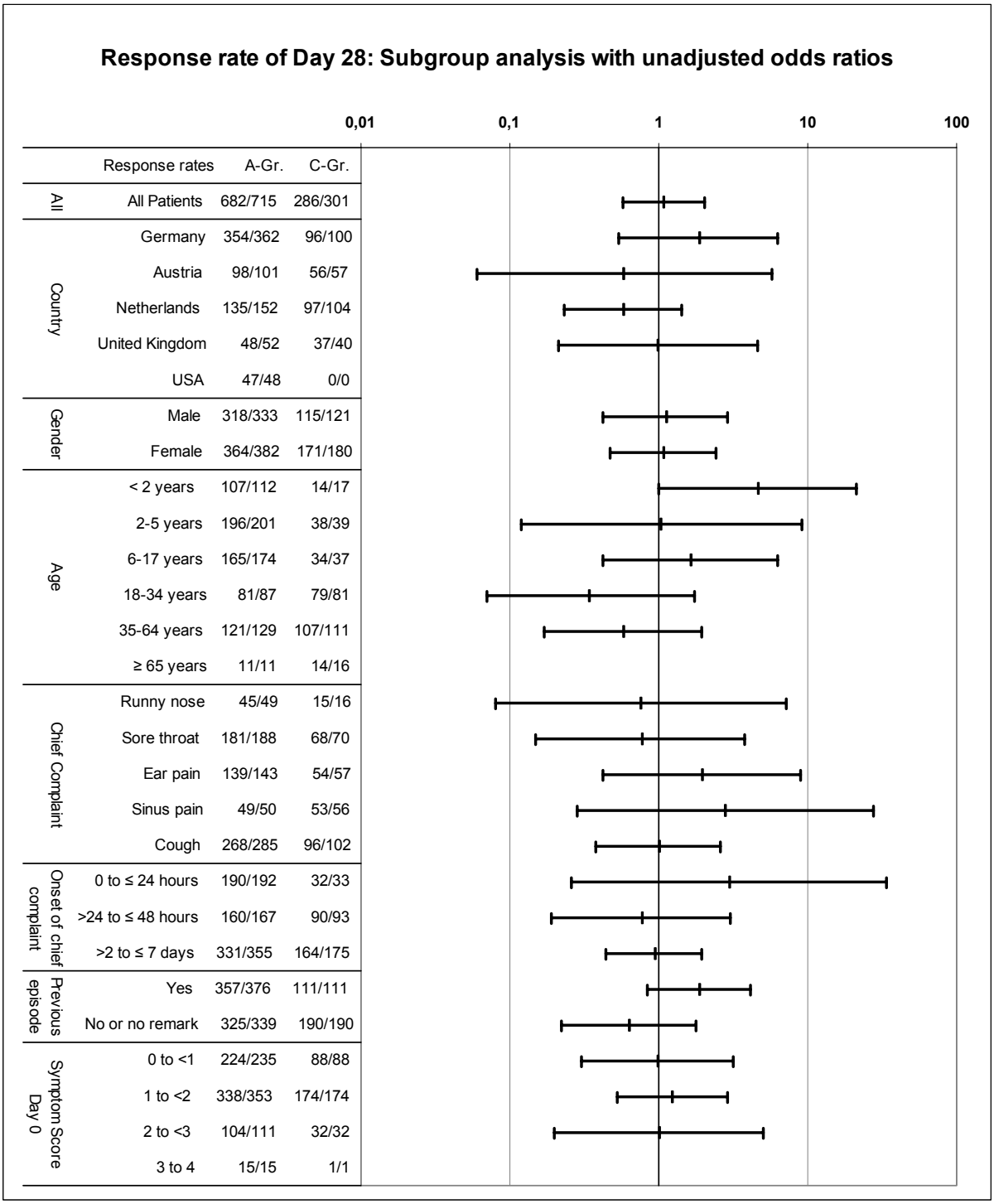


Figure 28 Unadjusted odds ratios (95%-CI) for response (treatment outcome = complete recovery or major improvement) by Day 28 in Anthroposophy Group (n = 715) vs. Conventional Group (n = 301), in whole sample and subgroups. Previous episode: Previous episode of chief complaint within the last 12 months. Response rates: number of patients with complete recovery or major improvement by Day 28 / number of patients. Odds ratio > 1 indicates higher response rate in Anthroposophy Group.

After multiple logistic regression analysis, adjusting for all prescribed covariates, the OR for response by Day 28 was 0.87 (95%-CI:0.45-1.69), favouring the C-group (Figure 29).

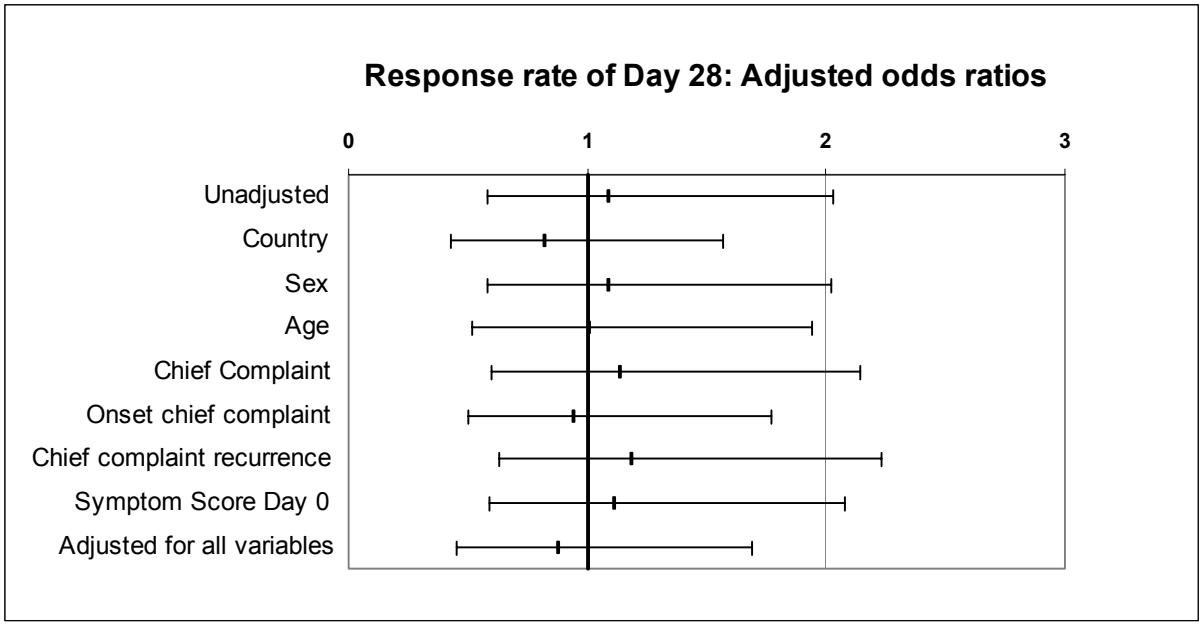


Figure 29 Adjusted odds ratios (95%-CI) for cumulative response rate (Treatment outcome: complete recovery or major improvement) by Day 28 in Anthroposophy Group (n = 715) vs. Conventional Group (n = 301): adjusting for country, gender, age, chief complaint, duration of chief complaint, chief complaint episode within the last 12 months, and Symptom Score at day 0 respectively, combined adjustment for all these variables using multiple logistic regression analysis. Odds ratio > 1 indicates higher response rate in Anthroposophy Group.

The proportion of patients with a complete recovery by Day 7 was 218 (30.5%) of 715 A-patients and 70 (23.3%) of 301 C-patients, resulting in an OR (A-group vs. C-group) for a complete recovery by Day 7 of 1.45 (95%-CI: 1.06-1.98) favouring the A-group. The A-group was favoured in all analysed subgroups except among patients from The Netherlands, patients aged 35-64 years, patients with a chief complaint of sinus pain, and patients with onset of chief complaint within 24 hours (Figure 30).

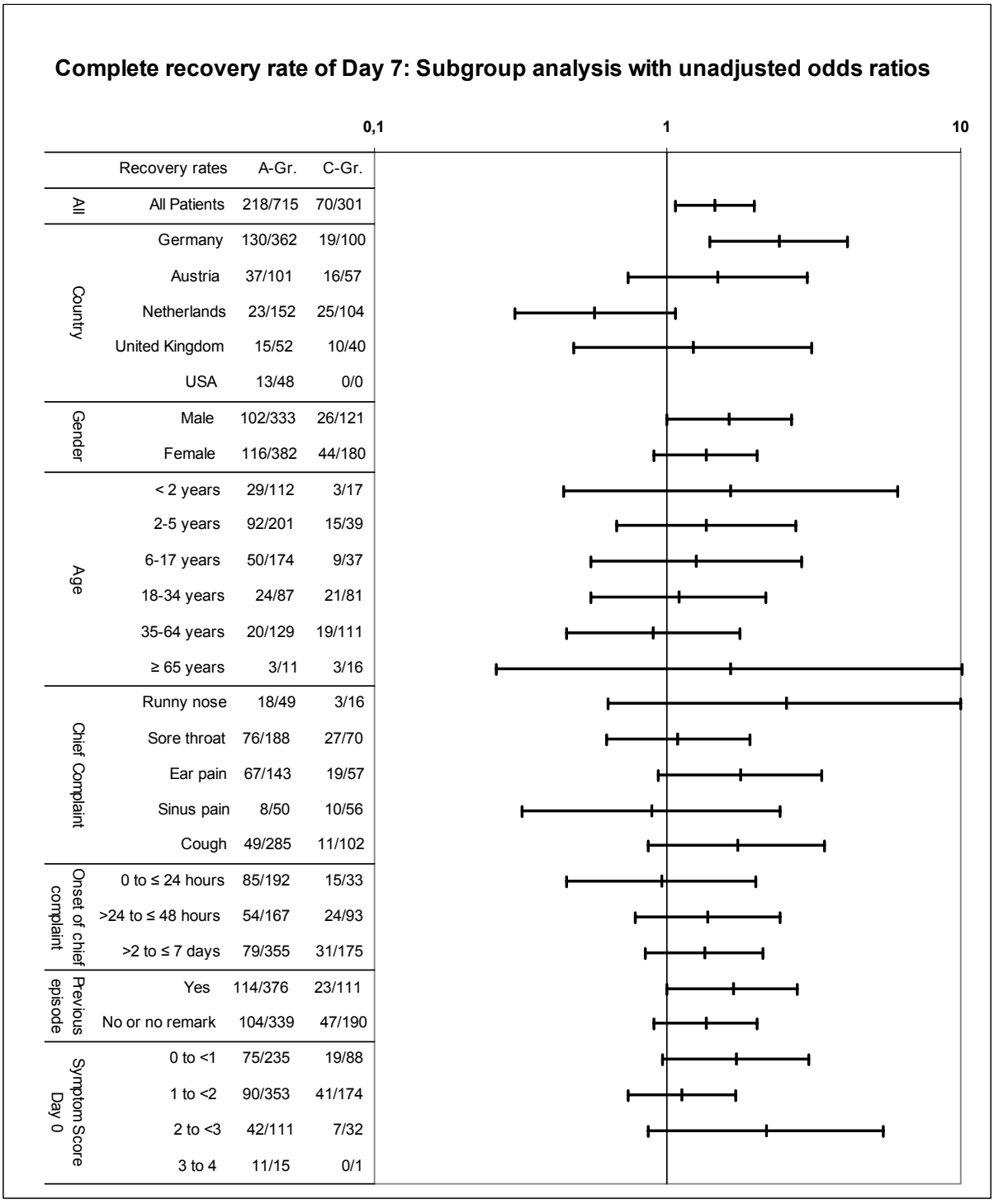


Figure 30 Unadjusted odds ratios (95%-CI) for complete recovery by Day 7 in Anthroposophy Group (n = 715) vs. Conventional Group (n = 301), in whole sample and subgroups. Previous episode: Previous episode of chief complaint within the last 12 months. Recovery rates: number of patients with recovery by Day 7 / number of patients. Odds ratio > 1 indicates higher recovery rate in Anthroposophy Group.

After multiple logistic regression analysis, adjusting for all prescribed covariates (Figure 31), the OR for complete recovery by Day 7 was 1.05 (95%-CI: 0.72-1.54), favouring the A-group.

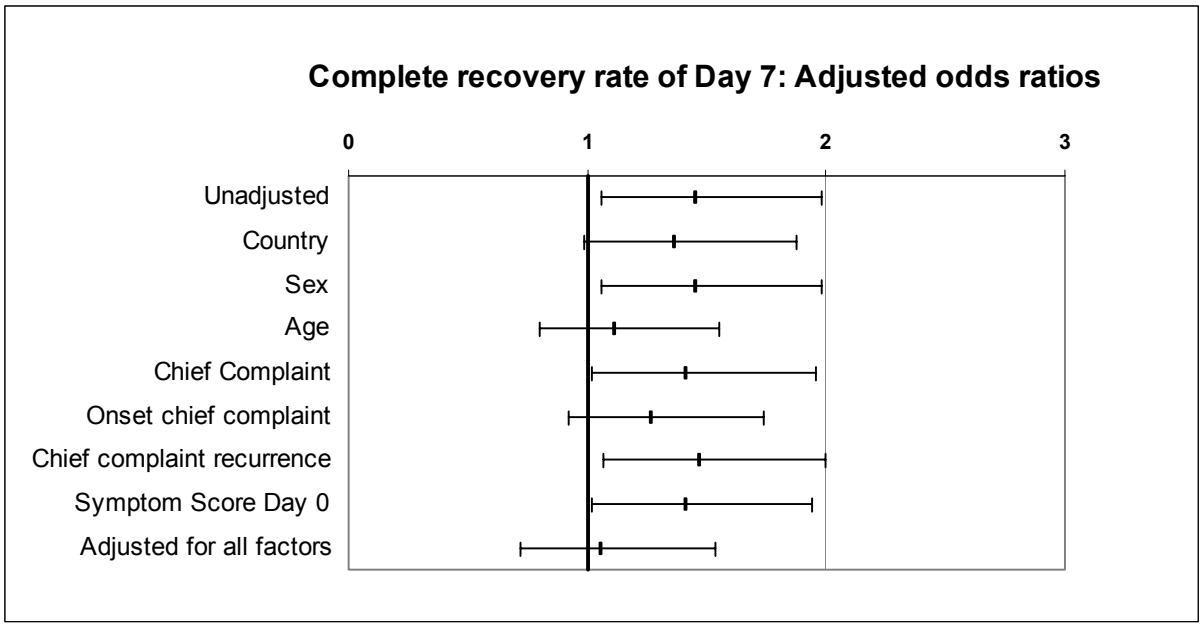


Figure 31 Adjusted odds ratios (95%-CI) for complete recovery by Day 7 in Anthroposophy Group (n = 715) vs. Conventional Group (n = 301): adjusting for country, gender, age, chief complaint, duration of chief complaint, chief complaint episode within the last 12 months, and Symptom Score at day 0 respectively, combined adjustment for all these variables using multiple logistic regression analysis. Odds ratio > 1 indicates higher recovery rate in Anthroposophy Group.

The proportion of patients with a complete recovery by Day 14 was 459 (64.2%) of 715 A-patients and 149 (49.5%) of 301 C-patients, resulting in an OR (A-group vs. C-group) for a complete recovery by Day 14 of 1.83 (95%-CI: 1.39-2.40), favouring the A-group. The A-group was favoured in all analysed subgroups except among patients from The Netherlands, patients aged ≥ 65 years, and patients with a chief complaint of sinus pain (Figure 32).

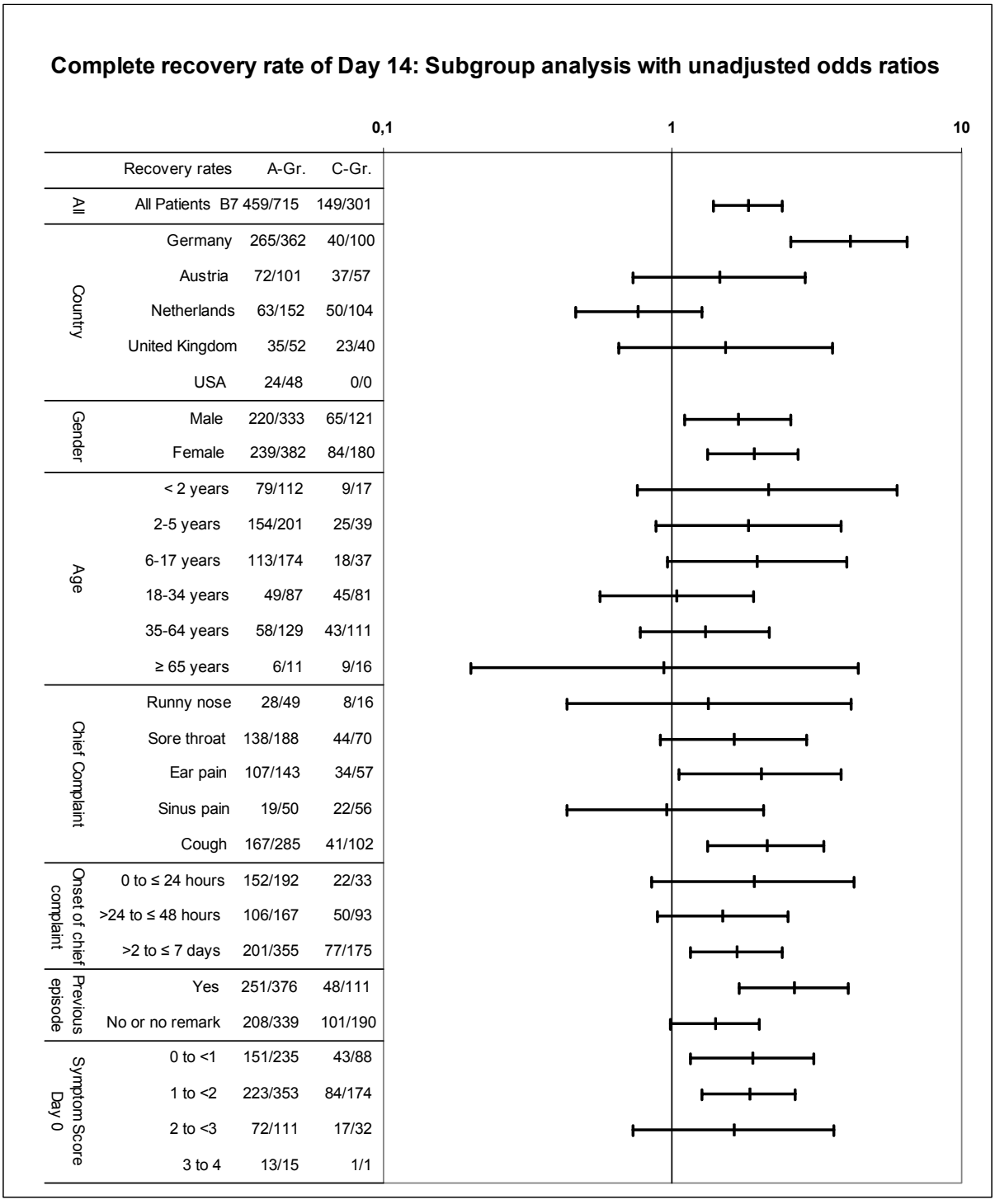


Figure 32 Unadjusted odds ratios (95%-CI) for complete recovery by Day 14 in Anthroposophy Group (n = 715) vs. Conventional Group (n = 301), in whole sample and subgroups. Previous episode: Previous episode of chief complaint within the last 12 months. Recovery rates: number of patients with complete recovery by Day 14 / number of patients. Odds ratio > 1 indicates higher recovery rate in Anthroposophy Group.

After multiple logistic regression analysis, adjusting for all prescribed covariates (Figure 33) the OR for complete recovery by Day 14 was 1.35 (95%-CI: 0.98-1.86), favouring the A-group.

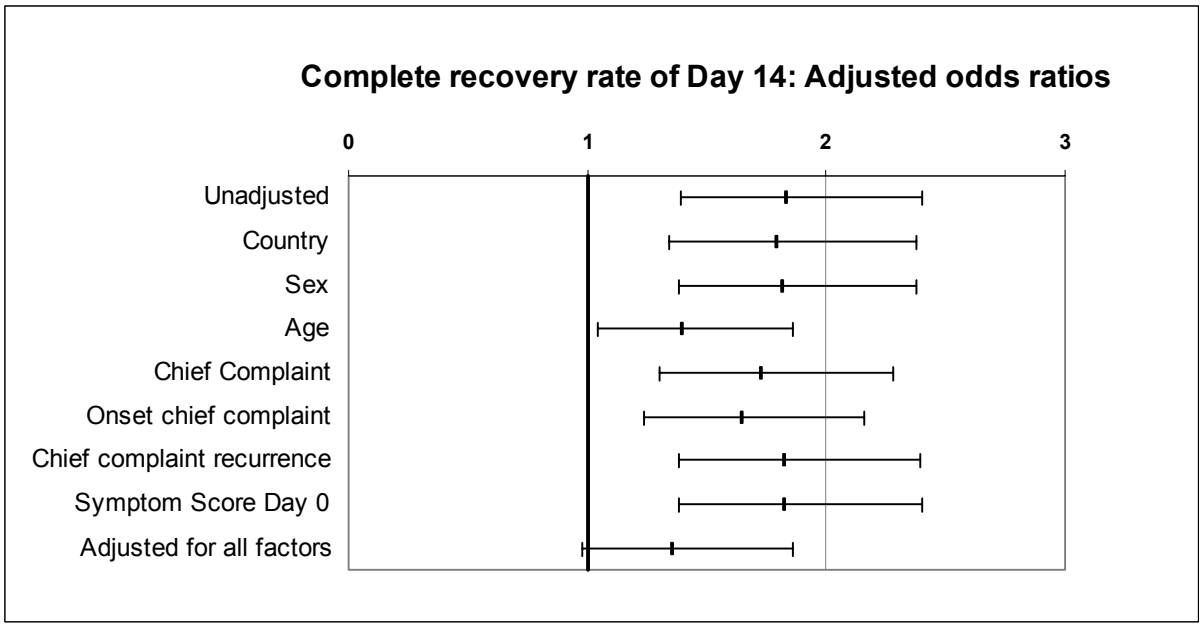


Figure 33 Adjusted odds ratios (95%-CI) for complete recovery by Day 14 in Anthroposophy Group (n = 715) vs. Conventional Group (n = 301): adjusting for country, gender, age, chief complaint, duration of chief complaint, chief complaint episode within the last 12 months, and Symptom Score at day 0 respectively, combined adjustment for all these variables using multiple logistic regression analysis. Odds ratio > 1 indicates higher recovery rate in Anthroposophy Group.

The proportion of patients with a complete recovery by Day 28 was 597 (83.5%) of 715 A-patients and 229 (76.1%) of 301 C-patients, resulting in an OR (A-group vs. C-group) for a complete recovery by Day 28 of 1.59 (95%-CI: 1.14-2.21) favouring the A-group. The A-group was favoured in all analysed subgroups except among patients from The Netherlands, patients aged 18-34 years, and patients with a chief complaint of sinus pain (Figure 34).

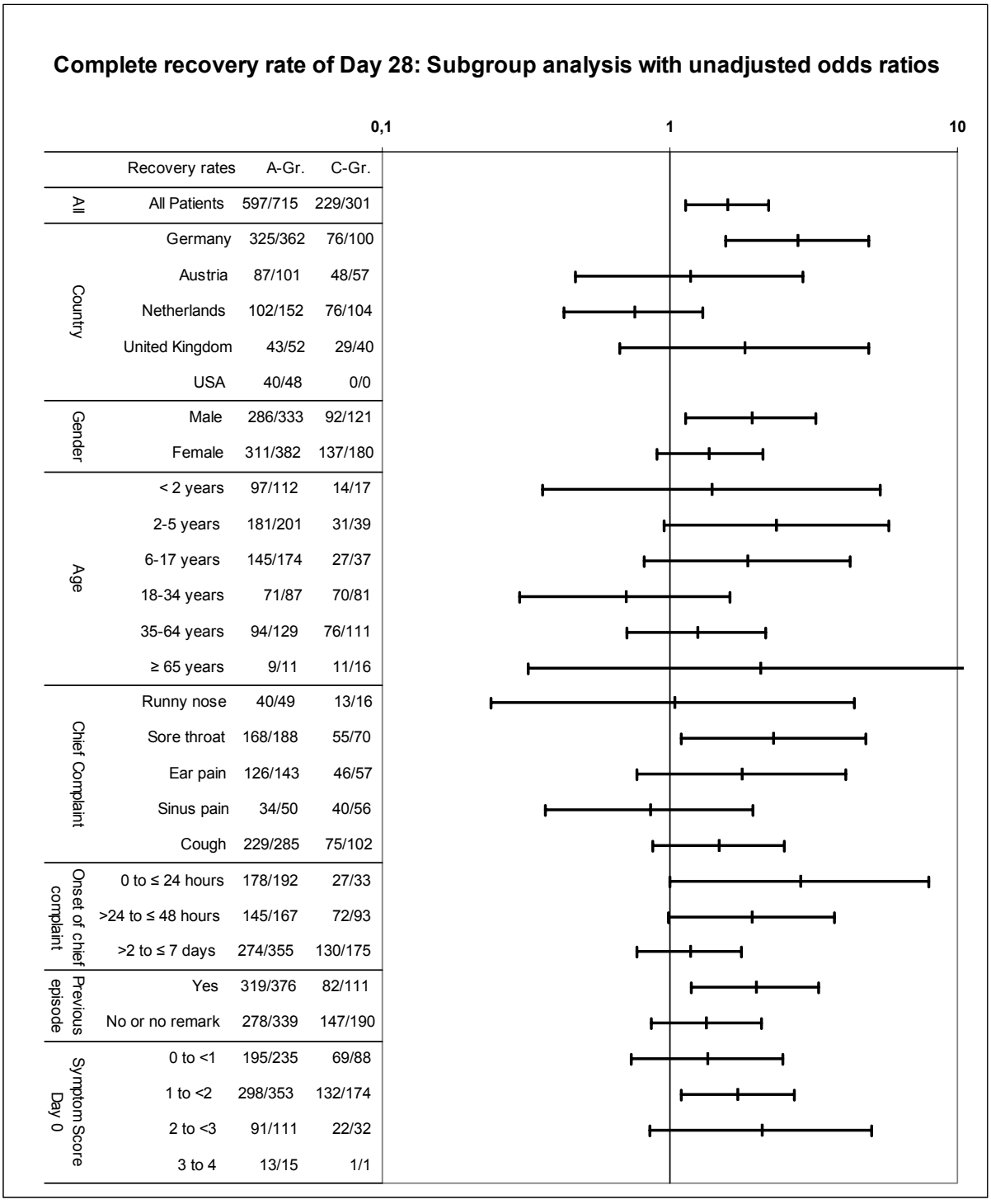


Figure 34 Unadjusted odds ratios (95%-CI) for complete recovery by Day 28 in Anthroposophy Group (n = 715) vs. Conventional Group (n = 301), in whole sample and subgroups. Previous episode: Previous episode of chief complaint within the last 12 months. Recovery rates: number of patients with complete recovery by Day 28 / number of patients. Odds ratio > 1 indicates higher recovery rate in Anthroposophy Group.

After multiple logistic regression analysis, adjusting for all prescribed covariates (Figure 35) the OR for complete recovery by Day 28 was 1.18 (95%-CI: 0.82-1.71), favouring the A-group.

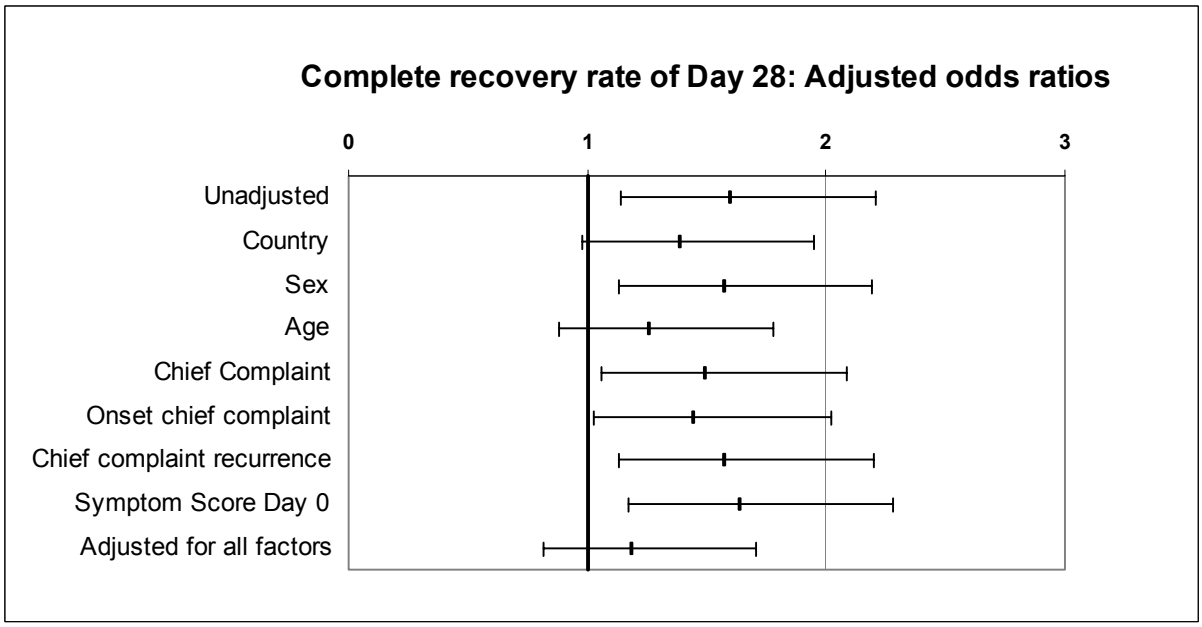


Figure 35 Adjusted odds ratios (95%-CI) for complete recovery by Day 28 in Anthroposophy Group (n = 715) vs. Conventional Group (n = 301): adjusting for country, gender, age, chief complaint, duration of chief complaint, chief complaint episode within the last 12 months, and Symptom Score at day 0 respectively, combined adjustment for all these variables using multiple logistic regression analysis. Odds ratio > 1 indicates higher recovery rate in Anthroposophy Group.

Time to first improvement

The time to first improvement noted by the patients was significantly shorter in the A-group than in the C-group ($p < 0.0001$) (Figure 36).

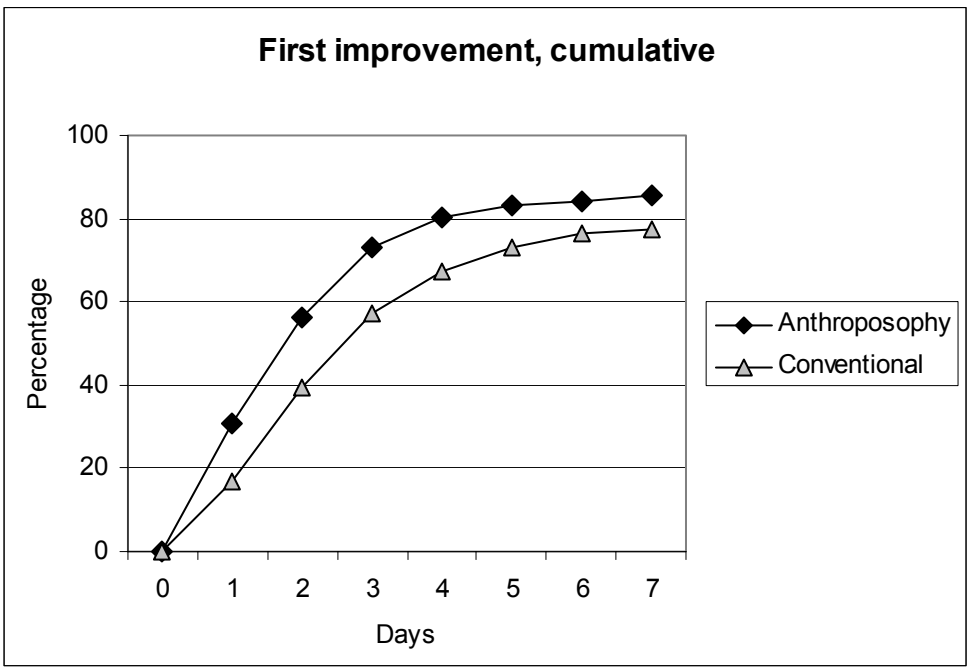


Figure 36 First improvement, cumulative percentage. A-group: n =715, C-group: n = 301

The proportion of patients with first improvement within 24 hours was 221 (30.9%) of 715 A-patients and 50 (16.6%) of 301 C-patients, resulting in an odds ratio (OR: A-group vs. C-group) for time to first improvement ≤ 24 hours of 2.25 (95%-CI: 1.59-3.16), favouring the A-group. The A-group was favoured in all analysed subgroups except among patients from the Netherlands, patients aged 35-64 years, and patients with a chief complaint of runny nose (Figure 37).

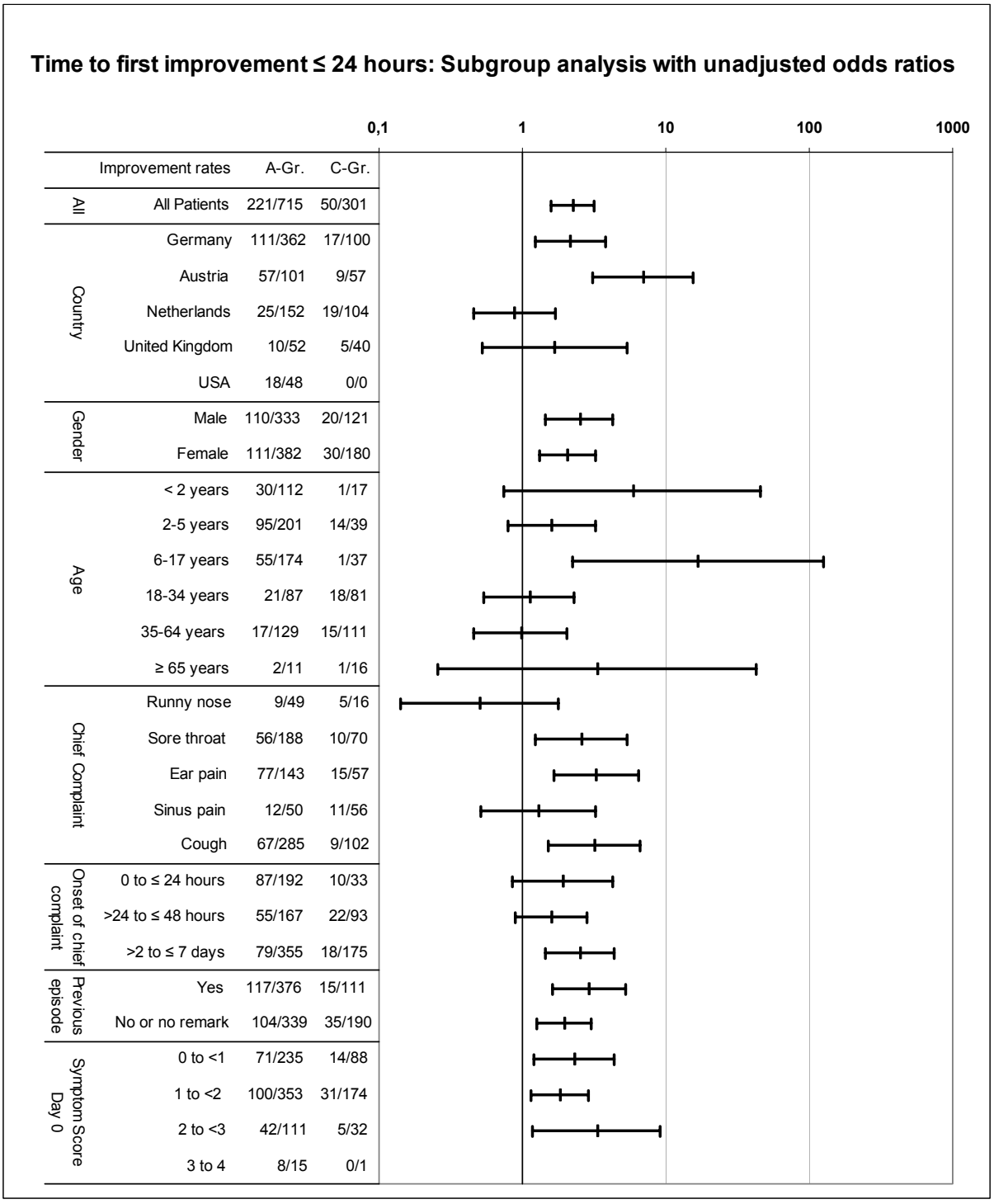


Figure 37 Unadjusted odds ratios (95%-CI) for time to first improvement < 24 hours in Anthroposophy Group (n = 715) vs. Conventional Group (n = 301), in whole sample and subgroups. Previous episode: Previous episode of chief complaint within the last 12 months. Improvement rates: number of patients with first improvement < 24 hours / number of patients. Odds ratio > 1 more frequent improvement within 24 hours in Anthroposophy Group.

Adjustment for age reduced the OR to 1.63 (95%-CI: 1.14-2.35), adjustment for other covariates had little influence on the OR (Figure 38). After adjustment for all prescribed covariates with multiple logistic regression, the OR for first improvement within 24 hours was 1.54 (95%-CI: 1.03-2.31), favouring the A-group.

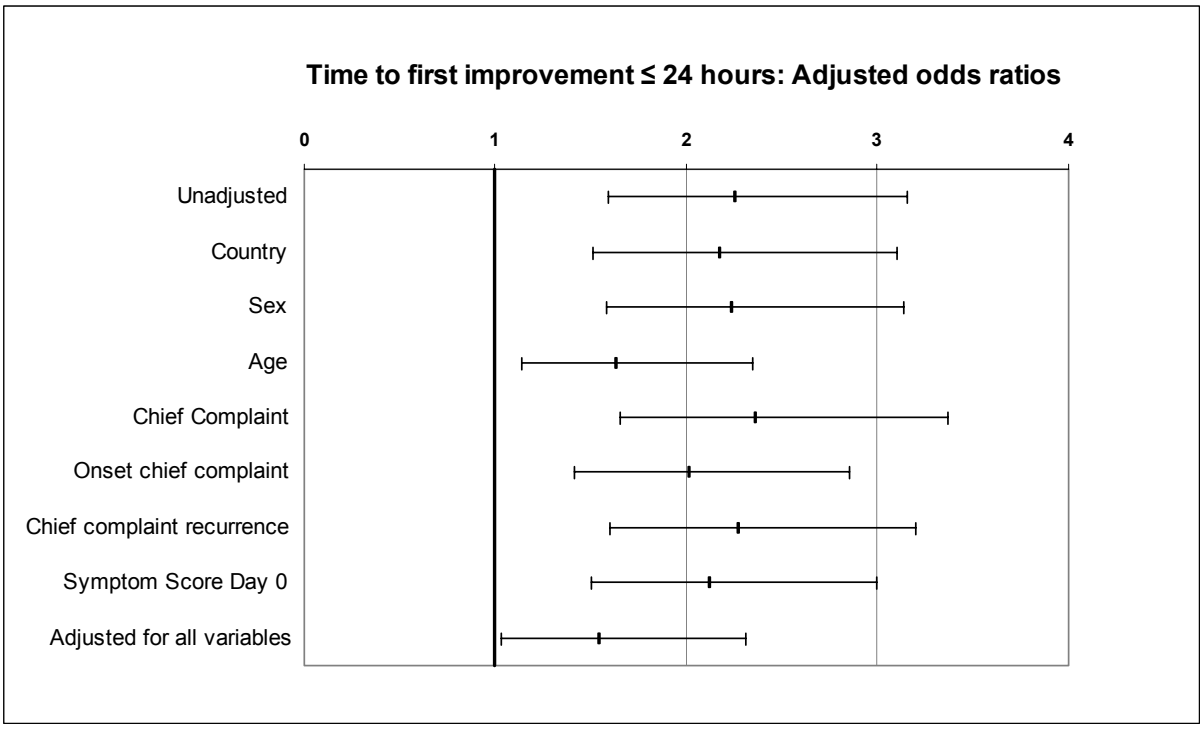


Figure 38 Adjusted odds ratios (95%-CI) for time to first improvement < 24 hours in Anthroposophy Group (n = 715) vs. Conventional Group (n = 301): adjusting for country, gender, age, chief complaint, duration of chief complaint, chief complaint episode within the last 12 months, and Symptom Score at day 0 respectively, combined adjustment for all these variables using multiple logistic regression analysis. Odds ratio > 1 indicates more frequent improvement within 24 hours in Anthroposophy Group.

The proportion of patients with first improvement within 3 days was 523 (73.1%) of 715 A-patients and 172 (57.1%) of 301 C-patients, resulting in an OR (A-group vs. C-group) for time to first improvement ≤ 3 days of 2.04 (95%-CI: 1.54-2.71), favouring the A-group. The A-group was favoured in all analysed subgroups except among patients from The Netherlands or UK, and patients aged ≥ 65 years (Figure 39)

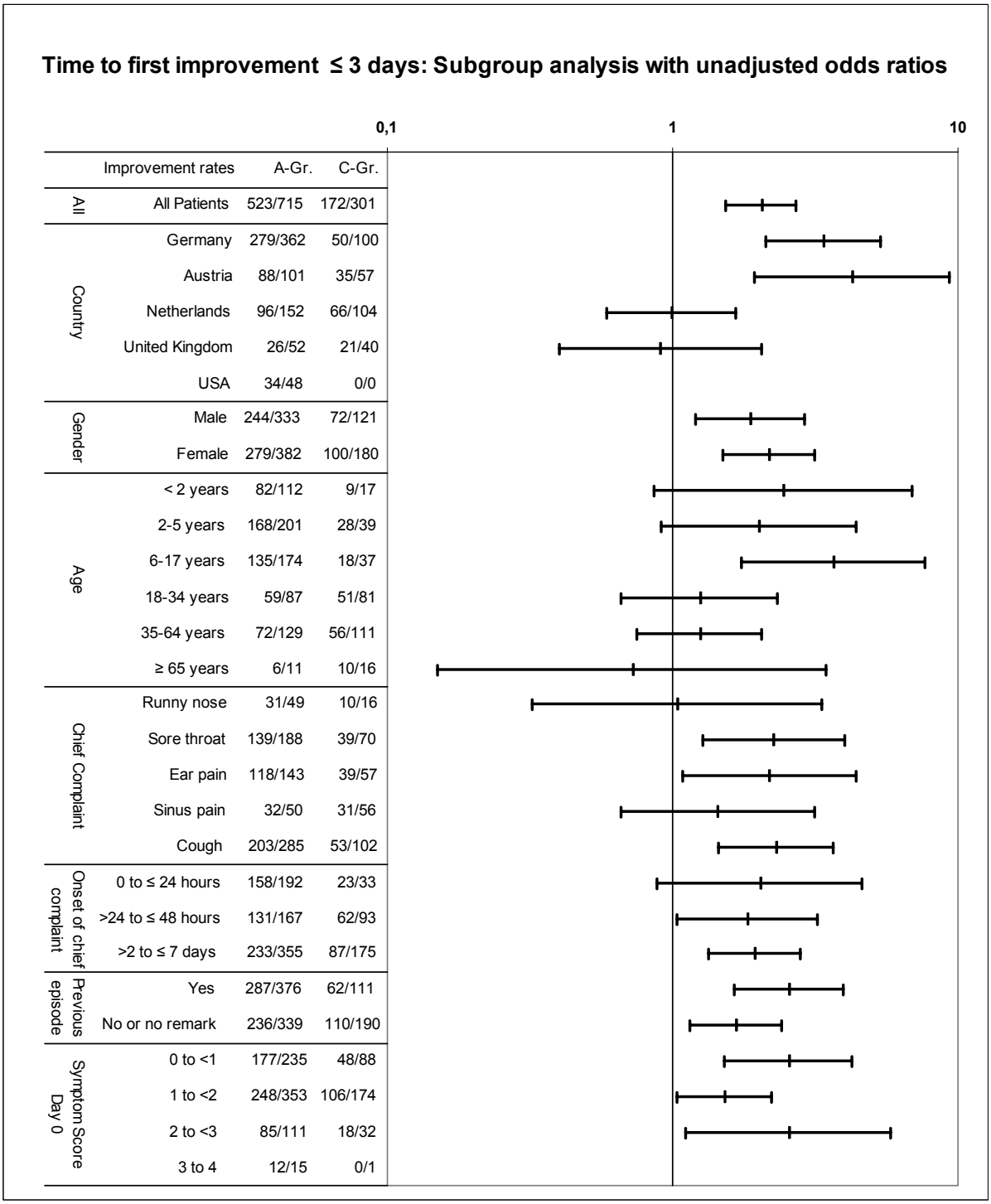


Figure 39 Unadjusted odds ratios (95%-CI) for time to first improvement < 3 days in Anthroposophy Group (n = 715) vs. Conventional Group (n = 301), in whole sample and subgroups. Previous episode: Previous episode of chief complaint within the last 12 months. Improvement rates: number of patients with first improvement < 3 days / number of patients. Odds ratio > 1 indicates more frequent improvement within 3 days in Anthroposophy Group.

Again adjustment for age had the strongest influence on the OR. After multiple logistic regression analysis, adjusting for all prescribed covariates (Figure 40), the OR for first improvement within 3 days was 1.61 (95%-CI: 1.16-2.22), favouring the A-group.

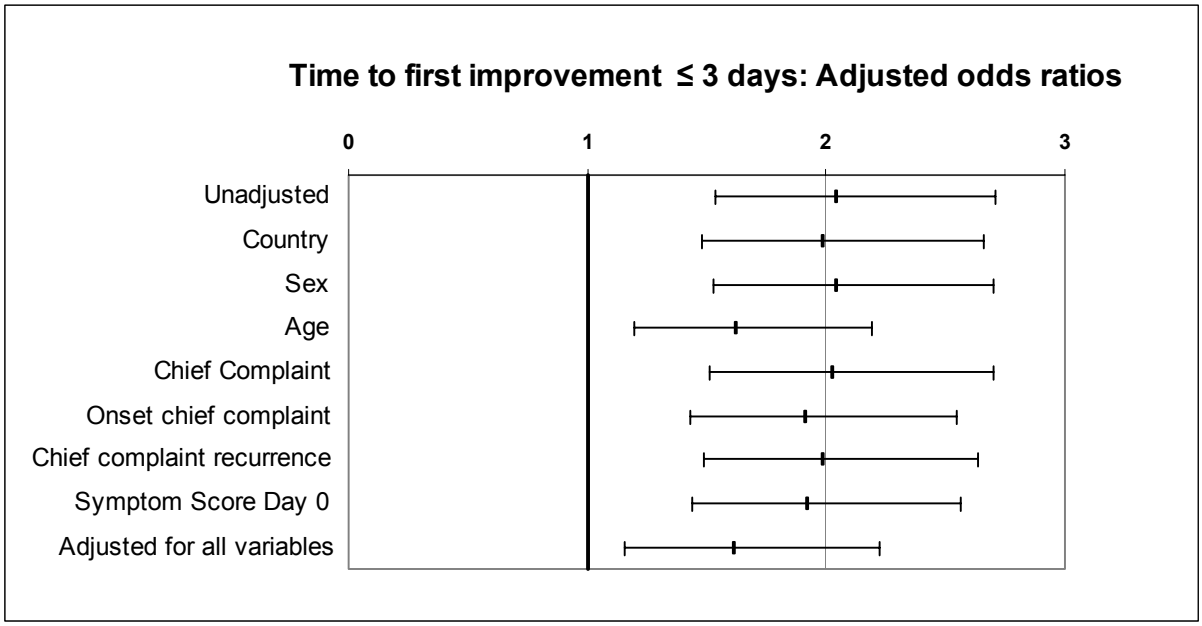


Figure 40 Adjusted odds ratios (95%-CI) for time to first improvement ≤ 3 days in Anthroposophy Group (n = 715) vs. Conventional Group (n = 301): adjusting for country, gender, age, chief complaint, duration of chief complaint, chief complaint episode within the last 12 months, and Symptom Score at day 0 respectively, combined adjustment for all these variables using multiple logistic regression analysis. Odds ratio > 1 indicates more frequent improvement within 3 days in Anthroposophy Group.

Summary of improvement, major improvement and recovery rates: Chief complaint subgroups, adults and children

Major clinical outcomes (first improvement, response and recovery rates) were analysed in chief complaint and age subgroups (Table 12).

Outcome rates differed considerably between chief complaint subgroups: In both the A- and C-group improvement within 3 days was observed more frequently among patients with chief complaint ear pain (82.5% and 68.4% of A- and C-group patients) than in other chief complaint subgroups. In the A-group improvement within 1 day (53.8%) and a response by Day 7 (89.5%) was also most frequent in the ear pain subgroup. An improvement within 1 day or a complete recovery by Day 7 was less frequent in patients with chief complaint cough in both groups and in patients with sinus pain in the A-group.

Comparing adults with children (Table 12), outcome rates were consistently higher in children than in adults in the A-group but not in the C-group.

Clinical outcomes: Chief complaint subgroups, adults and children

Subgroups	Number of patients		Percentages of patients											
			1 day		3 days		7 days				14 days			
			First Improvement				MI + CR		CR		MI + CR		CR	
	A	C	A	C	A	C	A	C	A	C	A	C	A	C
Runny nose	49	16	18.4	31.3	63.3	62.5	57.1	62.5	36.7	18.8	79.6	81.3	57.1	50.0
Sore throat	188	70	29.8	14.3	73.9	55.7	81.4	72.9	40.4	38.6	89.9	90.0	73.4	62.9
Ear pain	143	57	53.8	26.3	82.5	68.4	89.5	63.2	46.9	33.3	95.1	84.2	74.8	61.4
Sinus pain	50	56	24.0	19.6	64.0	55.4	76.0	62.5	16.0	17.9	90.0	83.9	38.0	39.3
Cough	285	102	23.5	8.8	71.2	52.0	71.6	65.7	17.2	10.8	88.4	81.4	58.6	40.2
Age 0-17 y	487	93	37.0	16.1	79.1	59.1	82.3	61.3	35.1	29.0	93.0	86.0	71.0	55.9
Age ≥ 18 y	227	208	17.6	16.3	60.4	56.3	65.6	68.3	20.7	20.7	82.4	83.7	49.8	46.6
All patients	715	301	30.9	16.6	73.1	57.1	77.1	66.1	30.5	23.3	89.7	84.4	64.2	49.5

Table 12 Percentage of patients with time to first improvement, MI = major improvement, CR = complete recovery. Subgroup analysis according to chief complaint and age.

Time to total recovery: Day 0-7

Time to total recovery (documented from Day 0 to Day 7) was shorter in the A-group than in the C-group (Figure 41) but this difference was not significant (p = 0.1691).

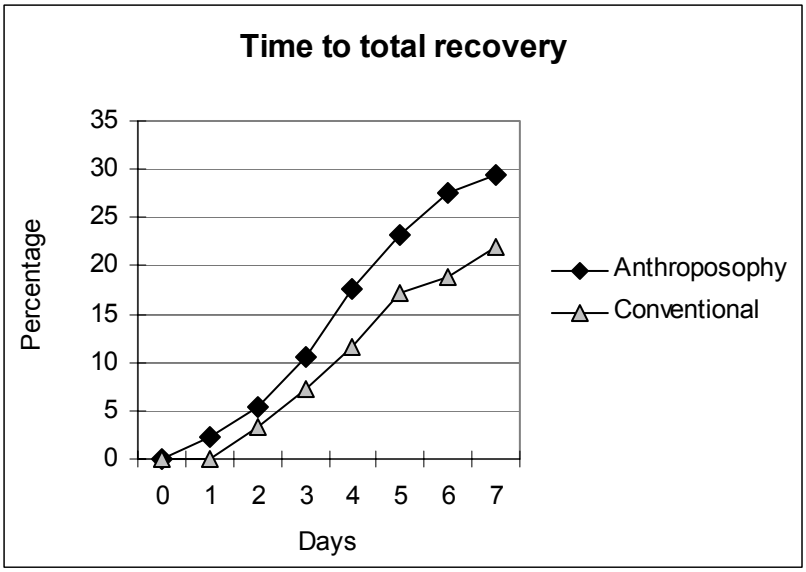


Figure 41 Time to total recovery. Percentage of patients. Patients with time to total recovery ≤ 7 days displayed, (for recovery rates at Day 14 and Day 28 cf. Figure 18). Anthroposophy Group: n = 715, Conventional Group: n = 301

Remission of chief complaint, Symptom Score, Quality of life

Figure 42, Figure 43 and Figure 44 display the proportions of patients with remission of chief complaint by Day 7, Day 14, and Day 28. Except for a higher remission rate of ear pain in the A-group on Day 7 (p = 0.0018), Day 14 (p = 0.0102), and Day 28 (p = 0.0137), a higher remission rate of sore throat in the A-group at Day 14 (p = 0.0121), and an overall higher remission rate in the A-group on Day 7 (p = 0.0319), differences between the groups were not significant.

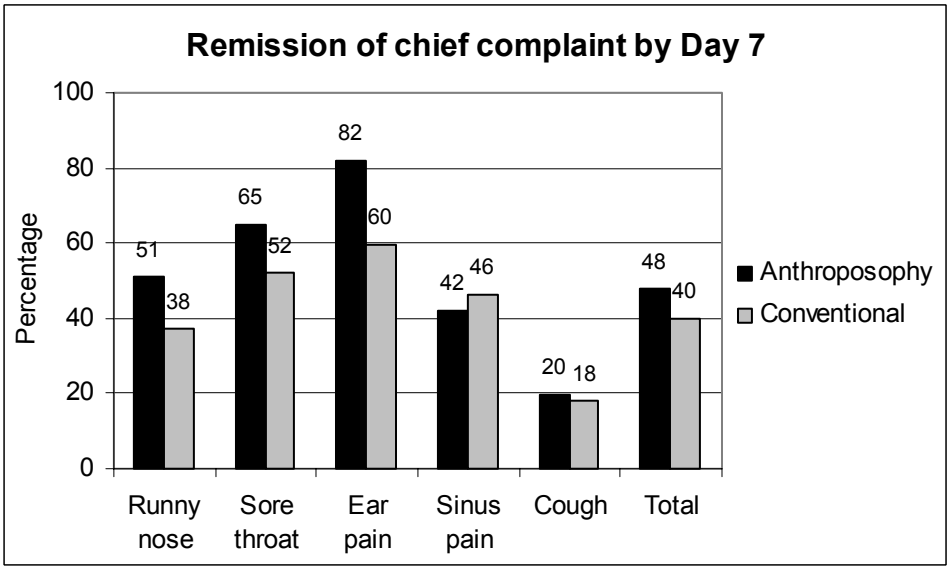


Figure 42 Chief complaint at Day 7: Percentage of patients with remission (chief complaint severity = not present). Anthroposophy Group: n = 713, Conventional Group: n = 299

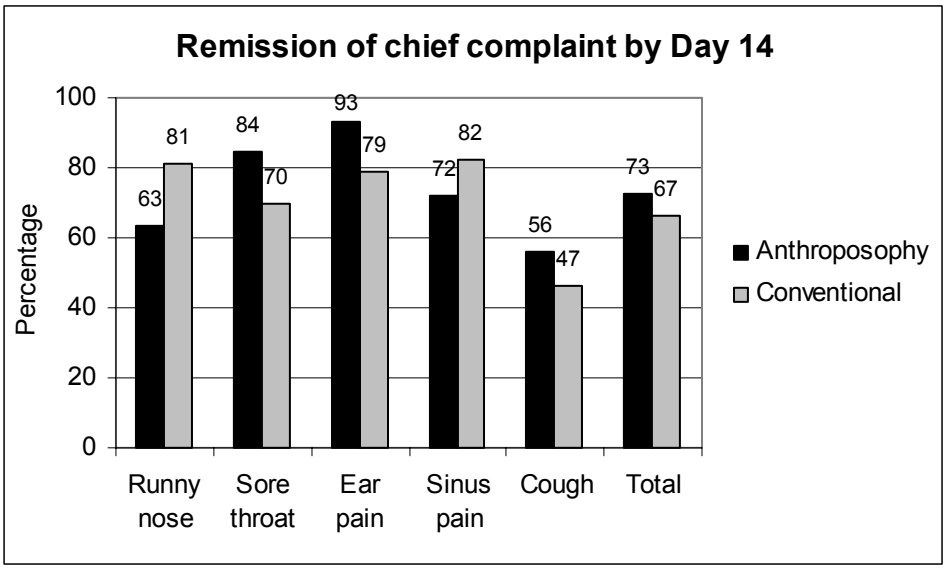


Figure 43 Chief complaint at Day 14: Percentage of patients with remission (chief complaint severity = not present). Anthroposophy Group: n = 713, Conventional Group: n = 299

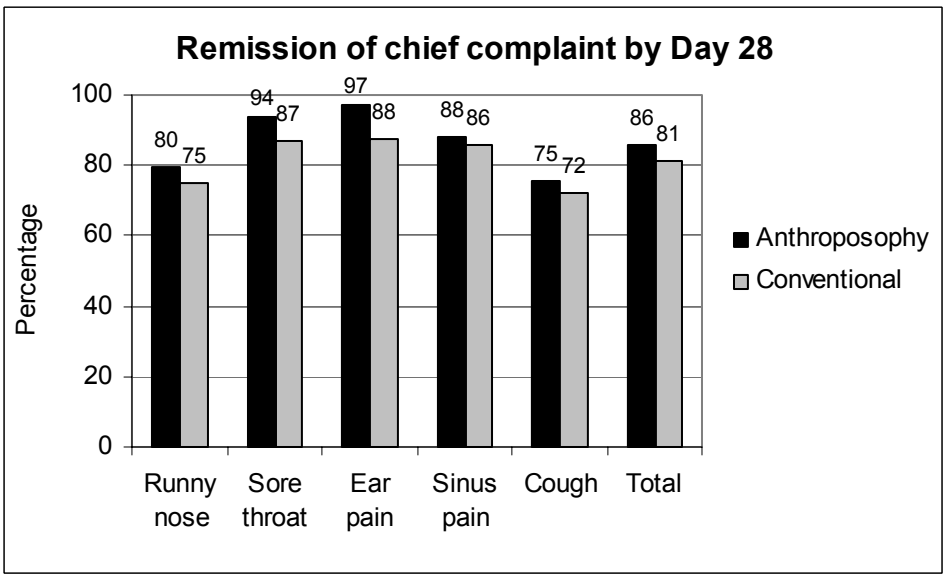


Figure 44 Chief complaint at Day 28: Percentage of patients with remission (chief complaint severity = not present). Anthroposophy Group: n = 713, Conventional Group: n = 299

Symptom Score (Figure 45), SF-12 Summary Score (Figure 46) and KINDL Summary Score (Figure 47) improved significantly in both groups. The magnitude of improvement did not differ significantly between the groups.

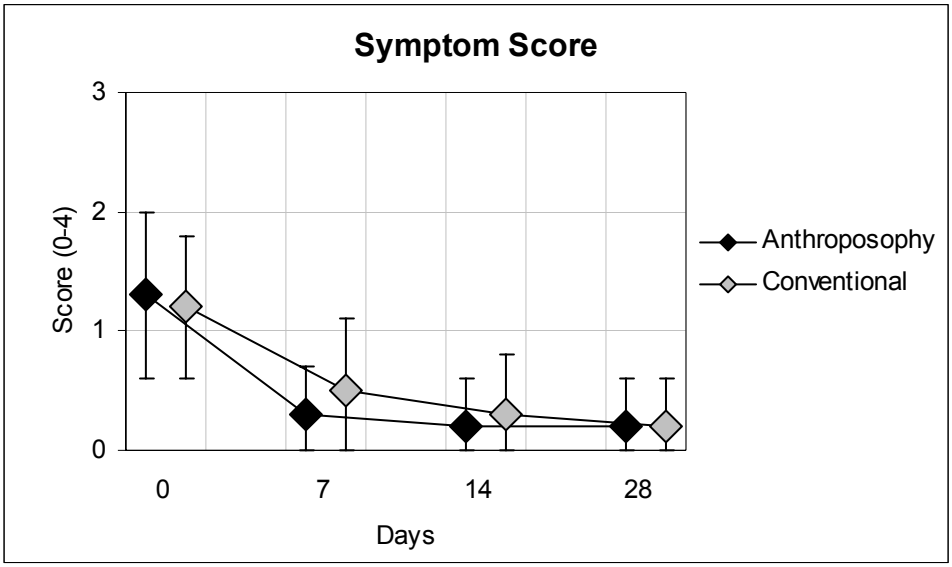


Figure 45 Symptom Score at Day 0, 7, 14, 28, mean and standard deviation in respondents. Anthroposophy Group: n = 714, n = 635, n = 453, n = 225. Conventional Group: n = 295, n = 262, n = 211, n = 145

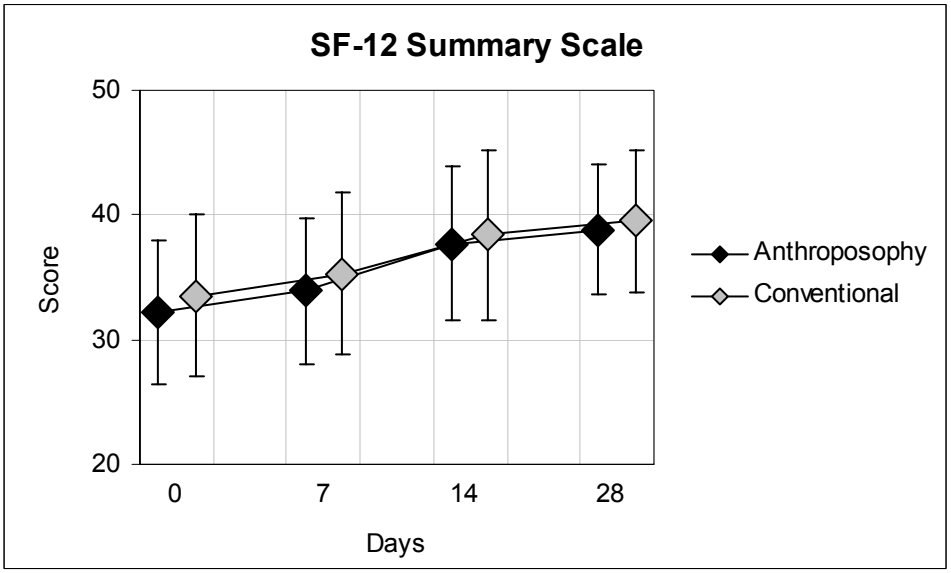


Figure 46 SF-12 Summary Scale at Day 0, 7, 14, 28, mean and standard deviation in respondents aged ≥ 16 years. Anthroposophy Group: n = 162, n = 195, n = 156, n = 103. Conventional Group: n = 165, n = 182, n = 149, n = 108

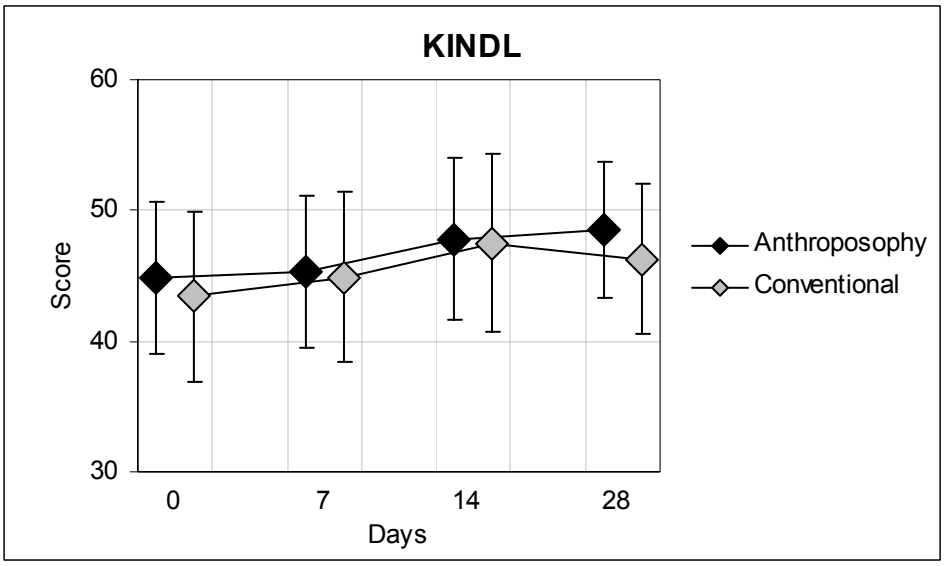


Figure 47 KINDL at Day 0, 7, 14, 28, mean and standard deviation in respondents aged < 16 years. Anthroposophy Group: n = 223, n = 256, n = 194, n = 187. Conventional Group: n = 57, n = 58, n = 49, n = 27

Patient satisfaction

Both patient satisfaction with the therapy (Figure 48) and patient satisfaction with the study doctor (Figure 49) were significantly higher in the A-group than in the C-group ($p < 0.0001$ and $p = 0.0028$ respectively).

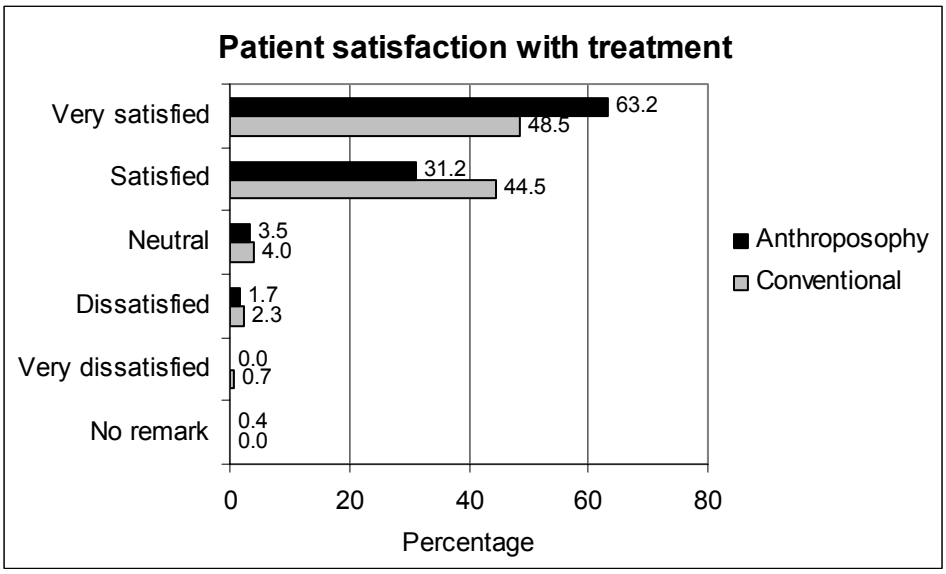


Figure 48 Patient satisfaction with treatment, last observation of each patient, Day 7-28. Anthroposophy Group: n = 715, Conventional Group: n = 301.

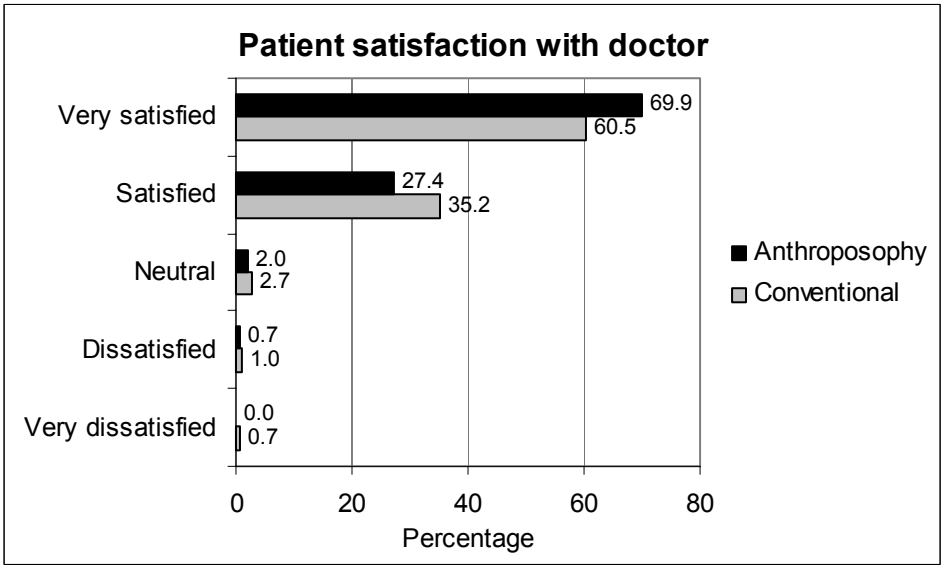


Figure 49 Patient satisfaction with study doctor, last observation of each patient Day 7-28. Anthroposophy Group: n = 715, Conventional Group: n = 301.

The proportion of patients very satisfied with the treatment at all evaluable follow-ups was 371 (51.9%) of 715 A-patients and 113 (37.5%) of 301 C-patients, resulting in an OR (A-group vs. C-group) for patient satisfaction of 1.79 (95%-CI: 1.36-2.36), favouring the A-group. The A-group was favoured in all analysed subgroups except among patients from the UK, patients aged 18-64 years, and patients with a chief complaint of runny nose or sinus pain (Figure 50).

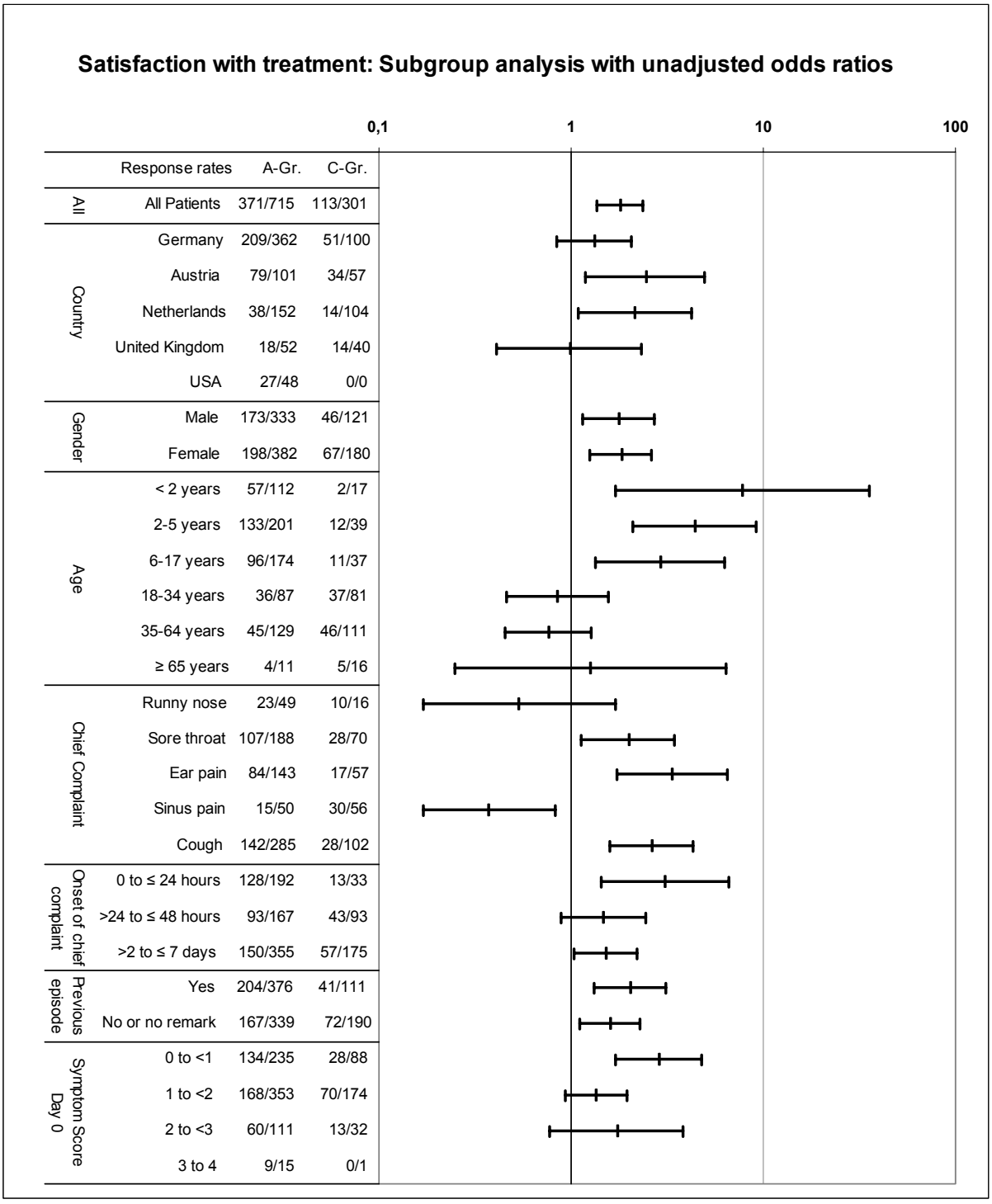


Figure 50 Unadjusted odds ratios for patient response = Very satisfied with the treatment at all evaluable follow-ups (2 missings permitted) in Anthroposophy Group (n = 715) vs. Conventional Group (n = 301), in whole sample and subgroups. Previous episode: Previous episode of chief complaint within the last 12 months. Response rates: number of patients very satisfied with the treatment at all evaluable follow-ups / number of patients. Odds ratio > 1 indicates higher response rate in Anthroposophy Group.

After multiple logistic regression analysis, adjusting for all prescribed covariates (Figure 51), the OR for patient satisfaction was 1.39 (95%-CI: 0.98-1.95), favouring the A-group.

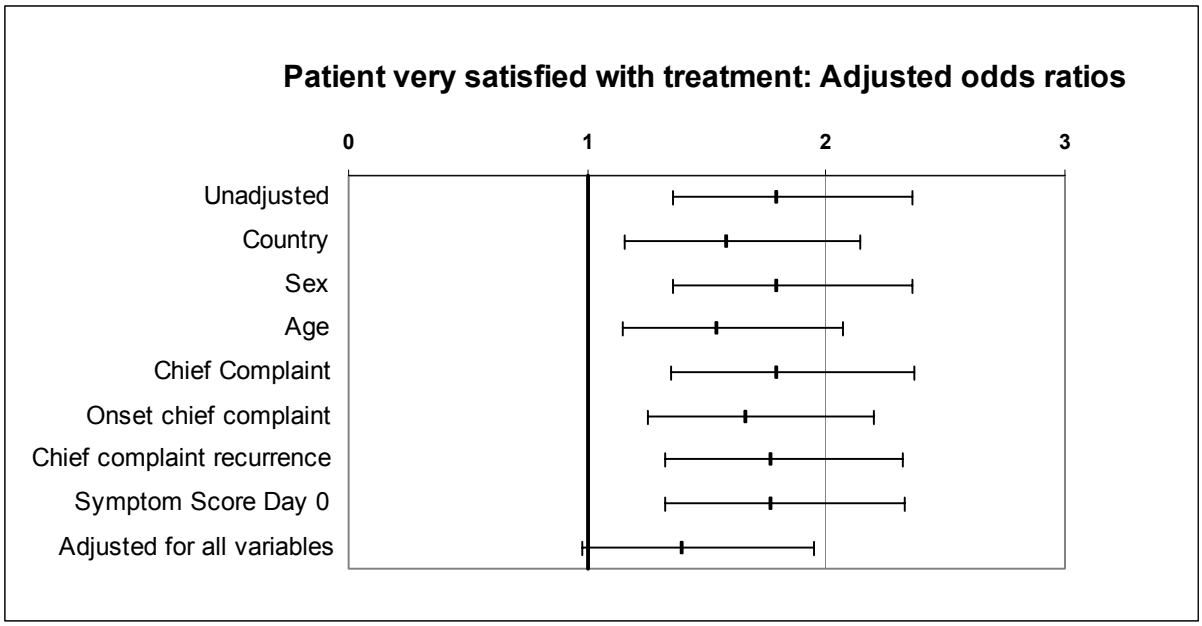


Figure 51 Adjusted odds ratios for patient response = Very satisfied with the treatment at all evaluable follow-ups (2 missings permitted) in Anthroposophy Group (n = 715) vs. Conventional Group (n = 301): adjusting for country, gender, age, chief complaint, duration of chief complaint, chief complaint episode within the last 12 months, and Symptom Score at day 0 respectively, combined adjustment for all these variables using multiple logistic regression analysis. Odds ratio > 1 indicates higher response rate in Anthroposophy Group.

684 (95.7%) of 715 A-patients and 251 (83.4%) of 301 C-patients answered the question "Would you choose this therapy again for your problem?" with yes at all follow-ups, resulting in an OR (A-group vs. C-group) for patients' choice of same therapy again of 4.40 (95%-CI: 2.74-7.04) favouring the A-group. The A-group was favoured in all analysed subgroups (Figure 52).

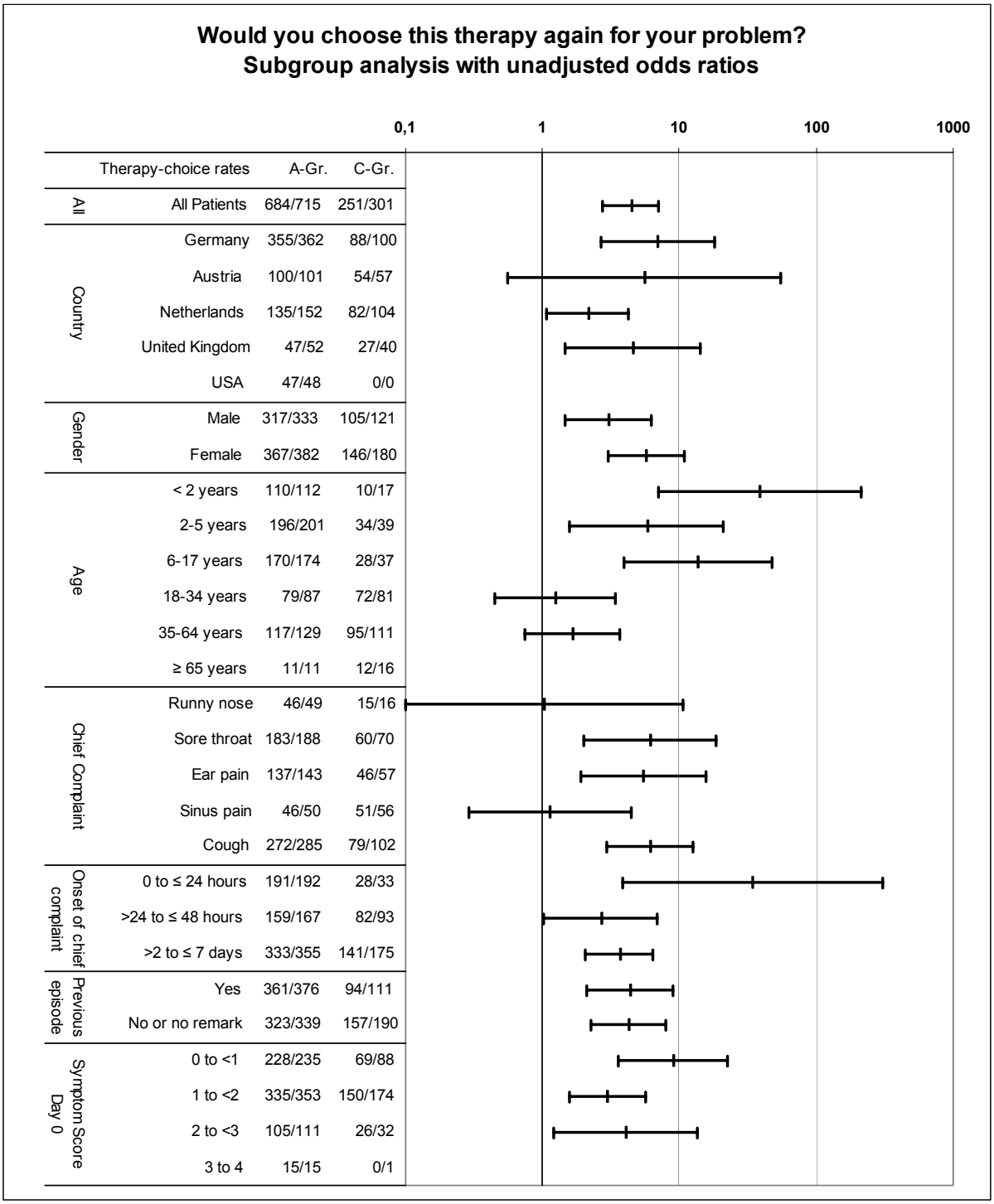


Figure 52 Unadjusted odds ratios for patient response = yes to question: "Would you choose this therapy again for your problem?" at all evaluable follow-ups (2 missings permitted) in Anthroposophy Group (n = 715) vs. Conventional Group (n = 301), in whole sample and subgroups. Previous episode: Previous episode of chief complaint within the last 12 months. Therapy-choice rates: number of patients with response = yes / number of patients. Odds ratio > 1 indicates higher response rate in Anthroposophy Group.

After multiple logistic regression analysis, adjusting for all prescribed covariates (Figure 53), the OR for patients' choice of same therapy again was 3.54 (95%-CI: 2.13-5.19), favouring the A-group.

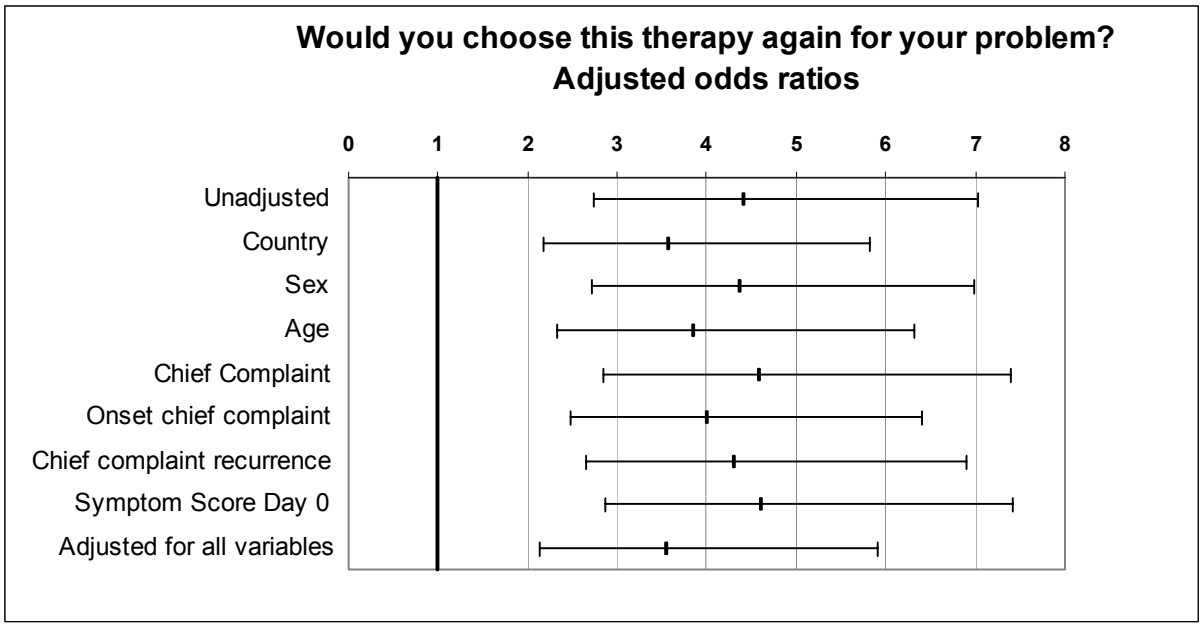


Figure 53 Odds ratios for patient response = yes to question: "Would you choose this therapy again for your problem?" at all evaluable follow-ups (2 missings permitted) in Anthroposophy Group (n = 715) vs. Conventional Group (n = 301): unadjusted, adjusting for country, gender, age, chief complaint, duration of chief complaint, chief complaint episode within the last 12 months, and Symptom Score at day 0 respectively, combined adjustment for all these variables using multiple logistic regression analysis. Odds ratio > 1 indicates more frequent response of "yes" in Anthroposophy Group.

The proportion of patients stating that they would choose this doctor again at all available follow-ups was 707 (98.9%) of 714 A-patients and 290 (96.3%) of 301 C-patients ($p = 0.0101$).

Summary of adjusted odds ratios for major outcomes

Figure 54 summarizes all odds ratios for major outcomes after multiple logistic regression analysis. Adjusted OR favoured the A-group for eight out of nine analysed outcomes and favoured the C-group for response by Day 28.

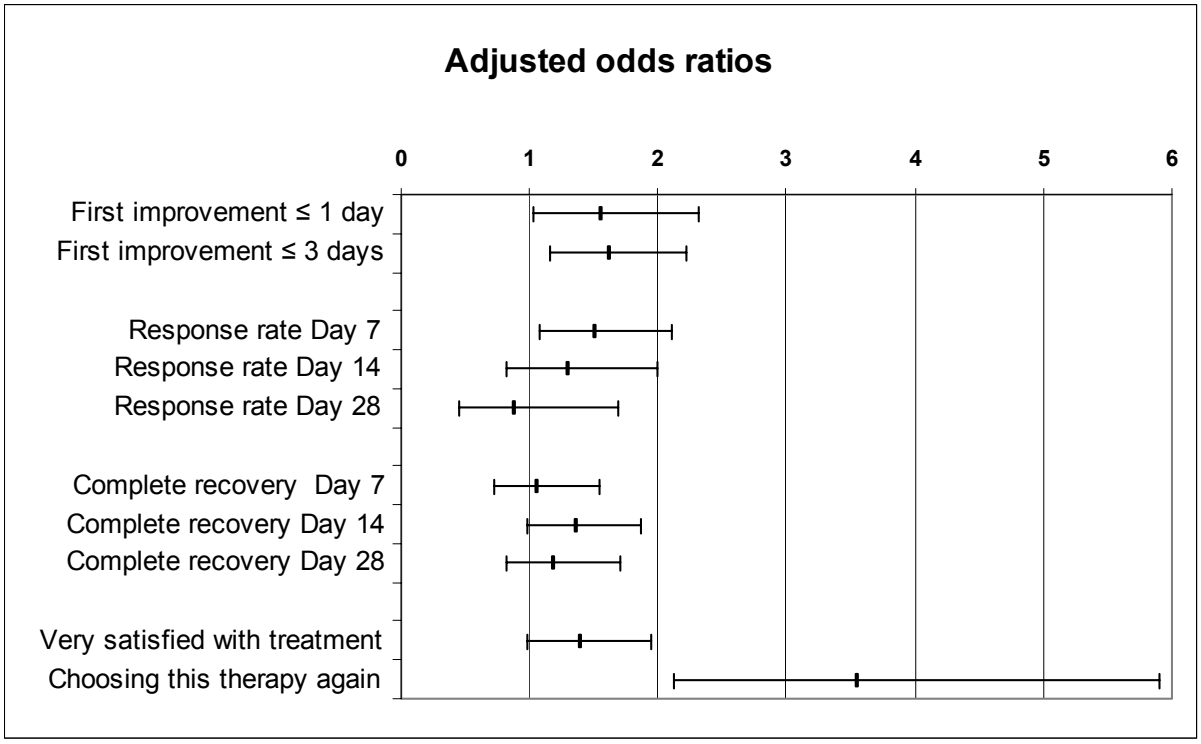


Figure 54 Odds ratios for major outcomes after multiple logistic regression analysis, adjusting for country, gender, age, chief complaint, duration of chief complaint, chief complaint episode within the last 12 months and Symptom Score at day 0. Odds ratio > 1 indicates higher improvement / response / recovery / satisfaction / therapy-choice rate in Anthroposophy Group.

Adverse Drug Reactions

Adverse Drug Reactions (Adverse Events with probable or possible causal relationship with any study medication, according to patient follow-up response) were reported by 6.0% of the C-patients and 2.7% of A-patients ($p = 0.0157$). Adverse Drug Reactions of severe intensity were also more frequent in C-patients (1.0%) than in A-patients (0.1%) ($p = 0.0805$). Necessary actions and outcomes of Adverse Drug Reactions are presented in Table 13.

Adverse Drug Reactions				
Patients with Adverse Drug Reactions	**Anthroposophy N=715**		**Conventional N=301**	
Relationship with study medication				
Probable	9	1.3%	16	5.3%
Possible	10	1.4%	2	0.7%
Total	19	2.7%	18	6.0%
Intensity				
Mild	17	2.4%	12	4.3%
Moderate	1	0.1%	3	1.0%
Severe	1	0.1%	3	1.0%
Total	19	2.7%	18	6.0%
Necessary actions				
None	8	1.1%	12	4.0%
Dose reduction of investigational medication	4	0.6%	0	0.0%
Withdrawal of investigational medication	4	0.6%	4	1.3%
Therapeutic counteractions	1	0.1%	2	0.7%
Others	2	0.3%	0	0.0%
Total	19	2.7%	18	6.9%
Outcome at last follow-up interview				
AE subsided	18	2.5%	12	4.0%
AE still being treated	0	0.0%	1	0.3%
Uncertain, AE still under observation	1	0.1%	5	1.7%
Total	19	2.7%	18	6.9%

Table 13 Patients with Adverse Drug Reactions (Adverse Events with probable or possible causal relationship with any study medication, according to patient follow-up response): relationship with study medication, intensity, necessary actions, outcome

Adverse Drug Reactions were more frequent in the C-group in 22 of 25 analysed subgroups, and more frequent in the A-group in patients from the UK, patients aged 0-2, and patients aged 2-5 (Figure 55). Grouping together all adults and all children, ADR rates were similar in children aged 0-17 years (2.1% and 2.2% in A- and C-group) but not in adults aged ≥ 18 years (4.0% and 7.7.%).

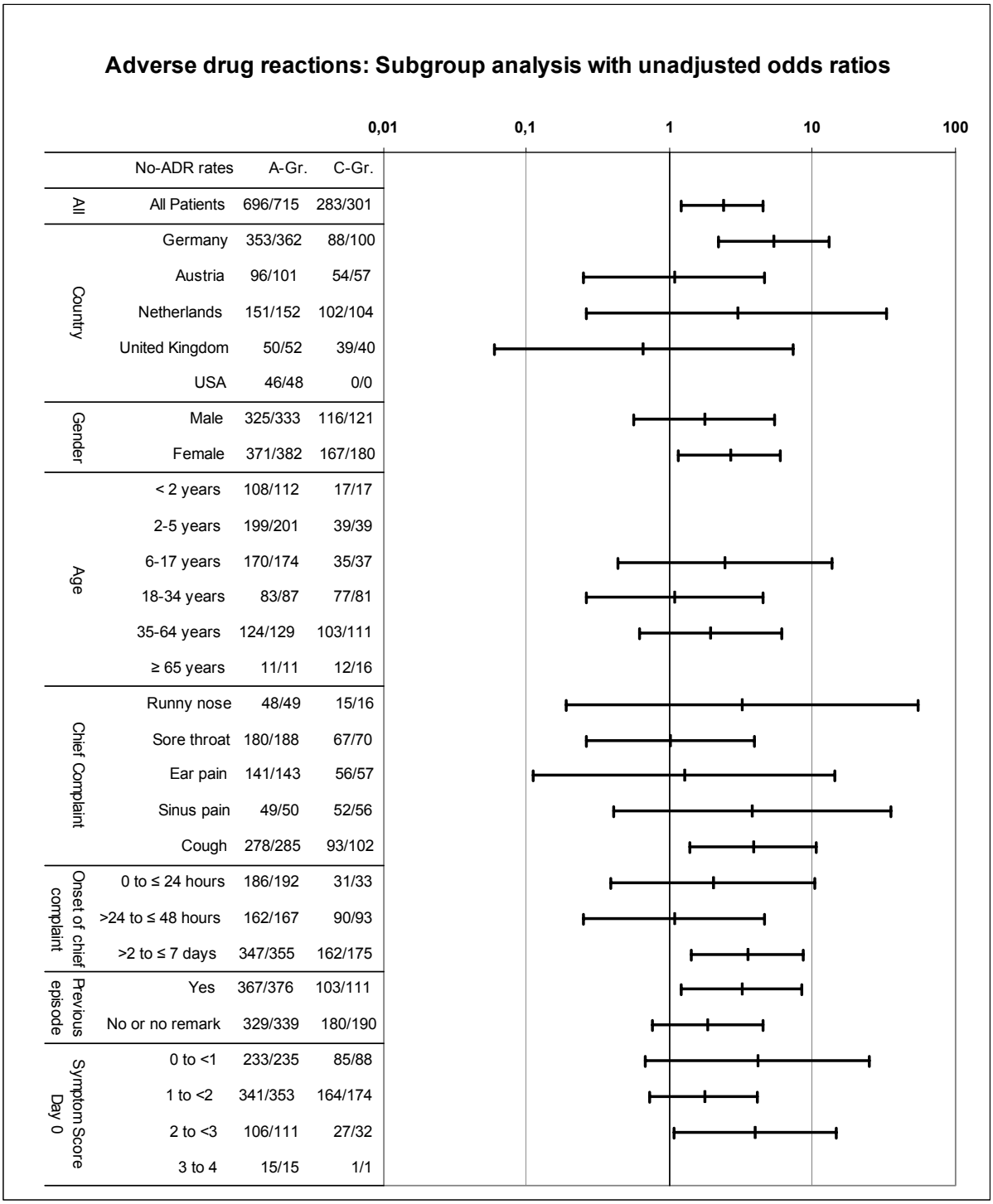


Figure 55 Unadjusted odds ratios for non-occurrence of adverse drug reaction (Adverse Events with probable or possible causal relationship with any study medication, according to patient follow-up response) in Anthroposophy Group (n = 715) vs. Conventional Group (n = 301), in whole sample and subgroups. Previous episode: Previous episode of chief complaint within the last 12 months. No-ADR rates: number of patients without adverse drug reactions at all evaluable follow-ups / number of patients. Odds ratio > 1 indicates less frequent adverse drug reactions in Anthroposophy Group.

Serious Adverse Events

Serious Adverse Events (SAE) occurred in 4 (0.6%) of 715 A-patients and 3 (1.0%) of 301 C-patients. All SAE were events of severe intensity, leading to acute hospital referrals. SAE in A-patients were: 1) patella fracture, 2) asthma, mesenteric adenitis, 3) gastroenteritis, vomiting, hypovolaemia, 4) suspected meningitis (suspicion not confirmed). SAE in C-patients were: 5) knee arthroscopy, 6) emotional lability, 7) tonsillectomy. At the last follow-up, SAE 1+6 were still being treated, the other SAE had subsided. None of the SAE were causally related to any study medication.

Comments

Overall study findings

This study compared primary care patients from five countries self-selected to treatment by anthroposophic (n = 715 patients) or conventional physicians (n = 301) for acute sore throat, ear pain, sinus pain, runny nose or cough. Clinical outcomes (improvement within 1 or 3 days, response and recovery by Days 7 and 14) were significantly more favourable after anthroposophic treatment. Outcomes were adjusted for age, gender, country, and four baseline symptom variables. All adjusted odds ratios favoured the A-group, results were statistically significant for early outcomes (improvement by 1 or 3 days, response by Day 7), but not for response by Day 14 (OR: 1.29, 95%-CI: 0.82-2.00).

During the four-week study period, 33.6% of C-patients but only 5.5% of A-patients were prescribed antibiotics. Another striking finding was that 21.9% of C-patients but only 3.2% of A-patients were prescribed analgesics, although at baseline both groups had similar frequency of symptoms often treated with analgesics (severe pain, high fever). Adverse drug reactions were relatively infrequent in C-patients (6.0%), but significantly less frequent in A-patients (3.7%). Complications related to chief complaint or its treatment occurred in the C-group only (n = 2: acute tonsillectomy, pneumonia) and not in the A-group. Patient satisfaction with treatment was higher in the A-group.

Study strengths and limitations

The following section discusses strengths and limitations of the study with respect to internal validity, representativity of participants and generalisability of study results.

Internal validity

Insensitive measure bias (86) probably applies to the primary comparison of Day 14 response rates, since most acute respiratory infections will have improved after 14 days. This outcome measure was adopted from a similar study on homeopathy (80), but the short-term follow-up data used for secondary comparisons (first improvement by 1 or 3 days, response by 7 days) are arguably more relevant.

Since clinical outcomes were analysed after 1, 3, 7, and 14 days, the issue of *multiple hypothesis-testing* arises. However, all comparisons favoured the A-group. Moreover, the time sequence of odds ratios (Figure 54 on p. 67) is compatible with short-time treatment effects (improvement by 1 and 3 days, response by Day 7) becoming attenuated (response by Day 14) and finally levelled out (response by Day 28) by spontaneous improvement in both groups.

Dropout bias: All patients were scheduled for follow-up telephone interviews on Day 7. Patients not completely recovered by Day 7 were also interviewed on Day 14, and, if not recovered by Day 14, on Day 28. Patients with at least one interview (1016 of 1171 enrolled patients) were included in the analysis; missing data from Days 14 or 28 were replaced by data from earlier follow-ups (Last Observation Carried Forward, LOCF).

Patients without any follow-up interviews (155 of 1171) were excluded from the analysis. Dropout analysis suggest that any dropout bias, if present, would be conservative, i. e. disfavouring the A-group, since evaluable A-patients had significantly higher baseline symptom severity than excluded A-patients (mean 1.3 vs. 1.0), whereas no such difference was observed in the C-group. Most exclusions were not related to treatment or clinical outcome (99 patients were excluded because one interviewer from a contract research organisation commissioned to perform the interviews had not performed interviews according to the protocol). For the remaining exclusions (see below: [a]) and missing follow-up interviews with included patients [b-c] the possibility of dropout bias will be further examined:

[a] 56 patients were excluded because no follow-up interview had been performed; mostly because patients were not reachable by telephone, or for technical reasons (remote data entry system error). 7/56 patients refused to participate in the interviews.

[b] 106/1016 scheduled Day 7 interviews were not performed (patient refusal: n = 2). For analysis of clinical outcomes of day 7, these 106 patients were classified as non-responder.

[c] 70/728 Day 14 interviews were not performed (refusal: n = 3). Missing data were replaced by Day 7 data when available, leaving 18 interviews without data. For outcome analysis of day 14, these 18 patients were classified as non-responders.

Proportions of patients without follow-up [a] or with missing data [b-c] did not differ significantly between A- and C-group.

To test the impact of alternative ways of dealing with missing data [a-c], we performed sensitivity analysis for unadjusted clinical outcomes. Patients without any follow-ups [a] or with missings [b-c] were alternatively classified as non-responder, or as responder, or excluded from the analysis; Day 14 outcomes were analysed with and without LOCF of Day 7 data. Altogether 31 alternative analyses were performed (Table 14, Table 15). All analyses resulted in superior outcomes in the A-group than in the C-group. For improvement ≤ 1 day and ≤ 3 days, Day 7 response and Day 14 recovery, all analyses showed highly significant A vs. C differences ($p = 0.001$ or lower). For Day 14 response, 8/9 alternative analyses had more significant differences than the primary analysis ($p = 0.0198$), one analysis had insignificant results ($p = 0.0586$). The most conservative analysis – not using LOCF and classifying patients [a+c] as non-responder – yielded a result ($p = 0.0148$) similar to the primary analysis. For Day 7 recovery, two alternative analyses – including the most conservative – had results similar to the primary analysis ($p = 0.0221$), two analyses had insignificant results. Altogether, 28 out of 31 analyses performed yielded statistically significant differences favouring the A-group. In conclusion, neither dropout bias as such, nor alternative ways of analysing missing data would change the overall results of this study.

Time to first improvement ≤ 1 day and ≤ 3 days, Day 14 response and recovery rates: Sensitivity analysis						
		A-group		C-group		Fisher's exact test
		N	%	N	%	
Time to first improvement ≤ 1 day						
Missing telephone interview of included patients (n = 106)	**Patients without any follow-up data (n = 56)**					
Classified as non-responder	Classified as non-responder	221/755	29.3%	50/317	15.8%	p < 0.0001
*Classified as non-responder**	*Excluded**	221/715	30.9%	50/301	16.6%	p < 0.0001
Excluded	Excluded	221/623	35.5%	50/247	20.2%	p < 0.0001
Classified as responder	Excluded	313/715	43.8%	104/301	34.6%	p = 0.0065
Classified as responder	Classified as responder	353/755	46.8%	120/317	37.9%	p = 0.0085
Time to first improvement ≤ 3 days						
Classified as non-responder	Classified as non-responder	523/755	69.3%	172/317	54.3%	p < 0.0001
*Classified as non-responder**	*Excluded**	*523/715*	*73.1%*	*172/301*	*57.1%*	*p < 0.0001*
Excluded	Excluded	523/623	83.9%	172/247	69.6%	p < 0.0001
Classified as responder	Excluded	615/715	86.0%	226/301	75.1%	p < 0.0001
Classified as responder	Classified as responder	655/755	86.8%	242/317	76.3%	p < 0.0001
Day 7 response rate						
Classified as non-responder	Classified as non-responder	551/755	73.0%	199/317	62.8%	p = 0.0010
*Classified as non-responder**	*Excluded**	*551/715*	*77.1%*	*199/301*	*66.1%*	*p = 0.0004*
Excluded	Excluded	551/645	85.4%	199/265	75.1%	p = 0.0004
Classified as responder	Excluded	621/715	86.9%	235/301	78.1%	p = 0.0007
Classified as responder	Classified as responder	661/755	87.5%	251/317	79.2%	p = 0.0007
Day 7 complete recovery rate						
Missing telephone interview of included patients (n = 106)	**Patients without any follow-up data (n = 56)**					
Classified as non-responder	Classified as non-responder	218/755	28.9%	70/317	22.1%	p = 0.0235
*Classified as non-responder**	*Excluded**	*218/715*	*30.5%*	*70/301*	*23.3%*	*p = 0.0221*
Excluded	Excluded	218/645	33.8%	70/265	26.4%	p = 0.0340
Classified as responder	Excluded	288/715	40.3%	106/301	35.2%	p = 0.1389
Classified as responder	Classified as responder	328/755	43.4%	122/317	38.5%	p = 0.1364

Table 14 Sensitivity analysis for time to first improvement ≤ 1 day and ≤ 3 days, Day response and recovery rates, classifying patients without any follow-up interviews and patients with missing data as non-responder or as responder or excluding them from the analysis. *The primary analysis used in this report.

Day 14 response and recovery rates: Sensitivity analysis						
		A-group		C-group		Fisher's exact test
		N	%	N	%	
Day 14 response rate						
Missing telephone interview of included patients after LOCF (n = 18)	**Patients without any follow-up data (n = 56)**					
Classified as non-responder	Classified as non-responder	641/755	84.9%	254/317	80.1%	p = 0.0586
*Classified as non-responder**	*Excluded**	*641/715*	*89.7%*	*254/301*	*84.4%*	*p = 0.0198*
Excluded	Excluded	641/701	91.4%	254/297	85.5%	p = 0.0062
Classified as responder	Excluded	655/715	91.6%	258/301	85.7%	p = 0.0061
Classified as responder	Classified as responder	695/755	92.1%	274/317	86.4%	p = 0.0062
Missing telephone interview of included patients without LOCF (n = 70)	**Patients without any follow-up data (n = 56)**					
Classified as non-responder	Classified as non-responder	620/755	82.1%	239/317	75.4%	p = 0.0148
Classified as non-responder	Excluded	620/715	86.7%	239/301	79.4%	p = 0.0043
Excluded	Excluded	620/669	92.7%	239/277	86.3%	p = 0.0029
Classified as responder	Excluded	666/715	93.1%	263/301	87.4%	p = 0.0044
Classified as responder	Classified as responder	706/755	93.5%	279/317	88.0%	p = 0.0045
Day 14 complete recovery rate						
Missing telephone interview of included patients after LOCF (n = 18)	**Patients without any follow-up data (n = 56)**					
Classified as non-responder	Classified as non-responder	459/755	60.8%	149/317	47.0%	p < 0.0001
*Classified as non-responder**	*Excluded**	459/715	64.2%	149/301	49.5%	p < 0.0001
Excluded	Excluded	459/701	65.5%	149/297	50.2%	p < 0.0001
Classified as responder	Excluded	473/715	66.2%	153/301	50.8%	p < 0.0001
Classified as responder	Classified as responder	513/755	67.9%	169/317	53.3%	p < 0.0001
Missing telephone interview of included patients without LOCF (n = 70)	**Patients without any follow-up data (n = 56)**					
Classified as non-responder	Classified as non-responder	As above				
Classified as non-responder	Excluded	As above				
Excluded	Excluded	As above				
Classified as responder	Excluded	505/715	70.6%	173/301	57.5%	p = 0.0001
Classified as responder	Classified as responder	545/755	72.2%	189/317	59.6%	p = 0.0001

Table 15 Sensitivity analysis for Day 14 response and recovery rates, classifying patients without any follow-up interviews and patients with missing data as non-responder or as responder or excluding them from the analysis. Analysis with and without LOCF (Day 7 observation carried forward) *The primary analysis used in this report.

Observation bias: In this study of real-world primary care treatment, patient blinding was neither wanted nor possible. Both treatment groups had high levels of satisfaction with their doctors. To diminish potential obsequiousness bias (86), follow-up data were not collected at doctors' offices but by telephone. For technical reasons, blinding of telephone interviewers towards patients' treatment setting was not possible. However, reporting bias is unlikely, since all interviews followed identical protocols and were performed by independent interviewers without financial or personal ties to any treatment regimen or any doctor.

Baseline differences: This study compared patients who had chosen to be treated by anthroposophic or conventional physicians. It was not purpose of this real-world comparison to have identical baseline groups. The largest baseline differences observed were related to country, age, frequency of chief complaint sinus pain, and recurrences of chief complaint. To

control for confounding, outcomes were adjusted for these variables, and for gender, duration of chief complaint, and symptom severity. The groups were similar regarding household size and income, smoking, previous treatment by doctor, body mass index, quality of life, and concomitant diseases; only a few percent of patients were using medication for chronic respiratory disease. Moreover, follow-up consultation rates and medication compliance were similar in both groups. Still, factors relating to patients' self-selection (e. g. motivation or lifestyle) may have affected outcomes.

Representativity of the participants

Settings and doctors: Patients were recruited by 36 doctors from 23 municipalities in five countries, allowing for a range of healthcare settings. All doctors had at least 5 years practice, A-doctors had median 15.5 years. For C-doctors this number was not documented, but was probably similar to that of A-doctors (W. Mayer, personal communication). Altogether, patients were treated by experienced primary care physicians with different (anthroposophic vs. conventional) practice profiles.

Eligibility criteria: In primary care, patients seek relief of symptoms, not diagnoses. General practitioners' treatment of acute respiratory and ear disease relies more on symptoms and signs than diagnoses or tests (4;11;44;77;100). Whereas clinical trials traditionally include patients with specific diagnoses, academic primary care medicine is now calling for trials focusing on patients' symptoms, to mirror the full disease spectrum seen in real-world practice (21). In this study patients were included if they had one out of five symptoms; patients were not required to fulfil a set of diagnostic criteria, the clinical and prognostic validity of which is often disputable (see Text Block).

TEXT BLOCK
In the case of patients with a sore throat, the clinical-anatomical diagnoses tonsillitis and pharyngitis are frequently used interchangeably (44). Doctors' major decision dilemma has been whether to prescribe antibiotics or not, consequently the diagnostic issue has been the presence of Group A Streptococci infection. Several diagnostic scores (12;18;66) have attempted to identify patients with a high probability of throat swab cultures positive for Group A Streptococci (gold standard). However, bacteria collected on throat swabs stem from the surface of the tonsils, whereas infection is more likely caused by the bacterial flora of the tonsillar crypts. Moreover, positive throat cultures are observed in up till 40% of asymptomatic patients (2). Therefore, even a positive Streptococci culture (gold standard) or antigen test (surrogate marker with lower sensitivity and specificity) does not prove that the Streptococci are causing the patients' symptoms of sore throat (58). A better gold standard for a diagnosis of Streptococcal infection would be serological tests, which are not useful in primary care. Finally, the clinical and prognostic significance of a diagnosis of bacterial vs. viral infection is uncertain: There is no conclusive evidence that bacterial sore throats are more severe or long-lasting than viral ones (2). Consequently, the Cochrane review of antibiotic trials in pharyngitis/tonsillitis used "symptoms of sore throat" as inclusion criteria – and found antibiotics to be only moderately more effective in people with Streptococci growing in the throat compared to people without Streptococci (22).

Study *exclusion criteria* were limited to severe non-respiratory conditions which might profoundly affect the physician's treatment of the patient (dementia, schizophrenia, psychosis, spinal cord injury, stroke, renal failure, severe hepatic disease, ongoing cancer therapy, alcohol or drug abuse). Whereas e. g. randomised trials of antibiotics in RTI and AOM frequently exclude patients "too ill not to have antibiotics" (15;37;43;45;51;54;59;60;110), patients with recurrent chief complaints (25;61;71;98) or patients with more than one respiratory organ acutely affected (9;13;24;39;50;52;53;71;73;75;96;102;103;107), such patients were not excluded from this trial. Thus, at study entry the chief complaint severity was "very severe" in 14.7% of A-patients and 6.0% of C-patients, a previous episode of the chief complaint had occurred within the last year in 52.7% and 37.0%, and a comorbid respiratory disorder was present in 9.1% and 10.0% of the patients. In conclusion: this study covers the full range of acute respiratory and ear symptoms seen in primary care and is therefore more representative for real-world practice than traditional clinical trials.

Selection bias: Screening data did not suggest selection bias in the A-group: reasons for non-inclusion of eligible A-patients (NE-A, n = 461) were lack of time or technical obstacles in 80%. Comparing NE-A-patients to evaluable A-patients, we found no significant differences (gender, chief complaint sinus pain or cough, chief complaint severity), or small differences of little clinical relevance (1.1 year age difference, frequency of runny nose 4.0% vs. 6.9%, sore throat 17.6% vs. 26.3%, Day 0 antibiotic prescription rate 2.8% vs. 0.8%). For the C-group no screening data were available, thus selection bias cannot be ruled out. In the C-group, lower occurrence of a chief complaint episode in the last year (C-group: 37.0%, A-group: 52.7%) or of "very severe" chief complaints (6.0% vs. 14.7%) could suggest selection

bias, but this could also reflect true differences between patients choosing anthroposophic or conventional therapy.

Generalisability of the study results

Patient numbers were limited in two subgroups: Only 16 C-patients had chief complaint runny nose, and only 27 A+C-patients were over 65 years. In children aged 0-17 years clinical outcomes were consistently more favourable in A-patients than in C-patients (Table 12 on p. 57), whereas adults had similar results in both groups. Antibiotic prescription rates were lower in A-patients across all ages. Thus, overall study results apply to patients aged < 65 years with sore throat, ear pain, sinus pain or cough, and the superior clinical outcomes of AM compared to conventional treatment may not be generalisable to adults.

Study implications

Implications for practice

In this study, real-world anthroposophic treatment was compared to real-world conventional treatment, not to placebo, minimal- or no-treatment. Therefore, adequate interpretation of study results requires an appreciation of the treatment in the conventional group. At study entry, 97% of C-patients received a medication prescription. The appropriateness of this treatment was not formally evaluated. Two points should be noted, however:

- Antibiotic prescription rates in the C-group (27% of all patients by Day 0) – albeit much higher than in the A-group (1%) – were much lower than in recent primary care samples (pharyngitis: 49%-94% (72;74;100), otitis media: 81%-97% (29;72;74), sinusitis: 80%-91% (72;74), bronchitis: 69%-89% (36;46;63;64;72;74), cough: 70%, (67), any RTI: 39%-54% (6;17;74)). This difference may partly stem from different diagnostic labelling between studies, but still suggest a judicious use of antibiotics by the conventional doctors in this study, as recommended by modern guidelines (23;35;40;90).
- This study included patients with severe (A-group: 60%, C-group: 54%) and recurrent symptoms (53% vs. 37%), often deemed to require antibiotics, i. e. patients for whom minimal treatment would not be appropriate.

The conventional group thus represents unselected patients receiving “modern” treatment-as-usual in countries (A, D, NL, UK) with varying antibiotic prescription traditions.

In conclusion: Anthroposophic treatment of primary care patients with symptoms of acute respiratory and ear infections is safe, allows for a very low antibiotic prescription rate, and may offer more favourable short-time outcomes than conventional treatment.

Implication for research

There is a need to study the effectiveness of anthroposophic treatments across a range of clinical conditions (1). This study, the first of its kind, shows that international multi-centre GCP-conform trials are possible in AM primary care settings.

To assess the feasibility of randomisation in future projects, patient willingness to be randomised was recorded. Only 3.2% of AM patients were willing to be randomised if their

treatment would be offered in a clinical trial. Thus, studying AM therapy of acute infections (and probably other conditions), randomisation will not be feasible in usual AM settings. If randomised trials of AM should be conducted in other settings, results may lack representativity and be misleading.

In this study, 266 different AM medicines were prescribed for acute respiratory or ear complaints, only four medicines were prescribed for > 10% of patients. Thus, single-drug trials, albeit often requested for regulatory purposes, will cover only small segments of real-world AM practice, and will not be feasible in many cases. Therefore, study designs enabling the simultaneous evaluation of many AM medicines should be developed and implemented.

My own contributions to the study

My own contributions to this study (1998-2004) were:

- Adaptation of Case Report Forms and Study Protocol
- Recruiting anthroposophic study doctors
- Correspondence with cooperation partners: participating doctors, ethics committees etc.
- On-site-monitoring of anthroposophic study doctors: Study Initiation Visits, Periodical Monitor Visits, Study Termination Visits including Source Data Verification, queries and corrections
- Preparation of the analysis plan, supervision of the statistical analysis
- Preparation of the study report and this dissertation, including tables

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Literature

(1) Akademische Forschung in der Anthroposophischen Medizin. Beispiel Hygiogenese: Natur- und geisteswissenschaftliche Zugänge zur Selbstheilungskraft des Menschen. Bern: Peter Lang; 1999, 375 p.

(2) Management of Sore Throat and Indications for Tonsillectomy. Edinburgh: Scottish Intercollegiate Guidelines Network; 1999, 32 p.

(3) Community Management of Lower Respiratory Tract Infection in Adults. Edinburgh: Scottish Intercollegiate Guidelines Network; 2002, 31 p.

(4) Diagnosis and management of childhood otitis media in primary care. A national clinical guideline. Edinburgh: Scottish Intercollegiate Guidelines Network; 2003, 21 p.

(5) American Academy of Pediatrics Subcommittee on Management of Sinusitis and Committee on Quality Improvement. Clinical practice guideline: management of sinusitis. Pediatrics 2001; 108(3):798-808.

(6) Andre M, Odenholt I, Schwan A, Axelsson I, Eriksson M, Hoffman M et al. Upper respiratory tract infections in general practice: diagnosis, antibiotic prescribing, duration of symptoms and use of diagnostic tests. Scand J Infect Dis 2002; 34(12):880-886.

(7) Appelman CLM, van Balen FA, van de Lisdonk E, van Weert HCPM, Eizenga WH. NHG Practice Guideline 'Acute otitis media'. Dutch College of General Practitioners published practice guidelines in English. Last update: 2002. Accessibility verified: 17-1-2004.

(8) Arroll B, Kenealy T. Antibiotics for the common cold. Cochrane Database Syst Rev 2002;(3):CD000247.

(9) Arroll B, Kenealy T, Kerse N. Do delayed prescriptions reduce the use of antibiotics for the common cold? A single-blind controlled trial. J Fam Pract 2002; 51(4):324-328.

(10) Arzneimittelkommission der deutschen Ärzteschaft. Empfehlungen zur Therapie von akuten Atemwegsinfektionen (einschließlich HNO-Bereich), abgestimmt mit der Deutschen Gesellschaft für Pneumonologie. 2. ed. Köln: 2002, 28 p.

(11) 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 2000; 122(1):1-7.

(12) Breese BB. A simple scorecard for the tentative diagnosis of streptococcal pharyngitis. Am J Dis Child 1977; 131(5):514-517.

(13) Brickfield FX, Carter WH, Johnson RE. Erythromycin in the treatment of acute bronchitis in a community practice. J Fam Pract 1986; 23(2):119-122.

(14) Bullinger M, von Mackensen S, Kirchberger I. KINDL - ein Fragebogen zur Erfassung der gesundheitsbezogenen Lebensqualität von Kindern. Zeitschrift für Gesundheitspsychologie 1994; 2(1):64-77.

(15) Burke P, Bain J, Robinson D, Dunleavey J. Acute red ear in children: controlled trial of non-antibiotic treatment in general practice. BMJ 1991; 303(6802):558-562.

(16) Büttner G. Die Behandlung der akuten Otitis media ohne Sulfonamide und Antibiotika in einer Allgemeinpraxis. Beiträge zu einer Erweiterung der Heilkunst 1973; 26:125-129.

(17) Cantrell R, Young AF, Martin BC. Antibiotic prescribing in ambulatory care settings for adults with colds, upper respiratory tract infections, and bronchitis. Clin Ther 2002; 24(1):170-182.

(18) Centor RM, Witherspoon JM, Dalton HP, Brody CE, Link K. The diagnosis of strep throat in adults in the emergency room. Med Decis Making 1981; 1(3):239-246.

(19) Cherry DK, Burt CW, Woodwell DA. National Ambulatory Medical Care Survey: 2001 summary. Adv Data 2003;(337):1-44.

(20) Dagnelie CF, Zwart S, Balder FA, Romeijnders ACM, Geijer RMM. NHG Standard 'Acute sore throat'. Dutch College of General Practitioners publishes practice guidelines in English. Last update: 2002. Accessibility verified: 17-1-2004.

(21) De Maeseneer JM, van Driel ML, Green LA, van Weel C. The need for research in primary care. Lancet 2003; 362(9392):1314-1319.

(22) Del Mar CB, Glasziou PP, Spinks AB. Antibiotics for sore throat. Cochrane Database Syst Rev 2000;(4):CD000023.

(23) Dowell SF, Marcy SM, Phillips WR, Gerber MA, Schwartz B. Principles of judicious use of antimicrobial agents for pediatric upper respiratory tract infections. Pediatrics 1998; 101(1):163-165.

(24) Dunlay J, Reinhardt R, Roi LD. A placebo-controlled, double-blind trial of erythromycin in adults with acute bronchitis. J Fam Pract 1987; 25(2):137-141.

(25) el Daher NT, Hijazi SS, Rawashdeh NM, al Khalil IA, Abu-Ektaish FM, Abdel-Latif DI. Immediate vs. delayed treatment of group A beta-hemolytic streptococcal pharyngitis with penicillin V. Pediatr Infect Dis J 1991; 10(2):126-130.

(26) Evans M, Rodger I. Anthroposophical medicine. London: Thorsons; 1992, 192 p.

(27) Evans M, Zimmermann P. Prospektive internationale Outcome-Studie zur Verschreibung anthroposophischer Arzneimittel: ein vorläufiger Bericht. Der Merkurstab 2000; 53(2):92-98.

(28) Fried R. My experiences with acute and chronic middle ear inflammations in children. Journal of Anthroposophic Medicine 1990; 7(1):48-51.

(29) Froom J, Culpepper L, Grob P, Bartelds A, Bowers P, Bridges-Webb C et al. Diagnosis and antibiotic treatment of acute otitis media: report from International Primary Care Network. BMJ 1990; 300(6724):582-586.

(30) Froom J, Culpepper L, Jacobs M. Antimicrobials for acute otitis media? A review from the International Primary Care Network. Br Med J 1997; 315:98-102.

(31) Gandek B, Ware JE, Aaronson NK, Apolone G, Bjorner JB, Brazier JE et al. Cross-validation of item selection and scoring for the SF-12 Health Survey in nine countries: results from the IQOLA Project. International Quality of Life Assessment. J Clin Epidemiol 1998; 51(11):1171-1178.

(32) Glasziou PP, Del Mar CB, Hayem M, Sanders SL. Antibiotics for acute otitis media in children. Cochrane Database Syst Rev 2000;(4):CD000219.

(33) Gonzales R, Bartlett JG, Besser RE, Cooper RJ, Hickner JM, Hoffman JR et al. Principles of appropriate antibiotic use for treatment of acute respiratory tract infections in adults: background, specific aims, and methods. Ann Intern Med 2001; 134(6):479-486.

(34) Gonzales R, Bartlett JG, Besser RE, Cooper RJ, Hickner JM, Hoffman JR et al. Principles of appropriate antibiotic use for treatment of uncomplicated acute bronchitis: background. Ann Intern Med 2001; 134(6):521-529.

(35) Gonzales R, Bartlett JG, Besser RE, Hickner JM, Hoffman JR, Sande MA. Principles of appropriate antibiotic use for treatment of nonspecific upper respiratory tract infections in adults: background. Ann Intern Med 2001; 134(6):490-494.

(36) Gonzales R, Steiner JF, Lum A, Barrett PH, Jr. Decreasing antibiotic use in ambulatory practice: impact of a multidimensional intervention on the treatment of uncomplicated acute bronchitis in adults. JAMA 1999; 281(16):1512-1519.

(37) Gordon M, Lovell S, Dugdale AE. The value of antibiotics in minor respiratory illness in children. A controlled trial. Med J Aust 1974; 1(9):304-306.

(38) Heikkinen T, Jarvinen A. The common cold. Lancet 2003; 361(9351):51-59.

(39) Herne N. Essai comparatif en double aveugle randomisé xibornol, tétracycline et placebo dans le infections saisonnières des voies aériennes superieures. Medicines et maladies infectieuses 1980; 10:185-190.

(40) 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 2001; 37(6):703-710.

(41) Hirschmann JV. Antibiotics for common respiratory tract infections in adults. Arch Intern Med 2002; 162(3):256-264.

(42) Hodges JL, Lehmann EL. Estimates of location based on rank tests. Ann Math Stat 1963; 34:598-611.

(43) Howe RW, Millar MR, Coast J, Whitfield M, Peters TJ, Brookes S. A randomized controlled trial of antibiotics on symptom resolution in patients presenting to their general practitioner with a sore throat. Br J Gen Pract 1997; 47(418):280-284.

(44) Howie JG. Research in general practice: pursuit of knowledge or defence of wisdom? Br Med J (Clin Res Ed) 1984; 289(6460):1770-1772.

(45) Howie VM, Ploussard JH. Efficacy of fixed combination antibiotics versus separate components in otitis media. Effectiveness of erythromycin estrolate, triple sulfonamide, ampicillin, erythromycin estolate- triple sulfonamide, and placebo in 280 patients with acute otitis media under two and one-half years of age. Clin Pediatr (Phila) 1972; 11(4):205-214.

(46) Huchon GJ, Gialdroni-Grassi G, Leophonte P, Manresa F, Schaberg T, Woodhead M. Initial antibiotic therapy for lower respiratory tract infection in the community: a European survey. Eur Respir J 1996; 9(8):1590-1595.

(47) Husemann F. Scharlach und eitrige Angina in zehn Jahren Praxis. Der Merkurstab 1998; 51(1):16-24.

(48) Husemann F, Wolff O. The anthroposophical approach to medicine. Volume 2. London: Rudolf Steiner Press; 1987, 460 p.

(49) Institute for Clinical Systems Improvement. Acute sinusitis in adults. 2002, 30 p.

(50) Kaiser L, Lew D, Hirschel B, Auckenthaler R, Morabia A, Heald A et al. Effects of antibiotic treatment in the subset of common-cold patients who have bacteria in nasopharyngeal secretions. Lancet 1996; 347(9014):1507-1510.

(51) Kaiser L, Morabia A, Stalder H, Ricchetti A, Auckenthaler R, Terrier F et al. Role of nasopharyngeal culture in antibiotic prescription for patients with common cold or acute sinusitis. Eur J Clin Microbiol Infect Dis 2001; 20(7):445-451.

(52) Kaleida PH, Casselbrant ML, Rockette HE, Paradise JL, Bluestone CD, Blatter MM et al. Amoxicillin or myringotomy or both for acute otitis media: results of a randomized clinical trial. Pediatrics 1991; 87(4):466-474.

(53) King DE, Williams WC, Bishop L, Shechter A. Effectiveness of erythromycin in the treatment of acute bronchitis. J Fam Pract 1996; 42(6):601-605.

(54) Krober MS, Bass JW, Michels GN. Streptococcal pharyngitis. Placebo-controlled double-blind evaluation of clinical response to penicillin therapy. JAMA 1985; 253(9):1271-1274.

(55) Kummer K-R. Scharlach und Streptokokkenkrankheiten - Versuch einer Systematik. Der Merkurstab 1999; 52(3):179-183.

(56) Liang MH, Fossel AH, Larson MG. Comparisons of five health status instruments for orthopedic evaluation. Med Care 1990; 28(7):632-642.

(57) Linder JA, Stafford RS. Antibiotic treatment of adults with sore throat by community primary care physicians: a national survey, 1989-1999. JAMA 2001; 286(10):1181-1186.

(58) Little P. Penicillin for acute sore throat in children: randomised, double blind trial. Commentary: More valid criteria may be needed. BMJ 2003; 327(7427):1327-1328.

(59) Little P, Gould C, Moore M, Warner G, Dunleavey J, Williamson I. Predictors of poor outcome and benefits from antibiotics in children with acute otitis media: pragmatic randomised trial. BMJ 2002; 325(7354):22.

(60) Little P, Gould C, Williamson I, Moore M, Warner G, Dunleavey J. Pragmatic randomised controlled trial of two prescribing strategies for childhood acute otitis media. BMJ 2001; 322(7282):336-342.

(61) Little P, Williamson I, Warner G, Gould C, Gantley M, Kinmonth AL. Open randomised trial of prescribing strategies in managing sore throat. Br Med J 1997; 314(7082):722-727.

(62) Lohn B, Schoorel E. Resultaten von pneumonie-behandeling op Anthroposophische grondslag bij kinderen. Integrale Geneeskunde 1993; 3:113-119.

(63) MacFarlane J, Holmes W, Gard P, Macfarlane R, Rose D, Weston V et al. Prospective study of the incidence, aetiology and outcome of adult lower respiratory tract illness in the community. Thorax 2001; 56(2):109-114.

(64) MacFarlane J, Lewis SA, Macfarlane R, Holmes W. Contemporary use of antibiotics in 1089 adults presenting with acute lower respiratory tract illness in general practice in the U.K.: implications for developing management guidelines. Respir Med 1997; 91(7):427-434.

(65) Majeed A, Harris T. Acute otitis media in children. Fewer children should be treated with antibiotics. BMJ 1997; 315(7104):321-322.

(66) McIsaac WJ, White D, Tannenbaum D, Low DE. A clinical score to reduce unnecessary antibiotic use in patients with sore throat. CMAJ 1998; 158(1):75-83.

(67) Metlay JP, Stafford RS, Singer DE. National trends in the use of antibiotics by primary care physicians for adult patients with cough. Arch Intern Med 1998; 158(16):1813-1818.

(68) Meyer U. Anwendungsbeobachtung WALA Plantago-Bronchialbalsam. Der Merkurstab 2003; 56(4):208-209.

(69) Monto AS. Epidemiology of viral respiratory infections. Am J Med 2002; 112 Suppl 6A:4S-12S.

(70) Murray CJ, Lopez AD. Global mortality, disability, and the contribution of risk factors: Global Burden of Disease Study. Lancet 1997; 349(9063):1436-1442.

(71) Mygind N, Meistrup-Larsen KI, Thomsen J, Thomsen VF, Josefsson K, Sorensen H. Penicillin in acute otitis media: a double-blind placebo-controlled trial. Clin Otolaryngol 1981; 6(1):5-13.

(72) Nash DR, Harman J, Wald ER, Kelleher KJ. Antibiotic prescribing by primary care physicians for children with upper respiratory tract infections. Arch Pediatr Adolesc Med 2002; 156(11):1114-1119.

(73) Nelson JD. The effect of penicillin therapy on the symptoms and signs of streptococcal pharyngitis. Pediatr Infect Dis 1984; 3(1):10-13.

(74) Pennie RA. Prospective study of antibiotic prescribing for children. Can Fam Physician 1998; 44:1850-1856.

(75) Petersen K, Phillips RS, Soukup J, Komaroff AL, Aronson M. The effect of erythromycin on resolution of symptoms among adults with pharyngitis not caused by group A streptococcus. J Gen Intern Med 1997; 12(2):95-101.

(76) Porzsolt F, Ohletz A. Kunstfehler und Phantom-Risiken. Dt Ärztebl 1999; 96(41):C-1902.

(77) Preston K. Pneumatic otoscopy: a review of the literature. Issues Compr Pediatr Nurs 1998; 21(2):117-128.

(78) Ravens-Sieberer U, Bullinger M. Assessing health-related quality of life in chronically ill children with the German KINDL: first psychometric and content analytical results. Qual Life Res 1998; 7(5):399-407.

(79) Ravens-Sieberer U, Bullinger M. KINDL® Fragebogen zur Erfassung der gesundheitsbezogenen Lebensqualität bei Kindern und Jugendlichen. Revidierte Form. Manual. 2000, 28 p.

(80) Riley D, Fischer M, Singh B, Haidvogl M, Heger M. Homeopathy and conventional medicine: an outcomes study comparing effectiveness in a primary care setting. J Altern Complement Med 2001; 7(2):149-159.

(81) Ritchie J, Wilkinson J, Gantley M, Feder G, Carter Y, Formby J. A model of integrated primary care: anthroposophic medicine. London: National Centre for Social Research. Department of General Practice and Primary Care, St Bartholomew's and the Royal London School of Medicine and Dentistry, Queen Mary University of London; 2001, 158 p.

(82) Rosenfeld RM, Kay D. Natural history of untreated otitis media. Laryngoscope 2003; 113(10):1645-1657.

(83) Rosenstein N, Phillips WR, Gerber MA, Marcy SM, Schwartz B, Dowell SF. The common cold - principles of judicious use of antimicrobial agents. Pediatrics 1998; 101(1):181-184.

(84) Royal College of Paediatrics and Child Health. Guidelines for good practice: management of acute and recurring sore throat and indications for tonsillectomy. London: Royal College of Paediatrics and Child Health; 2000, 4 p.

(85) Royal College of Paediatrics and Child Health. RCPCH Guideline appraisal: Scottish Intercollegiate Guidelines Network (SIGN) - Evidence-based guidelines for the diagnosis and management of childhood otitis media in primary care. London: Royal College of Paediatrics and Child Health; 2003, 2 p.

(86) Sackett DL. Bias in analytical research. J Chron Dis 1979; 32:51-63.

(87) Schwarz R. Otitis, Tubenkatarrh und Sinusitis in der pädiatrischen Praxis. Der Merkurstab 2002; 55(Sonderheft IV):S30-S39.

(88) Smucny J, Fahey T, Becker L, Glazier R, McIsaac W. Antibiotics for acute bronchitis. Cochrane Database Syst Rev 2000;(4):CD000245.

(89) Snow V, Mottur-Pilson C, Cooper RJ, Hoffman JR. Principles of appropriate antibiotic use for acute pharyngitis in adults. Ann Intern Med 2001; 134(6):506-508.

(90) Snow V, Mottur-Pilson C, Gonzales R. Principles of appropriate antibiotic use for treatment of nonspecific upper respiratory tract infections in adults. Ann Intern Med 2001; 134(6):487-489.

(91) Snow V, Mottur-Pilson C, Hickner JM. Principles of appropriate antibiotic use for acute sinusitis in adults. Ann Intern Med 2001; 134(6):495-497.

(92) Soldner G. Akute und chronische Rhinitis und Sinusitis. In: Medizinisches Seminar Bad Boll, editor. Anthroposophische Medizin in der Praxis, Band 1. Bad Boll: Natur Mensch Medizin Verlags GmbH, 1998: 35-57.

(93) Soldner G, Stellmann HM. Leibliche, seelische und geistige Aspekte in Diagnostik und Beratung. Anthroposophisch-homöopathische Therapie. Stuttgart: Wissenschaftliche Verlagsgesellschaft mbH; 2001, 626 p.

(94) Sommer M. Aus der Praxis der anthroposophischen Medizin. Behandlung der Otitis media ohne Antibiotika. Der Merkurstab 1998; 51(6):373-374.

(95) Steiner R, Wegman I. Extending practical medicine. Fundamental principles based on the science of the spirit. GA 27. Bristol: Rudolf Steiner Press; 2000, 144 p.

(96) Taylor B, Abbott GD, Kerr MM, Fergusson DM. Amoxycillin and co-trimoxazole in presumed viral respiratory infections of childhood: placebo-controlled trial. Br Med J 1977; 2(6086):552-554.

(97) The European Agency for the Evaluation of Medicinal Products CfPMPC. Points to consider on switching between superiority and non-inferiority, CPMP/EWP/482/99. London: 2000, 10 p.

(98) Todd JK, Todd N, Damato J, Todd WA. Bacteriology and treatment of purulent nasopharyngitis: a double blind, placebo-controlled evaluation. Pediatr Infect Dis 1984; 3(3):226-232.

(99) Toedt R. Anwendungsbeobachtung WALA Aconit Ohrentropfen. Der Merkurstab 2001; 54(5):313-314.

(100) Touw-Otten FW, Johansen KS. Diagnosis, antibiotic treatment and outcome of acute tonsillitis: report of a WHO Regional Office for Europe study in 17 European countries. Fam Pract 1992; 9(3):255-262.

(101) Turner RB. Epidemiology, pathogenesis, and treatment of the common cold. Ann Allergy Asthma Immunol 1997; 78(6):531-539.

(102) Van Buchem FL, Knottnerus JA, Schrijnemaekers VJ, Peeters MF. Primary-care-based randomised placebo-controlled trial of antibiotic treatment in acute maxillary sinusitis. Lancet 1997; 349(9053):683-687.

(103) Verheij TJ, Hermans J, Mulder JD. Effects of doxycycline in patients with acute cough and purulent sputum: a double blind placebo controlled trial. Br J Gen Pract 1994; 44(386):400-404.

(104) von Zabern B. Case report: recurrent otitis media. Journal of Anthroposophic Medicine 1995; 12(1):86-88.

(105) Ware J, Jr., Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. Med Care 1996; 34(3):220-233.

(106) Williams JW, Jr., Aguilar C, Cornell J, Chiquette ED, Makela M, Holleman DR et al. Antibiotics for acute maxillary sinusitis. Cochrane Database Syst Rev 2003;(2):CD000243.

(107) Williamson HA, Jr. A randomized, controlled trial of doxycycline in the treatment of acute bronchitis. J Fam Pract 1984; 19(4):481-486.

(108) Wise R, Hart T, Cars O, Streulens M, Helmuth R, Huovinen P et al. Antimicrobial resistance is a major threat to public health. BMJ 1998; 317(7159):609-610.

(109) Zentralinstitut für die kassenärztliche Versorgung. ZI-ADT-Panel Nordrhein, Patienten-/Praxenstichprobe: I/2001. Köln: 2001.

(110) Zwart S, Sachs AP, Ruijs GJ, Gubbels JW, Hoes AW, de Melker RA. Penicillin for acute sore throat: randomised double blind trial of seven days versus three days treatment or placebo in adults. BMJ 2000; 320(7228):150-154.

Appendix: Tables

Participating doctors

Participating doctors* by country				
	Anthroposophy		Conventional	
	N	%	N	%
USA	8	31%	0	0%
Germany	7	27%	3	20%
Austria	3	12%	3	30%
Netherlands	6	23%	2	20%
United Kingdom	2	8%	2	20%
Total	26	100%	10	100%

*Participating doctor: doctor who enrolled at least one patient evaluable for efficacy

Participating doctors: Name, gender, therapy setting, city, country and practice				
Name (Country)	**Gender**	**Therapy setting**	**City**	**Practice***
USA				
Molly McMullen-Laird	Female	Anthroposophy	Ann Arbor, MI	1
Quentin McMullen	Male	Anthroposophy	Ann Arbor, MI	1
Gerald Karnow	Male	Anthroposophy	Spring Valley, NY	2
Paul Scharff	Male	Anthroposophy	Spring Valley, NY	2
Kent Hesse	Male	Anthroposophy	Spring Valley, NY	2
Mark Eisen	Male	Anthroposophy	Chapel Hill, NC	3
Bob Dudney	Male	Anthroposophy	Sebastopol, CA	4
Peter Hinderberger	Male	Anthroposophy	Baltimore, MD	5
Germany				
Sabine Schaefer	Female	Anthroposophy	Kassel	6
Peter Fischer-Wasels	Male	Anthroposophy	Dortmund	7
Heidi Pechmann	Female	Anthroposophy	Dingelstädt	8
Hendrik Voegler	Male	Anthroposophy	Dortmund	9
Tatjana Grah	Female	Anthroposophy	Berlin	10
Erika Richter	Female	Anthroposophy	Marburg	11
Karl-Reinhard Kummer	Male	Anthroposophy	Karlsruhe	12
Michael Bach	Male	Conventional	Stuttgart	13
Eberhard Bock	Male	Conventional	Berlin	14
Lutz Duerrschnabel	Male	Conventional	Bühl	15
Austria				
Elisabeth Krainer	Female	Conventional	Graz	16
Susanne Pruegger	Female	Conventional	Graz	17
Alexander Kozel	Male	Conventional	Graz	18
Reinhard Schwarz	Male	Anthroposophy	Graz	19
Harald Siber	Male	Anthroposophy	Wien	20
Mario Mayrhoffer	Male	Anthroposophy	Klagenfurt	21
Netherlands				
Henri Zomer	Male	Conventional	Tilburg	22
Rob Stok	Male	Conventional	Tilburg	22
Thomas Kelling	Male	Anthroposophy	Amsterdam	23
Arie Bos	Male	Anthroposophy	Amsterdam	23
Marco Ephraim	Male	Anthroposophy	Zoetermeer	24
Peter Staal	Male	Anthroposophy	Tilburg	25
Madeleen Winkler	Female	Anthroposophy	Gouda	26
George Maissan	Male	Anthroposophy	Gouda	26
United Kingdom				
Bernhard Bedford	Male	Conventional	Southampton	27
Andrew Hamilton	Male	Conventional	Southampton	27
Stefan Gaidar	Male	Anthroposophy	Aberdeen	28
Andrew Maendl	Male	Anthroposophy	Bristol	29

*Each individually located medical practice is allocated a number

Participating anthroposophic doctors: number of years in practice		
	Years in medical practice	**Years in anthroposophic medical practice**
N	26	26
Mean	18.00	14.50
SD	8.80	8.51
Minimum	6.00	6.00
Maximum	40.00	40.00
25 percentile	11.75	8.00
50 percentile	15.50	13.50
75 percentile	23.25	18.25

Patient recruitment and follow-up

Overview

Patient recruitment: overview				
	Anthroposophy		**Conventional**	
	N	%	N	%
Screened patients	1731	100.0%	No data	
Included patients	853	49.3%		
Not included patients	878	50.7%	No data	
Included patients	853	100.0%	318	100.0%
Evaluable for efficacy	715	83.8%	301	94.7%
Excluded from analysis	138	16.2%	17	5.3%

Evaluable patients: Availability of baseline and follow-up data

Evaluable patients: Availability of baseline and follow-up data							
	Anthroposophy N=715			Conventional N=301			Fisher's exact test
Day 0 Doctor's documentation	N	%		N	%		
Respondent	715	100.0%		301	100.0%		
Missing	0	0.0%		0	0.0%		
Total	715	100.0%		301	100.0%		
Day 0 Patient questionnaire	N	%		N	%		
Respondent	574	80.3%		264	87.7%		p = 0.0049
Missing	141	19.7%		37	12.3%		
Total	715	100.0%		301	100.0%		
Day 7 Telephone interview with patient	N	%		N	%		
Interviewed*	645	90.2%		265	88.0%		p = 0.3126
Not interviewed	70	9.8%		36	12.0%		
Total	715	100.0%		301	100.0%		
Day 14 Telephone interview with patient	N	%		N	%		
Interviewed*	451	63.1%		207	68.8%		
No interview scheduled (Complete Recovery at Day 7**)	218	30.5%		70	23.3%		
Not interviewed	46	6.4%		24	7.8%		
Total	715	100.0%		301	100.0%		
-Excluding patients without scheduled interviews							
Interviewed*	451	90.7%		207	89.6%		p = 0.6855
Not interviewed	46	9.3%		24	10.4%		
Total	497	100.0%		231	100.0%		
Day 28 Telephone interview with patient	N	%		N	%		
Interviewed*	221	30.9%		134	44.5%		
No interview scheduled (Complete Recovery at Day 7**)	459	64.2%		149	49.5%		
Not interviewed	35	4.9%		18	6.0%		
Total	715	100.0%		301	100.0%		
-Excluding patients without scheduled interviews							
Interviewed*	221	86.3%		134	88.2%		p = 0.6498
Not interviewed	35	13.7%		18	11.8%		
Total	256	100.0%		152	100.0%		
Follow-up period in days (Day 0 – Follow-up)	Mean	SD	N	Mean	SD	N	
Day 7	7.3	1.2	624	7.8	2.4	222	
Day 14	14.2	1.0	440	15.0	3.0	189	
Day 28	28.0	1.9	220	28.8	2.8	132	

* Interviewed = Status of follow-up: agreed to participate

** Patients with Treatment outcome = Complete Recovery at a follow-up were not interviewed at subsequent follow-up days

Missing follow-up interview data on Day 7-21: reasons						
	Anthroposophy N=715		Conventional N=301		Total	
Number of scheduled interviews: Reason for missing data	N	%	N	%	N	%
Refused to participate	1	0.7%	7	10.3%	8	3.7%
Unreachable	79	52.3%	37	54.4%	116	53.0%
Other	71	47.0%	24	35.3%	95	43.4%
Total number of scheduled interviews with missing data	151	100.0%	68	100.0%	219	100.0%

Screened, not enrolled patients

Patient screening data availability in Anthroposophy Group by country and doctor								
Participating doctors	**Screening data available?**		**Enrolled patients**					
			All patients		**Screening data available**		**Screening data not available**	
USA	Yes	No	N	%	N	%	N	%
Quentin McMullen	X		7		7			
Gerald Karnow	X		4		4			
Paul Scharff	X		9		9			
Molly McMullen-Laird	X		7		7			
Mark Eisen	X		3		3			
Bob Dudney	X		6		6			
Peter Hinderberger	X		3		3			
Kent Hesse		X	9				9	
Germany								
Sabine Schaefer		X	3				3	
Peter Fischer-Wasels	X		91		91			
Heidi Pechmann	X		68		68			
Hendrik Voegler	X		59		59			
Tatjana Grah	X		28		28			
Erika Richter	X		41		41			
Karl-Reinhard Kummer	X		72		72			
Austria								
Reinhard Schwarz	X		86		86			
Harald Siber		X	3				3	
Mario Mayrhoffer		X	12				12	
Netherlands								
Thomas Kelling		X	3				3	
Marco Ephraim	X		35		35			
Arie Bos		X	7				7	
Peter Staal	X		39		39			
Madeleen Winkler	X		27		27			
George Maissan	X		41		41			
United Kingdom								
Stefan Gaidar		X	8				8	
Andrew Maendl	X		44		44			
Total	19	7	715	100.0%	679	95.0%	36	5.0%

Patient screening for Anthroposophy group: Reasons for non-inclusion		
Reasons for non-inclusion	N	%
1. Chief complaint > 7 days' duration	226	25.7%
2. Patient too young	42	4.8%
3. No informed consent	111	12.6%
4. Previous participation in this study	7	0.8%
5. Other chief complaint	20	2.3%
6. Language problems	11	1.3%
7. Doctor: lack of time	314	35.8%
8. Practical or technical obstacles	56	6.4%
9. Ongoing therapy for chief complaint	9	1.0%
10. Special diagnoses	26	3.0%
11. Others + not specified	56	6.4%
Total	878	100.0%
Study inclusion criteria fulfilled?	N	%
No: Reason 1-6	417	47.5%
Yes: Reason 7-11	461	52.5%
Total	878	100.0%

Screened patients of Anthroposophy group fulfilling study inclusion criteria: Demographics							
	Not included patients N = 461			**Evaluable patients N=715**			**Fisher's exact test**
Gender (excluding missings)	N	%		N	%		
Male	201	44.5%		333	46.6%		p = 0.5072
Female	251	55.5%		382	53.4%		
Total	452	100.0%		715	100.0%		
Age (years)	Median	l.q.r.		Median	l.q.r.		**Mann-Whitney U-test**
	5.3	2.9-16.0		6.0	3.0-28.0		p = 0.0036
Age groups	N	%		N	%		
< 2 years	80	17.4%		112	15.7%		Median difference evaluable minus not included: 1.13 (95%-CI: 0.38-1.95)
2-5 years	152	33.0%		201	28.1%		
6-11 years	90	19.5%		135	18.9%		
12-17 years	24	5.2%		39	5.5%		
18-34 years	37	8.0%		87	12.2%		
35-64 years	62	13.4%		129	18.0%		
≥ 65 years	5	1.1%		11	1.5%		
Missing	11	2.4%		1	0.1%		
Total	461	100.0%		715	100.0%		
Country	N	%		N	%		
USA	17	3.7%		48	6.7%		p = 0.0266
Germany	353	76.6%		362	50.6%		p < 0.0001
Austria	11	2.4%		101	14.1%		p < 0.0001
Netherlands	80	17.4%		152	21.3%		p = 0.0004
United Kingdom	0	0.0%		52	7.3%		p < 0.0001
Total	461	100.0%		715	100.0%		
Chief Complaint (excluding missings)	N	%		N	%		
Runny nose	18	4.0%		49	6.9%		p = 0.0392
Sore throat	80	17.6%		188	26.3%		p = 0.0006
Ear pain	126	27.7%		143	20.0%		p = 0.0027
Sinus pain	32	7.0%		50	7.0%		p = 1.0000
Cough	199	43.7%		285	39.9%		p = 0.2012
Total	455	100.0%		715	100.0%		
Severity of Chief Complaint (1-4)	Mean	SD	N	Mean	SD	N	**Mann-Whitney U-test**
Severity: 0-4	2.9	0.9	451	2.7	0.8	714	p = 0.0022
j							
	N	%		N	%		
0: Not present	0	0.0%		1	0.1%		Median difference evaluable minus not included: 0.00 (95%-CI: 0.00-0.00)
1: Mild	14	3.0%		35	4.9%		
2: Moderate	160	34.7%		248	34.7%		
3: Severe	150	32.5%		325	45.5%		
4: Very severe	127	27.5%		105	14.7%		
Missing	10	2.2%		1	0.1%		
Total	461	100.0%		715	100.0%		

Screened patients of Anthroposophy group fulfilling study inclusion criteria: Medication prescribed at Day 0					
	Not included patients N = 461		**Included patients N=715**		**Fisher's exact test**
Patients with prescribed medications*	N	%	N	%	
No medication	37	8.0%	0	0.0%	p < 0.0001
Anthroposophic medicines	383	83.1%	715	100.0%	p < 0.0001
Antibacterials for systemic use	13	2.8%	6	0.8%	p = 0.0153
Analgesics	5	1.1%	14	2.0%	p = 0.3442
Cough and cold preparations	31	6.7%	5	0.7%	p < 0.0001
Anti-inflammatory and antirheumatic products	3	0.7%	2	0.3%	p = 0.3860
Antihistamines for systemic use	0	0.0%	0	0.0%	
Nasal preparations	6	1.3%	29	4.1%	p = 0.0075
Homeopathic preparations, not listed above	3	0.7%	96	13.4%	p < 0.0001

*multiple responses possible, sum of percentages > 100.0%

Patient exclusions

Patient recruitment: exclusion after recruitment							
	Anthroposophy			**Conventional**			
Included patients	N	%		N	%		
Excluded from analysis	138	16.2%		17	5.3%		
-Incorrect follow-up interview	98	11.5%		1	0.3%		
-No follow-up data	40	4.7%		16	5.0%		
Evaluable for efficacy	715	83.8%		301	94.7%		
Total	853	100.0%		318	100.0%		
Included patients minus patients with incorrect follow-up interview	N	%		N	%		**Fisher's exact test**
No follow-up data	40	5.3%		16	5.0%		p = 1.0000
Evaluable for efficacy	715	94.7%		301	95.0%		
Total	755	100.0%		317	100.0%		
Patients / caregivers who refused to participate in at least one follow-up telephone interview	Proportion	%		Proportion	%		
No follow-up data	5/40	12.5%		2/16	12.5%		p = 1.0000
Evaluable for efficacy	1/715	0.1%		5/301	1.7%		p = 0.0101
Total	6/755	0.8%		7/317	2.2%		
Excluded patient with adverse events	N			N			
Serious	0			1			
Not serious	1			0			
Total	1			1			
Symptom Score Day 0	Mean	SD	N	Mean	SD	N	
Excluded from analysis	1.0	0.6	138	1.3	0.4	16	
Evaluable for efficacy	1.3	0.7	714	1.2	0.6	295	
-Mann-Whitney-U-test	p < 0.0001			p = 0.4205			

Baseline characteristics

Demographics

Patients by country					
	Anthroposophy N=715		Conventional N=301		Fisher's exact test
Country	N	%	N	%	
USA	48	6.7%	0	0.0%	p < 0.0001
Germany	362	50.6%	100	33.2%	p < 0.0001
Austria	101	14.1%	57	18.9%	p = 0.0581
Netherlands	152	21.3%	104	34.6%	p = 0.0543
United Kingdom	52	7.3%	40	13.3%	p = 0.0038
Total	715	100.0%	301	100.0%	

Patients by country and doctor						
	Anthroposophy N=715		Conventional N=301		Total	
USA: doctors	N	%	N	%	N	%
Quentin McMullen	7	14.6%	0	0.0%	7	14.6%
Gerald Karnow	4	8.3%	0	0.0%	4	8.3%
Paul Scharff	9	18.8%	0	0.0%	9	18.8%
Molly McMullen-Laird	7	14.6%	0	0.0%	7	14.6%
Mark Eisen	3	6.3%	0	0.0%	3	6.3%
Bob Dudney	6	12.5%	0	0.0%	6	12.5%
Peter Hinderberger	3	6.3%	0	0.0%	3	6.3%
Kent Hesse	9	18.8%	0	0.0%	9	18.8%
Total patients USA					48	100.0%
Germany: doctors	N	%	N	%	N	%
Sabine Schaefer	3	0.6%	0	0.0%	3	0.6%
Peter Fischer-Wasels	91	19.7%	0	0.0%	91	19.7%
Heidi Pechmann	68	14.7%	0	0.0%	68	14.7%
Hendrik Voegler	59	12.8%	0	0.0%	59	12.8%
Tatjana Grah	28	6.1%	0	0.0%	28	6.1%
Erika Richter	41	8.9%	0	0.0%	41	8.9%
Karl-Reinhard Kummer	72	15.6%	0	0.0%	72	15.6%
Michael Bach	0	0.0%	29	6.3%	29	6.3%
Eberhard Bock	0	0.0%	14	3.0%	14	3.0%
Lutz Duerrschnabel	0	0.0%	57	12.3%	57	12.3%
Total patients Germany					462	100.0%
Austria: doctors	N	%	N	%	N	%
Elisabeth Krainer	0	0.0%	2	1.3%	2	1.3%
Susanne Pruegger	0	0.0%	34	21.5%	34	21.5%
Alexander Kozel	0	0.0%	21	13.3%	21	13.3%
Reinhard Schwarz	86	54.4%	0	0.0%	86	54.4%
Harald Siber	3	1.9%	0	0.0%	3	1.9%
Mario Mayrhoffer	12	7.6%	0	0.0%	12	7.6%
Total patients Austria					158	100.0%
Netherlands: doctors	N	%	N	%	N	%
Henri Zomer	0	0.0%	86	33.6%	86	33.6%
Rob Stok	0	0.0%	18	7.0%	18	7.0%
Thomas Kelling	3	1.2%	0	0.0%	3	1.2%
Marco Ephraim	35	13.7%	0	0.0%	35	13.7%
Arie Bos	7	2.7%	0	0.0%	7	2.7%
Peter Staal	39	15.2%	0	0.0%	39	15.2%
Madeleen Winkler	27	10.5%	0	0.0%	27	10.5%
George Maissan	41	16.0%	0	0.0%	41	16.0%
Total patients Netherlands					256	100.0%
United Kingdom: doctors	N	%	N	%	N	%
Bernhard Bedford	0	0.0%	10	10.9%	10	10.9%
Andrew Hamilton	0	0.0%	30	32.6%	30	32.6%
Stefan Gaidar	8	8.7%	0	0.0%	8	8.7%
Andrew Maendl	44	47.8%	0	0.0%	44	47.8%
Total patients UK					92	100.0%

Number of patients per doctor		
	Anthroposophy N=715 patients	**Conventional N=301 patients**
Mean	27.5	30.1
SD	27.9	24.8
Median	10.5	25.0
25-Percentile	6.3	15.0
75-Percentile	41.0	33.0
Minimum	3.0	2.0
Maximum	91.0	86.0

Country according to patient's chief complaint						
Chief complaint	**Country**	**Anthroposophy N=715**		**Conventional N=301**		
		N	%	N	%	**Fisher's exact test**
Runny nose	USA	6	12.2%	0	0.0%	p = 0.3228
	Germany	32	65.3%	5	31.3%	p = 0.0220
	Austria	3	6.1%	5	31.3%	p = 0.0179
	Netherlands	6	12.2%	6	37.5%	p = 0.0569
	United Kingdom	2	4.1%	0	0.0%	p = 1.0000
	Total	49	100.0%	16	100.0%	
Sore throat	USA	18	9.6%	0	0.0%	p = 0.0044
	Germany	96	51.1%	11	15.7%	p < 0.0001
	Austria	16	8.5%	23	32.9%	p < 0.0001
	Netherlands	44	23.4%	25	35.7%	p = 0.0576
	United Kingdom	14	7.4%	11	15.7%	p = 0.0581
	Total	188	100.0%	70	100.0%	
Ear pain	USA	8	5.6%	0	0.0%	p = 0.1082
	Germany	69	48.3%	8	14.0%	p < 0.0001
	Austria	37	25.9%	1	1.8%	p < 0.0001
	Netherlands	20	14.0%	34	59.6%	p < 0.0001
	United Kingdom	9	6.3%	14	24.6%	p = 0.0008
	Total	143	10.0%	57	100.0%	
Sinus pain	USA	2	4.0%	0	0.0%	p = 0.2201
	Germany	18	36.0%	45	80.4%	p < 0.0001
	Austria	4	8.0%	4	7.1%	p = 1.0000
	Netherlands	26	52.0%	5	8.9%	p < 0.0001
	United Kingdom	0	0%	2	3.6%	p = 0.4969
	Total	50	100.0%	56	100.0%	
Cough	USA	14	4.9%	0	0.0%	p = 0.0255
	Germany	147	51.6%	31	30.4%	p = 0.0003
	Austria	41	14.4%	24	23.5%	p = 0.0442
	Netherlands	56	19.6%	34	33.3%	p = 0.0063
	United Kingdom	27	9.5%	13	12.7%	p = 0.3483
	Total	285	100.0%	102	100.0%	

Gender, age, race/ethnicity					
	Anthroposophy N=715		**Conventional N=301**		**Fisher's exact test**
Gender	N	%	N	%	
Male	333	46.6%	121	40.2%	p = 0.0626
Female	382	53.4%	180	59.8%	
Total	715	100.0%	301	100.0%	
					Mann-Whitney U-test
Age					
Mean	15.7		29.9		
SD	17.9		20.5		
25-percentile	3.0		10.0		p < 0.0001
Median	6.0		32.0		
75-percentile	28.0		42.0		
Age groups	N	%	N	%	
< 2 years	112	15.7%	17	5.6%	
2-5 years	201	28.1%	39	13.0%	
6-11 years	135	18.9%	26	8.6%	
12-17 years	39	5.5%	11	3.7%	
18-34 years	87	12.2%	81	26.9%	
35-64 years	129	18.0%	111	36.9%	
≥ 65 years	11	1.5%	16	5.3%	
Missing	1	0.1%	0	0.0%	
Total	715	100.0%	301	100.0%	
Race/Ethnicity	N	%	N	%	
White	554	77.5%	258	85.7%	
Other or mixed	20	2.8%	2	0.7%	
Missing	141	19.7%	41	13.6%	
Total	715	100.0%	301	100.0%	
-excluding missings	N	%	N	%	**Fisher's exact test**
White	554	96.5%	258	99.2%	p = 0.0200
Other or mixed	20	3.5%	2	0.8%	
Sum respondents	574	100.0%	260	100.0%	

Age groups according to patient's chief complaint					
Chief complaint	**Age group**	**Anthroposophy N=715**		**Conventional N=301**	
		N	%	N	%
Runny nose	< 2 years	23	46.9%	0	0%
	2 – 5 years	5	10.2%	0	0%
	6 – 11 years	4	8.2%	2	12.5%
	12 – 17 years	2	4.1%	1	6.3%
	18 – 34 years	4	8.2%	7	43.8%
	35 – 64 years	9	18.4%	5	31.3%
	≥ 65 years	2	4.1%	1	6.3%
	Total	49	100.0%	16	100.0%
Sore throat	< 2 years	11	5.9%	3	4.3%
	2 – 5 years	32	17.0%	6	8.6%
	6 – 11 years	39	20.7%	2	2.9%
	12 – 17 years	16	8.5%	3	4.3%
	18 – 34 years	41	21.8%	28	40.0%
	35 – 64 years	47	25.0%	26	37.1%
	≥ 65 years	2	1.1%	2	2.9%
	Total	188	10.0%	70	100.0%
Ear pain	< 2 years	20	14.0%	4	7.0%
	2 – 5 years	76	53.1%	18	31.6%
	6 – 11 years	28	19.6%	12	21.1%
	12 – 17 years	6	4.2%	3	5.3%
	18 – 34 years	7	4.9%	10	17.5%
	35 – 64 years	5	3.5%	10	17.5%
	≥ 65 years	1	0.7%	0	0%
	Total	143	100.0%	57	100.0%
Sinus pain	< 2 years	1	2.0%	0	0%
	2 – 5 years		%	2	3.6%
	6 – 11 years	6	12.0%	1	1.8%
	12 – 17 years	4	8.0%	1	1.8%
	18 – 34 years	12	24.0%	16	28.6%
	35 – 64 years	27	54.0%	35	62.5%
	≥ 65 years	0	0.0%	1	1.8%
	Total	50	100.0%	56	100.0%
Cough	< 2 years	58	20.4%	10	9.8%
	2 – 5 years	88	30.9%	13	12.7%
	6 – 11 years	58	20.4%	9	8.8%
	12 – 17 years	11	3.9%	3	2.9%
	18 – 34 years	23	8.1%	20	19.6%
	35 – 64 years	41	14.4%	35	34.3%
	≥ 65 years	6	2.1%	12	11.8%
	Total	285	100.0%	102	100.0%

Baseline characteristics: Body mass index, smoking, household size							
	Anthroposophy N=715			**Conventional N=301**			
Body mass index	Mean	SD	N	Mean	SD	N	
Patients aged < 18 years	16.2	2.7	336	16.5	3.1	65	
Patients aged ≥ 18 years	24.1	4.4	163	24.6	4.1	170	
Smoking	N	%		N	%		
Yes	42	5.9%		41	13.6%		
No	531	74.3%		220	73.1%		
Missing	142	19.9%		40	13.3%		
Total	715	100.0%		301	100.0%		
-excluding missings	N	%		N	%		**Fisher's exact test**
Yes	42	7.3%		41	15.7%		p = 0.0122
No	531	92.7%		220	84.3%		
Sum respondents	573	100.0%		261	100.0%		
Total number of persons in household	Mean	SD	N	Mean	SD	N	
	3.6	1.7	557	3.4	1.3	260	

Payment source, willingness to pay for treatment, household income, freedom to choose doctor					
	Anthroposophy N=715		**Conventional N=301**		**Mann-Whitney U-test**
Payment source	N	%	N	%	
Self-pay	113	15.8%	2	0.7%	
Third party	87	12.2%	63	20.9%	
Government	336	47.0%	184	61.1%	
Combinations and other source	26	3.6%	9	3.0%	
Missing	153	21.4%	43	14.3%	
Total	715	100.0%	301	100.0%	
-excluding missings	N	%	N	%	
Self-pay	113	20.1%	2	0.8%	
Third party	87	15.5%	63	24.4%	
Government	336	59.8%	184	71.3%	p = 0.0002
Combinations and other source	26	4.6%	9	3.5%	
Total	562	100.0%	258	100.0%	
Patient willingness to pay for the treatment he/she will receive	N	%	N	%	
Willing to pay the entire costs	168	23.5%	32	10.6%	
Willing to pay some of the costs	299	41.8%	157	52.2%	
Not willing to pay any portion of costs	78	10.9%	68	22.6%	
Missing	170	23.8%	44	14.6%	
Total	715	100.0%	301	100.0%	
-excluding missings					**Fisher's exact test**
Willing to pay the entire costs	168	30.8%	32	12.5%	
Willing to pay some of the costs / Not willing to pay any portion of costs	377	69.2%%	225	87.5%	p < 0.0001
Total	545	100.0%	257	100.0%	
Total annual household income (excluding missings)	N	%	N	%	**Mann-Whitney U-test**
< 15.000 €	75	21.5%	31	20.7%	
15.000-29.999 €	95	27.2%	42	28.0%	
30.000-44.999 €	88	25.2%	45	30.0%	p = 0.5856
45.000-59.999 €	47	13.5%	22	14.7%	
60.000-74.999 €	28	8.0%	7	4.7%	
≥ 75.000 €	16	4.6%	3	2.0%	
Sum respondents	349	100.0%	150	100.0%	
Did you have freedom to choose this doctor?	N	%	N	%	**Fisher's exact test**
Yes	525	73.4%	203	67.4%	
No or other response	48	6.7%	57	18.9%	
Missing	142	19.9%	41	13.6%	
Total	715	100.0%	301	100.0%	
-excluding missings	N	%	N	%	
Yes	525	91.6%	203	78.1%	p < 0.0001
No or other response	48	8.4%	57	21.9%	
Total	573	100.0%	260	100.0%	

Chief complaint

Chief complaint: name, duration, previous episode					
	Anthroposophy N=715		**Conventional N=301**		**Fisher's exact test**
Chief Complaint	N	%	N	%	
Runny nose	49	6.9%	16	5.3%	p = 0.4020
Sore throat	188	26.3%	70	23.3%	p = 0.3436
Ear pain	143	20.0%	57	18.9%	p = 0.7302
Sinus pain	50	7.0%	56	18.6%	p < 0.0001
Cough	285	39.9%	102	33.9%	p = 0.0772
Total	715	100.0%	301	100.0%	
Duration of chief complaint	N	%	N	%	**Mann-Whitney U-test**
0- ≤24h	192	26.9%	33	11.0%	
>24h - ≤48h	167	23.4%	93	30.9%	
>2 days - ≤ 3 days	134	18.7%	85	28.2%	
>3 days - ≤ 5 days	153	21.4%	62	20.6%	p = 0.0043
> 5 days - ≤7 days	68	9.5%	28	9.3%	
Missing	1	0.1%	0	0.0%	
Total	715	100.0%	301	100.0%	
Chief complaint episode within last 12 months?	N	%	N	%	**Fisher's exact test**
Yes	376	52.6%	111	36.9%	p < 0.0001
No	338	47.3%	189	62.8%	
Missing	1	0.1%	1	0.3%	
Total	715	100.0%	301	100.0%	
How often has this complaint recurred within the past 12 month?	N	%	N	%	
No recurrence	338	47.3%	189	62.8%	
1-2 times	227	31.7%	78	25.9%	
3-4 times	114	15.9%	22	7.3%	
5-6 times	22	3.1%	6	2.0%	
> 6 times	13	1.8%	3	1.0%	
Missing	1	0.1%	3	1.0%	
Total	715	100.0%	301	100.0%	

Diagnosis of chief complaint					
	Anthroposophy N=715		Conventional N=301		Fisher's exact test
Diagnosis of chief complaint*	N	%	N	%	
Pharyngitis or tonsillitis	185	25.9%	60	19.9%	p = 0.0449
Bronchitis	138	19.3%	42	14.0%	p = 0.0475
Otitis media	123	17.2%	39	13.0%	p = 0.1103
Laryngotracheitis	108	15.1%	43	14.3%	p = 0.7727
Tonsillitis	81	11.3%	12	4.0%	p = 0.0001
Rhinitis or common cold	81	11.3%	32	10.6%	p < 0.8272
Sinusitis	53	7.4%	59	19.6%	p < 0.0001
Acute URI unspecified	22	3.1%	16	5.3%	p = 0.1025
Eustachian tube disease	11	1.5%	8	2.7%	p = 0.3086
Viral infection unspecified	11	1.5%	0	0.0%	p = 0.0401
Other	11	1.5%	5	0.7%	p = 1.0000
Asthma, obstructive bronchitis	8	1.1%	2	0.7%	p = 0.7319
Pneumonia	6	0.8%	0	0.0%	p = 0.1877
Tympanic membrane disease	6	0.8%	0	0.0%	p = 0.1877
Otitis externa	5	0.7%	6	2.0%	p = 0.0935
Scarlet fever	5	0,7%	0	0.0%	p = 0.3295
Cough	3	0.4%	0	0.0%	p = 0.5591
Influenza	3	0.4%	1	0.3%	p = 1.0000
Allergy	0	0.0%	3	1.0%	p = 0.0258
Total*	781	109.2%*	316	104.0%*	

* Multiple responses possible, sum of percentages > 100.0%

Confidence in diagnosis of chief complaint							
	Anthroposophy N=715			Conventional N=301			
Confidence in diagnosis	N	%		N	%		
No remark	1	0.1%		1	0.3%		
0 (= none)	0	0.0%		0	0.0%		
1	0	0.0%		0	0.0%		
2	0	0.0%		0	0.0%		
3	0	0.0%		0	0.0%		
4	0	0.0%		3	1.0%		
5	5	0.7%		3	1.0%		
6	10	1.4%		1	0.3%		
7	41	5.7%		29	9.6%		
8	132	18.5%		48	15.9%		
9	187	26.2%		67	22.3%		
10 (= total)	339	47.4%		149	49.5%		
Total	715	100.0%		301	100.0%		
Confidence in diagnosis (0-10)	Mean	SD	N	Mean	SD	N	**Mann-Whitney U-test**
Mean / SD	9.1	1.1	714	9.0	1.2	300	p = 0.9586
Reason for confidence	N	%		N	%		**Fisher's exact test**
Clinical symptoms	53	7.4%		53	17.6%		p < 0.0001
Clinical symptoms and/or nose check / tonsil check / ear check / other	661	92.4%		247	82.1%		
No remark	1	0.1%		1	0.3%		
Total	715	100.0%		301	100.0%		

Baseline severity of chief complaint							
	Anthroposophy N=715			**Conventional N=301**			**Fisher's exact test**
Severity of Chief Complaint	N	%		N	%		
0: Not present	1	0.1%		1	0.3%		
1: Mild	35	4.9%		16	5.3%		
2: Moderate	248	34.7%		122	40.5%		
3: Severe	325	45.5%		143	47.5%		
4: Very severe	105	14.7%		18	6.0%		
Missing	1	0.1%		1	0.3%		
Total	715	100.0%		301	100.0%		
-excluding missings							
Not present, mild or moderate	284	39.8%		139	46.3%		p = 0.0596
Severe or very severe	430	60.2%		161	53.7%		
Total	714	100.0%		300	100.0%		
	Mean	SD	N	Mean	SD	N	**Mann-Whitney U-test**
Severity of Chief Complaint (0-4)							
Runny nose	2.6	0.7	49	2.5	0.6	16	p = 0.8208
Sore throat	2.6	0.8	188	2.6	0.7	69	p = 0.6545
Ear pain	2.9	0.8	143	2.3	0.8	57	p < 0.0001
Sinus pain	2.6	0.8	50	2.7	0.7	2.5	p = 0.5774
Cough	2.7	0.7	284	2.5	0.7	102	p = 0.0339
All patients	2.7	0.8	714	2.5	0.7	300	p = 0.0031
	Hodges-Lehmann estimate						
Severity of Chief Complaint (0-4)	Median diff.: Anthr. minus Convent.	95%-CI					
		Lower	upper				
Runny nose	0.00	0.00	0.00				
Sore throat	0.00	0.00	0.00				
Ear pain	1.00	0.00	1.00				
Sinus pain	0.00	0.00	0.00				
Cough	0.00	0.00	0.00				
All patients	0.00	0.00	0.00				

Chief complaint runny nose: duration, diagnosis, previous episodes					
	Anthroposophy N=49		**Conventional N=16**		**Fisher's exact test**
Duration of chief complaint	N	%	N	%	
0- ≤24h	11	22.4%	2	12.5%	
>24h - ≤48h	19	38.8%	6	37.5%	
>2 days - ≤ 3 days	9	18.4%	3	18.8%	
>3 days - ≤ 5 days	5	10.2%	3	18.8%	
> 5 days - ≤7 days	5	10.2%	2	12.5%	
Total	49	100.0%	16	100.0%	
Diagnosis of chief complaint	N	%	N	%	
Rhinitis	44	89.8%	10	62.5%	p = 0.0200
Allergy	0	0.0%	1	6.3%	
Other	5	10.2%	5	31.3%	
Total	49	100.0%	16	100.0%	
Reason for the value for confidence in diagnosis					
Clinical symptoms alone	12	24.5%	7	43.8%	p = 0.2051
Nose check	37	75.5%	9	56.3%	
Total	49	100.0%	16	100.0%	
Chief complaint episode within last 12 months?	N	%	N	%	
Yes	32	65.3%	4	25.0%	p = 0.0082
No	17	34.7%	12	75.0%	
Total	49	100.0%	16	100.0%	
How often has this complaint recurred within the past 12 month?					
No recurrence	17	34.7%	12	75.0%	
1-2 times	20	40.8%	3	18.8%	
3-4 times	11	22.4%	1	6.3%	
5-6 times	0	0.0%	0	0.0%	
> 6 times	1	2.0%	0	0.0%	
Total	49	100.0%	16	100.0%	

Chief complaint Sore throat: duration, diagnosis, previous episodes					
	Anthroposophy N=188		**Conventional N=70**		**Fisher's exact test**
Duration of chief complaint	N	%	N	%	
0- ≤24h	45	23.9%	10	14.3%	
>24h - ≤48h	38	20.2%	23	32.9%	
>2 days - ≤ 3 days	47	25.0%	18	25.7%	
>3 days - ≤ 5 days	48	25.5%	11	15.7%	
>5 days - ≤7 days	10	5.3%	8	11.4%	
Total	188	100.0%	70	100.0%	
Diagnosis of chief complaint	N	%	N	%	
Pharyngitis	84	44.7%	46	65.7%	p = 0.0032
Tonsillitis	69	36.7%	12	17.1%	p = 0.0025
Other	35	18.6%	11	15.7%	
No remark	0	0.0%	1	1.4%	
Total	188	100.0%	70	100.0%	
Reason for the value for confidence in diagnosis	N	%	N	%	
Clinical symptoms alone	12	6.4%	22	31.4%	
Throat check	174	92.6%	46	65.7%	
Other	2	1.1%	1	1.4%	
Missing	0	0.0%	1	1.4%	
Total	188	100.0%	70	100.0%	
-excluding missings					
Clinical symptoms alone	12	6.4%	22	31.9%	p < 0.0001
Throat check or other	176	93.6%	47	68.1%	
Total	188	100.0%	69	100.0%	
Chief complaint episode within last 12 months?	N	%	N	%	
Yes	78	41.5%	18	25.7%	
No	110	58.5%	51	72.9%	
Missing	0	0.0%	1	1.4%	
Total	188	100.0%	70	100.0%	
-excluding missings					
Yes	78	41.5%	18	26.1%	p = 0.0288
No	110	58.5%	51	73.9%	
Total	188	100.0%	69	100.0%	
How often has this complaint recurred within the past 12 month?	N	%	N	%	
No recurrence	110	58.5%	51	73.9%	
1-2 times	52	27.7%	13	18.6%	
3-4 times	20	10.6%	4	5.7%	
5-6 times	4	2.1%	0	0.0%	
> 6 times	2	1.1%	0	0.0%	
Missing	0	0.0%	1	1.4%	
Total	188	100.0%	70	100.0%	

Chief complaint ear pain: duration, diagnosis, previous episodes					
	Anthroposophy N=143		**Conventional N=57**		**Fisher's exact test**
Duration of chief complaint	N	%	N	%	
0- ≤24h	80	55.9%	12	21.1%	
>24h - ≤48h	40	28.0%	19	33.3%	
>2 days - ≤ 3 days	12	8.4%	10	17.5%	
>3 days - ≤ 5 days	4	2.8%	12	21.1%	
>5 days - ≤7 days	7	4.9%	4	7.0%	
Total	143	100.0%	57	100.0%	
Diagnosis of chief complaint	N	%	N	%	
Otitis media	123	86.0%	39	68.4%	p = 0.0085
Otitis externa	5	3.5%	6	10.5%	
Other	15	10.5%	12	26.7%	
Total	143	100.0%	57	100.0%	
Reason for the value for confidence in diagnosis	N	%	N	%	
Clinical symptoms alone	1	0.7%	2	3.5%	p = 0.1960
Ear check	142	99.3%	55	96.5%	
Total	143	100.0%	57	100.0%	
Chief complaint episode within last 12 months?	N	%	N	%	
Yes	77	53.8%	22	38.6%	p = 0.0606
No	66	46.2%	35	61.4%	
Total	143	100.0%	57	100.0%	
How often has this complaint recurred within the past 12 month?	N	%	N	%	
No recurrence	66	46.2%	35	61.4%	
1-2 times	44	30.8%	15	26.3%	
3-4 times (>3 = recurrent OM)	26	18.2%	4	7.0%	
5-6 times	7	4.9%	2	3.5%	
> 6 times	0	0.0%	0	0.0%	
Total	143	100.0%	57	100.0%	

Chief complaint sinus pain: duration, diagnosis, previous episodes					
	Anthroposophy N=50		Conventional N=56		Fisher's exact test
Duration of chief complaint	N	%	N	%	
0- ≤24h	5	10.0%	1	1.8%	
>24h - ≤48h	4	8.0%	18	32.1%	
>2 days - ≤ 3 days	14	28.0%	24	42.9%	
>3 days - ≤ 5 days	22	44.0%	7	12.5%	
> 5 days - ≤7 days	5	10.0%	6	10.7%	
Total	50	100.0%	56	100.0%	
Diagnosis of chief complaint	N	%	N	%	
Sinusitis	48	96.0%	33	58.9%	p < 0.0001
Allergy	0	0.0%	1	1.8%	
Other	2	4.0%	22	39.3%	
Total	50	100.0%	56	100.0%	
Reason for the value for confidence in diagnosis	N	%	N	%	
Clinical symptoms alone	14	28.0%	12	21.4%	p = 0.5008
Nose check	31	62.0%	43	76.8%	
Other	5	10.0%	1	1.8%	
Total	50	100.0%	56	100.0%	
Chief complaint episode within last 12 months?	N	%	N	%	
Yes	18	36.0%	29	51.8%	p = 0.1199
No	32	64.0%	27	48.2%	
Total	50	100.0%	56	100.0%	
How often has this complaint recurred within the past 12 month?	N	%	N	%	
No recurrence	32	64.0%	27	48.2%	
1-2 times	13	26.0%	22	39.3%	
3-4 times	5	10.0%	5	8.9%	
5-6 times	0	0.0%	1	1.8%	
> 6 times	0	0.0%	0	0.0%	
Missing	0	0.0%	1	1.8%	
Total	50	100.0%	56	100.0%	

Chief complaint cough: duration, diagnosis, previous episodes					
	Anthroposophy N=285		**Conventional N=102**		**Fisher's exact test**
Duration of chief complaint	N	%	N	%	
0- ≤24h	51	17.9%	8	7.8%	
>24h - ≤48h	66	23.2%	27	26.5%	
>2 days - ≤ 3 days	52	18.2%	30	29.4%	
>3 days - ≤ 5 days	74	26.0%	29	28.4%	
> 5 days - ≤7 days	41	14.4%	8	7.8%	
Missing	1	0.4%	0	0.0%	
Total	285	100.0%	102	100.0%	
Diagnosis of chief complaint	N	%	N	%	
Bronchitis	128	44.9%	35	34.3%	p = 0.0794
Laryngotracheitis	60	21.1%	40	39.2%	p = 0.0006
Other	96	33.7%	27	26.5%	
No remark	1	0.4%	0	0.0%	
Total	285	100.0%	102	100.0%	
Reason for the value for confidence in diagnosis	N	%	N	%	
Clinical symptoms alone	14	4.9%	10	9.8%	p = 0.0941
Lung check	269	94.4%	92	90.2%	
Other	1	0.4%	0	0.0%	
Missing	1	0.4%	0	0.0%	
Total	285	100.0%	102	100.0%	
Chief complaint episode within last 12 months?	N	%	N	%	
Yes	171	60.0%	38	37.3%	
No	113	39.6%	64	62.7%	
Missing	1	0.4%	0	0.0%	
Total	285	100.0%	102	100.0%	
-excluding missings	N	%	N	%	
Yes	171	60.2%	38	37.3%	p = 0.0001
No	113	39.8%	64	62.7%	
Total	284	100.0%	102	100.0%	
How often has this complaint recurred within the past 12 month?	N	%	N	%	
No recurrence	113	39.6%	64	62.7%	
1-2 times	98	34.4%	25	24.5%	
3-4 times	52	18.2%	8	7.8%	
5-6 times	11	3.9%	3	2.9%	
> 6 times	10	3.5%	2	2.0%	
Missing	1	0.4%	0	0.0%	
Total	285	100.0%	102	100.0%	

Complaint-related symptoms, quality of life, concomitant medical problems

Complaint-related symptoms: Chief complaint runny nose					
	Anthroposophy N=49		Conventional N=16		
Patients with complaint-related symptoms present	N	%	N	%	**Fisher's exact test**
Runny nose	49	100.0%	16	100.0%	
Sneezing	23	46.9%	15	93.8%	p = 0.0010
Itchy nose	13	26.5%	12	75.0%	p = 0.0009
Nasal congestion	44	89.8%	15	93.8%	p = 1.0000
Loss of smell	17	34.7%	12	75.0%	p = 0.0082
Post-nasal drip	40	81.6%	11	68.8%	p = 0.3057
Itchy eyes	3	6.1%	8	50.0%	p = 0.0003
Red/watery eyes	10	20.4%	7	43.8%	p = 0.0998
Patients with complaint-related symptoms severe or very severe	N	%	N	%	
Runny nose	27	55.1%	9	56.3%	p = 1.0000
Sneezing	3	6.1%	1	6.3%	p = 1.0000
Itchy nose	1	2.0%	0	0.0%	p = 1.0000
Nasal congestion	16	32.7%	9	56.3%	p = 0.1386
Loss of smell	5	10.2%	5	31.3%	p = 0.1032
Post-nasal drip	13	26.5%	3	18.8%	p = 0.7409
Itchy eyes	0	0.0%	2	12.5%	p = 0.0577
Red/watery eyes	0	0.0%	0	0.0%	

Complaint-related symptoms: Chief complaint sore throat					
	Anthroposophy N=188		Conventional N=70		
Patients with complaint-related symptoms present	N	%	N	%	**Fisher's exact test**
Sore throat	187	99.5%	69	98.6%	p = 0.4698
Difficulty swallowing	176	93.6%	63	90.0%	p = 0.4203
Lump in throat	119	63.3%	46	65.7%	p = 0.7717
Swollen glands	123	65.4%	41	58.6%	p = 0.3128
Fever (≥ 99.5°F or ≥ 37.5°C)	94	50.0%	31	44.3%	p = 0.4840
Cough	33	17.6%	15	21.4%	
Patients with complaint-related symptom severity: severe or very severe	Proportion of patients	%	Proportion of patients	%	
Sore throat	101/188	53.7%	39/68	57.4%	p = 0.6705
Difficulty swallowing	53/188	28.2%	21/68	30.9%	p = 0.7551
Lump in throat	36/188	19.1%	6/68	8.8%	p = 0.0562
Swollen glands	37/188	19.7%	4/68	5.9%	p = 0.0067
Fever ≥103.1°F / 39.5°C	13/188	6.9%	2/68	2.9%	p = 0.3668

Complaint-related symptoms: Chief complaint ear pain					
	Anthroposophy N=143		Conventional N=57		
Patients with complaint-related symptoms present	N	%	N	%	**Fisher's exact test**
Ear pain	143	100.0%	57	100.0%	
Feeling of 'plugged ear'	83	58.0%	28	49.1%	p = 0.2728
Discharge from air	38	26.6%	10	17.5%	p = 0.2027
Hearing loss	82	57.3%	25	43.9%	p = 0.1159
Fever (≥ 99.5°F or ≥ 37.5°C)	78	54.5%	20	35.1%	p = 0.0184
Patients with complaint-related symptom severity: severe or very severe	N	%	N	%	
Ear pain	99	69.2%	25	43.9%	p = 0.0012
Feeling of 'plugged ear'	45	31.5%	5	8.8%	p = 0.0005
Discharge from air	3	2.1%	6	10.5%	p = 0.0172
Hearing loss	35	24.4%	5	8.8%	p = 0.0112
Fever ≥ 103.1°F / 39.5°C	11	7.7%	2	3.5%	p = 0.3566

Complaint-related symptoms: Chief complaint sinus pain					
	Anthroposophy N=50		Conventional N=56		
Patients with complaint-related symptoms present	N	%	N	%	**Fisher's exact test**
Sinus pain	50	100.0%	56	100.0%	
Headache	47	94.0%	53	94.6%	p = 1.0000
Post-nasal drip	39	78.0%	28	50.0%	p = 0.0045
Purulent discharge	32	64.0%	19	33.9%	p = 0.0033
Fever (≥ 99.5°F or ≥ 37.5°C)	19	38.0%	7	12.5%	p = 0.0031
Patients with complaint-related symptom severity: severe or very severe	N	%	N	%	
Sinus pain	27	54.0%	36	64.3%	p = 0.3249
Headache	21	42.0%	9	16.1%	p = 0.0046
Post-nasal drip	8	16.0%	8	14.3%	p = 1.0000
Purulent discharge	8	16.0%	1	1.8%	p = 0.0122
Fever ≥ 103.1°F / 39.5°C	1	2.0%	1	1.8%	p = 1.0000

Complaint-related symptoms: Chief complaint cough					
	Anthroposophy N=285		Conventional N=102		
Complaint-related symptoms present	N	%	N	%	**Fisher's exact test**
Cough	284	99.6%	101	99.0%	p = 0.4582
Expiratory wheezing	104	36.5%	38	37.3%	p = 0.9051
Sputum expectoration	139	48.8%	61	59.8%	p = 0.0648
Pain with coughing/breathing	154	54.0%	60	58.8%	p = 0.4190
Shortness of breath	83	29.1%	33	32.4%	p = 0.5322
Fever (≥ 99.5°F or ≥ 37.5°C)	129	45.3%	40	39.2%	p = 0.2981
Patients with complaint-related symptom severity: severe or very severe	N	%	N	%	
Cough	176	61.8%	54	52.9%	p = 0.1278
Expiratory wheezing	19	6.7%	2	2.0%	p = 0.0786
Sputum expectoration	18	6.3%	9	8.8%	p = 0.3743
Pain with coughing/breathing	36	12.6%	13	12.7%	p = 1.0000
Shortness of breath	13	4.6%	5	4.9%	p = 1.0000
Fever ≥ 103.1°F / 39.5°C	6	2.1%	3	2.9%	p = 0.7034

Complaint-related symptoms: Chief complaint sore throat, ear pain, sinus pain, or cough					
	Anthroposophy N=666		Conventional N=283		Fisher's exact test
	N	%	N	%	
Patients with complaint-related symptom sore throat / ear pain / sinus pain / pain with coughing/breathing – severity: severe or very severe	238	35.8%	113	39.9%	p = 0.2397
Patients with fever ≥ 99.5°F or ≥ 37.5°C	148	22.2%	47	16.6%	p = 0.0535
Patients with fever ≥ 103.1°F / 39.5°C	31	4.7%	8	2.8%	p = 0.2158

Quality of life, Symptom Score at baseline							
	Anthroposophy N=715			Conventional N=301			
Age groups for quality of life documentation	N	%		N	%		
SF-12 Health survey: ≥ 16 years	237	33.1%		212	70.4%		
KINDL Children's Questionnaire: ≥ 8 to < 16 years	76	10.6%		25	8.3%		
KINDL Parents' Questionnaire: > 1 month to < 8 years	402	56.2%		64	21.3%		
Total	715	100.0%		301	100.0%		
Quality of life, Symptom Score at baseline	**Mean**	**SD**	**N**	**Mean**	**SD**	**N**	**Mann-Whitney U-test**
SF-12 Summary Score	32.2	5.8	162	33.5	6.5	165	p = 0.0561
KINDL Summary Score	44.9	6.9	223	43.4	5.6	57	p = 0.0745
Symptom Score (0-4)	1.3	0.7	714	1.2	0.6	295	p = 0.5197

Concomitant medical problems present at baseline					
	Anthroposophy N=715		**Conventional N=301**		**Fisher's exact test**
Concomitant medical problems present	N	%	N	%	
Yes	226	31.6%	97	32.2%	p = 0.8827
No	489	68.4%	204	67.8%	
Total	715	100.0%	301	100.0%	
ICD-9 classification of concomitant medical problems	N	%	N	%	
Diseases of the respiratory system	65	9.1%	30	10.0%	p = 0.6392
Endocrine, nutritional and metabolic diseases, immunity disorders	35	4.9%	16	5.3%	p = 0.7552
Diseases of the nervous system and sense organs	30	4.2%	6	2.0%	p = 0.0951
Symptoms, signs, and ill-defined conditions	29	4.1%	14	4.7%	p = 0.7330
Diseases of the skin and subcutaneous tissue	28	3.9%	1	0.3%	p = 0.0007
Diseases of the digestive system	23	3.2%	8	2.7%	p = 0.6953
Injury and poisoning	18	2.5%	1	0.3%	p = 0.0197
Diseases of the musculoskeletal system and connective tissue	16	2.2%	11	3.7%	p = 0.2047
Diseases of the genitourinary system	15	2.1%	4	1.3%	p = 0.6122
Diseases of the circulatory system	14	2.0%	17	5.6%	p = 0.0041
Infectious and parasitic diseases	14	2.0%	1	0.3%	p = 0.0500
Mental disorders	13	1.8%	11	3.7%	p = 0.1103
Injury and poisoning	7	1.0%	7	2.3%	p = 0.1358
Congenital anomalies	7	1.0%	2	0.7%	p = 1.0000
Factors influencing health status and contact with health services	2	0.3%	0	0.0%	p = 1.0000
Diseases of the blood and blood-forming organs	1	0.1%	2	0.7%	p = 0.2111
Complications of pregnancy, childbirth, and the puerperium	1	0.1%	0	0.0%	p = 1.0000
Certain conditions originating in the perinatal period	1	0.1%	0	0.0%	p = 1.0000
Neoplasms	0	0.0%	2	0.7%	p = 0.0876
Chronic respiratory or ear disease					
Asthma / obstructive chronic bronchitis / chronic airway obstruction / bronchitis, unqualified	22	3.1%	18	6.0%	p = 0.0345
Allergic / chronic rhinitis / hay fever	21	2.9%	3	1.0%	p = 0.0711
Chronic sinusitis	5	0.7%	1	0.3%	p = 0.6761
Hypertrophy of tonsils or adenoids	3	0.4%	1	0.3%	p = 1.0000
Ear operation	1	0.1%	0	0.0%	p = 1.0000

Medication use for concomitant medical problems					
	Anthroposophy N=715		**Conventional N=301**		**Fisher's exact test**
Any medication use for concomitant medical problems	N	%	N	%	
Yes	128	17.9%	62	20.6%	p = 0.3327
No	587	82.1%	239	79.4%	
Total	715	100.0%	301	100.0%	
Main medication groups*					
Anti-asthmatics	12	1.7%	10	3.3%	p = 0.1043
Thyroid therapy	5	0.7%	4	1.3%	p = 0.4626
Nasal preparations	4	0.6%	5	1.7%	p = 0.1350
Cough and cold preparations	1	0.1%	7	2.3%	
Sex hormones and modulators of the genital system	3	0.4%	4	1.3%	
Analgesics	4	0.6%	3	1.0%	
Antiseptics and disinfectants	5	0.7%	1	0.3%	
Psychoanaleptics	1	0.1%	5	1.7%	
Antacids, drugs for treatment of peptic ulcer and flatulence	3	0.4%	2	0.7%	
Drugs used in diabetes	2	0.3%	3	1.0%	
Cardiac therapy	0	0.0%	5	1.7%	
Calcium channel blockers	3	0.4%	2	0.7%	
Agents acting on the renin-angiotensin system	1	0.1%	4	1.3%	
Serum lipid reducing agents	2	0.3%	3	1.0%	

Multiple responses possible, coding according to Drug dictionary. Only groups with medication used by at least 1% of the patients in the Anthroposophy Group or Conventional Group are listed.

Previous experience with doctor, confidence in doctor, consultation type and length

Previous experience with doctor and therapy system					
	Anthroposophy N=715		Conventional N=301		Fisher's exact test
Previous experience with this doctor	N	%	N	%	
Yes	507	70.9%	236	78.4%	
No	59	8.3%	24	8.0%	
Missing	149	20.8%	41	13.6%	
Total	715	100.0%	301	100.0%	
-excluding missings					
Yes	507	89.6%	236	90.8%	p = 0.0161
No	59	10.4%	24	9.2%	
Sum respondents	566	100.0%	260	100.0%	
Previous experience with anthroposophic medicine					
	N	%	**Not asked**		
Yes	498	69.7%			
No	69	9.7%			
Missing	148	20.7%			
Total	715	100.0%			
-excluding missings					
Yes	498	87.8%			
No	69	12.2%			
Total	567	100.0%			

Confidence in doctor, consultation type and length					
	Anthroposophy N=715		**Conventional N=301**		
Patient confidence in doctor's professional skills	N	%	N	%	
Not at all	2	0.3%	0	0.0%	
Slightly	1	0.1%	2	0.7%	
Moderately	11	1.5%	24	8.0%	
Quite a bit	161	22.5%	90	29.9%	
Extremely	388	54.3%	148	49.2%	
Missing	152	21.3%	37	12.3%	
Total	715	100.0%	301	100.0%	
-excluding missings	N	%	N	%	**Mann-Whitney U-test**
Not at all	2	0.4%	0	0.0%	
Slightly	1	0.2%	2	0.8%	
Moderately	11	2.0%	24	9.1%	p < 0.0001
Quite a bit	161	28.6%	90	34.1%	
Extremely	388	68.9%	148	56.1%	
Sum respondents	563	100.0%	264	100.0%	
Patient's confidence that the doctor will solve his/her medical problem	N	%	N	%	**Fisher's exact test**
Yes	556	77.8%	258	85.7%	
No (or yes and no)	4	0.6%	4	1.3%	
Missing	155	21.7%	39	13.0%	
Total	715	100.0%	301	100.0%	
-excluding missings	N	%	N	%	
Yes	556	99.3%	258	98.5%	p = 0.2742
No (or yes and no)	4	0.7%	4	1.5%	
Total	560	100.0%	262	100.0%	
Consultation type	N	%	N	%	
Office visit	682	97.3%	284	94.4%	p = 0.5256
Telephone consultation only	10	1.4%	5	1.7%	
Home visit	23	3.2%	2	0.7%	
Total	715	100.0%	301	100.0%	
Consultation length	N	%	N	%	**Mann-Whitney U-test**
< 5 min.	8	1.1%	62	20.6%	
>5 - ≤ 15 min	442	61.8%	217	72.1%	
>15 - ≤ 30 min	261	36.5%	22	7.3%	p < 0.0001
>30 - ≤ 60 min	4	0.6%	0	0.0%	
Total	715	100.0%	301	100.0%	

Patients' and doctors' therapy preferences for the chief complaint, willingness to be randomised

Treatment preference, willingness to be randomized					
	Anthroposophy N=715		Conventional N=301		
Patient preference for treatment of today's chief complaint	N	%	N	%	**Fisher's exact test**
No preference	25	3.5%	97	32.2%	
Preference for anthroposophic treatment	676	94.5%	Not asked		
Preference for conventional treatment	5	0.7%	200	66.4%	
Other	8	1.1%	3	1.0%	
No remark	1	0.1%	1	0.3%	
Total	715	100.0%	301	100.0%	
Doctor preference for treatment for the patient's chief complaint	N	%	N	%	
No preference	4	0.6%	9	3.0%	
Preference for anthroposophic treatment	709	99.2%	Not asked		
Preference for conventional treatment	1	0.1%	286	95.0%	
Other	0	0.0%	5	1.7%	
No remark	1	0.1%	1	0.3%	
Total	715	100.0%	301	100.0%	
Willingness to be randomized	N	%	N	%	
Yes	23	3.2%	105	34.9%	
No	691	96.6%	195	64.8%	
Missing	1	0.1%	1	0.3%	
Total	715	100.0%	301	100.0%	
-excluding missings					
Yes	23	3.2%	105	35.0%	p < 0.0001
No	691	96.8%	195	65.0%	
Total	714	100.0%	300	100.0%	
If no: Reason for unwillingness to be randomized	N	%	N	%	
Patient has a treatment preference	645	93.3%	164	84.1%	
Patient does not want to be randomized	41	5.9%	27	13.8%	
Patient perceived risk of at least one treatment option	1	0.1%	1	0.5%	
Other	4	0.6%	2	1.0%	
No remark	0	0.0%	1	0.5%	
Total	691	100.0%	195	100.0%	

Interventions

Primary and adjunctive therapy prescribed on Day 0: main groups

Primary therapy prescribed							
	Anthroposophy N=715			**Conventional N=301**			
Primary therapy prescribed at study entry	N	%		N	%		
Anthroposophic medicines (1 or 2 remedies)	714	99.9%		0	0.0%		
All other medicines (1 remedy)	1	0.1%		292	97.0%		
No medicines	0	0.0%		9	3.0%		
Total	715	100.0%		301	100.0%		
-Number of days prescribed	Mean	SD	N	Mean	SD	N	
	6.3	3.0	700	4.6	2.5	269	
Mann-Whitney U-test							p < 0.0001
Hodges-Lehmann estimate: Median difference (anthroposophy minus conventional)							1.00
95%-CI:							1.00-2.00
-Confidence in prescription (0=none. 10=total)	N	%		N	%		
0	0	0.0%		0	0.0%		
1	0	0.0%		0	0.0%		
2	0	0.0%		1	0.3%		
3	0	0.0%		6	2.0%		
4	0	0.0%		6	2.0%		
5	2	0.3%		10	3.3%		
6	13	1.8%		17	5.6%		
7	68	9.5%		73	24.3%		
8	179	25.0%		59	19.6%		
9	176	24.6%		49	16.3%		
10	256	35.8%		80	26.6%		
no remark	21	2.9%		0	0.0%		
Total	715	100.0%		301	100.0%		
-Confidence in prescription (0-10)	**Mean**	**SD**	**N**	**Mean**	**SD**	**N**	
	8.8	1.1	694	8.0	1.7	301	
Mann-Whitney U-test							p < 0.0001
Hodges-Lehmann estimate: Median difference (anthroposophy minus conventional)							1.00
95%-CI:							0.00-1.00

Adjunctive therapy					
	Anthroposophy N=715		Conventional N=301		
Adjunctive therapy prescribed at study entry*	N	%	N	%	**Fisher's exact test**
Anthroposophic medicines (1 to 3 remedies)	388	54.3%	0	0.0%	p < 0.0001
Homeopathic medicines (1 to 3 remedies)	96	13.4%	0	0.0%	p < 0.0001
Herbal medicines (1 to 3 remedies)	80	11.2%	10	3.3%	p < 0.0001
Conventional medicines = not anthroposophic. homeopathic or herbal (1 to 3 remedies)	72	10.1%	34	11.3%	p = 0.5748
External applications	61	8.5%		Not asked	
Steam	35	4.9%	0	0.0%	p < 0.0001
Nasal lavage	34	4.8%	0	0.0%	p < 0.0001
Saline lavage	24	3.4%	0	0.0%	p = 0.0004
Gargle	13	1.8%	0	0.0%	p = 0.0135
Ear oil	9	1.3%	1	0.3%	p = 0.2967
Diet	3	0.4%		Not asked	
Enema	1	0.1%		Not asked	
Other adjunctive therapy	59	8.3%	1	0.3%	p < 0.0001
No adjunctive therapy	171	23.9%	260	86.4%	p < 0.0001

*Multiple responses possible, sum of percentages > 100.0%

Anthroposophic medicine use in the A-Group

Anthroposophic medicines in Anthroposophy Group: Dosage Forms												
Dosage Form	**Concomitant***		**Primary Day 0**		**All Day 0**		**Day 1-28**		**Day 0-28**		**All**	
	N	%	N	%	N	%	N	%	N	%	N	%
Liquid	30	24,0%	526	38,6%	759	35,5%	71	31,0%	830	35,1%	860	34,5%
Pillules	14	11,2%	174	12,8%	216	10,1%	47	20,5%	263	11,1%	277	11,1%
Powder	34	27,2%	201	14,7%	237	11,1%	22	9,6%	259	11,0%	293	11,8%
Ointment	6	4,8%	89	6,5%	183	8,6%	22	9,6%	205	8,7%	211	8,5%
Ampoule	25	20,0%	77	5,6%	120	5,6%	17	7,4%	137	5,8%	162	6,5%
Tablets	2	1,6%	75	5,5%	95	4,4%	15	6,6%	110	4,7%	112	4,5%
Ear drops	1	0,8%	24	1,8%	81	3,8%	7	3,1%	88	3,7%	89	3,6%
Syrup	0	0,0%	55	4,0%	80	3,7%	2	0,9%	82	3,5%	82	3,3%
Suppositories	3	2,4%	28	2,1%	51	2,4%	4	1,7%	55	2,3%	58	2,3%
Bath preparations	1	0,8%	0	0,0%	52	2,4%	1	0,4%	53	2,2%	54	2,2%
Nose spray	1	0,8%	27	2,0%	49	2,3%	2	0,9%	51	2,2%	52	2,1%
Mouth spray	0	0,0%	39	2,9%	49	2,3%	0	0,0%	49	2,1%	49	2,0%
Bath oil	0	0,0%	6	0,4%	46	2,2%	1	0,4%	47	2,0%	47	1,9%
Oil	3	2,4%	9	0,7%	31	1,5%	4	1,7%	35	1,5%	38	1,5%
Cream	0	0,0%	2	0,1%	31	1,5%	2	0,9%	33	1,4%	33	1,3%
Nose drops	0	0,0%	8	0,6%	15	0,7%	1	0,4%	16	0,7%	16	0,6%
Eye drops	0	0,0%	4	0,3%	12	0,6%	3	1,3%	15	0,6%	15	0,6%
Eye ointment	0	0,0%	0	0,0%	1	0,0%	3	1,3%	4	0,2%	4	0,2%
Capsules	0	0,0%	0	0,0%	0	0,0%	3	1,3%	3	0,1%	3	0,1%
Tincture for external use	1	0,8%	1	0,1%	2	0,1%	1	0,4%	3	0,1%	4	0,2%
Gel	1	0,8%	0	0,0%	1	0,0%	1	0,4%	2	0,1%	3	0,1%
Unknown	3	2,4%	18	1,3%	18	1,3%	0	0,0%	25	1,1%	28	1,1%
Total	125	100.0%	1363	100.0%	2136	100.0%	229	100.0%	2365	100.0 %	2490	100.0 %

Concomitant: used at study intake for concomitant medical problems.

Most common ATC groups prescribed Day 0, Day 1-28, Day 0-28

Prescribed medicines: six most common ATC groups					
Prescription (primary or adjunctive: conventional, anthroposophic, homeopathic or herbal medicine)	**Anthroposophy N=715**		**Conventional N=301**		**Fisher's exact test**
Day 0	N	%	N	%	
J01 Antibacterials for systemic use	6	0.8%	80	26.6%	p < 0.0005
N02 Analgesics	14	2.0%	65	21.6%	p < 0.0001
R01 Nasal preparations	127	17.8%	61	20.3%	p = 0.3764
R05 Cough and cold preparations*	130	18.2%	46	15.3%	p = 0.2774
M01 Anti-inflammatory and antirheumatic products	2	0.3%	24	8.0%	p < 0.0001
R06 Antihistamines for systemic use	0	0.0%	14	4.7%	p < 0.0001
Days 1-28	N	%	N	%	
J01 Antibacterials for systemic use	35	4.9%	30	10.0%	p = 0.0045
N02 Analgesics	9	1.3%	4	1.3%	p = 1.0000
R01 Nasal preparations	14	2.0%	9	3.0%	p = 0.3559
R05 Cough and cold preparations*	27	3.8%	21	7.0%	p = 0.0348
M01 Anti-inflammatory and antirheumatic products	0	0.0%	4	1.3%	p = 0.0076
R06 Antihistamines for systemic use	1	0.1%	3	1.0%	p = 0.0805
Days 0-28	N	%	N	%	
J01 Antibacterials for systemic use	39	5.5%	101	33.6%	p < 0.0001
N02 Analgesics	23	3.2%	66	21.9%	p < 0.0001
R01 Nasal preparations	137	19.2%	67	22.3%	p = 0.2657
R05 Cough and cold preparations*	147	20.6%	56	18.7%	p = 0.4932
M01 Anti-inflammatory and antirheumatic products	2	0.3%	26	8.6%	p < 0.0001
R06 Antihistamines for systemic use	1	0.1%	16	5.3%	p < 0.0001

*In the Conventional Group, the number of patients prescribed cough and cold preparations may vary by ± 3 (±1.0%) due to unknown degree of overlap between patients prescribed such medication as conventional or "herbal" medicine.

Antibiotic prescription: Subgroup analysis with unadjusted odds ratios							
Response = No antibacterials for systemic use prescribed Day 0-28	**Anthroposophy N**		**Conventional N**		**Odds ratio Anthroposophy vs. Conventional**		
	Respon-ders	**Patients**	**Respon-ders**	**Patients**	**Value**	**95% CI**	
						Lower limit	**Upper limit**
All Patients	676	715	200	301	8.75	5.86	13.08
Country							
Germany	346	362	58	100	15.66	8.26	29.68
Austria	95	101	29	57	15.29	5.77	40.52
Netherlands	145	152	94	104	2.20	0.81	5.99
United Kingdom	43	52	19	40	5.28	2.04	13.65
USA	47	48	0	0			
Gender							
Male	310	333	88	121	5.05	2.82	9.05
Female	366	382	112	180	13.89	7.74	24.91
Age							
< 2 years	105	112	14	17	3.21	0.74	13.88
2-5 years	105	112	30	39	3.21	0.74	13.88
6-17 years	168	174	27	37	10.37	3.48	30.86
18-34 years	81	87	52	81	7.53	2.92	19.38
35-64 years	120	129	70	111	7.81	3.58	17.03
≥ 65 years	10	11	7	16	12.86	1.31	125.78
Chief Complaint							
Runny nose	49	49	15	16			
Sore throat	179	188	48	70	9.12	3.94	21.08
Ear pain	133	143	39	57	6.14	2.62	14.38
Sinus pain	48	50	30	56	20.80	4.60	94.05
Cough	267	285	68	102	7.42	3.95	13.93
Duration of chief complaint							
0 to ≤ 24 hours	183	192	22	33	10.17	3.79	27.24
>24 to ≤ 48 hours	158	167	62	93	8.78	3.95	19.50
>2 to ≤ 7 days	334	355	116	175	8.09	4.71	13.90
Chief complaint episode within last 12 months							
Yes	358	376	76	111	9.16	4.93	17.03
No or no remark	318	339	124	190	8.06	4.73	13.74
Symptom Score at Day 0							
0 to <1	225	235	64	88	8.44	3.84	18.56
1 to <2	334	353	114	174	9.25	5.30	16.17
2 to <3	103	111	19	32	8.81	3.22	24.13
3 to 4	13	15	0	1			

Follow-up contact with doctor, medication intake

Follow-up contact with doctor, medication intake					
	Anthroposophy N=715		**Conventional N=301**		**Fisher's exact test**
Follow-up recommendations at study entry	N	%	N	%	
Yes, appointment	200	28.0%	42	14.0%	
Yes, telephone	168	23.5%	7	2.3%	
No	347	48.5%	252	83.7%	
Total	715	100.0%	301	100.0%	
Yes (appointment or telephone)	368	51.5%	49	16.3%	p < 0.0001
No	347	48.5%	252	83.7%	
Total	715	100.0%	301	100.0%	
Follow-up contacts with doctor (yes)	N	%	N	%	
-office or home visit or telephone					
0-7 days	233	32.6%	92	30.6%	p = 0.5561
0-14 days	301	42.1%	122	40.5%	p = 0.6760
0-28 days	336	47.0%	135	44.9%	p = 0.5362
-office or home visit					
0-7 days	165	23.5%	73	24.3%	p = 0.6857
0-14 days	236	33.0%	104	34.6%	p = 0.6624
0-28 days	268	37.5%	116	38.5%	p = 0.7770
Other therapies prescribed for chief complaint Day 1-28	N	%	N	%	
Yes	130	18.2%	57	18.9%	p = 0.7906
No	585	81.8%	244	81.1%	
Total	715	100.0%	301	100.0%	
Medication taken as prescribed since the initial contact?	N	%	N	%	
Yes (continuously during the study)	641	89.7%	262	87.0%	
No (continuously during the study)	28	3.9%	25	8.3%	
Yes and no at different follow-ups	46	6.4%	14	4.7%	
Total	715	100.0%	301	100.0%	
Yes (continuously during the study)	641	89.7%	262	87.0%	p = 0.2308
No (continuously during the study) or Yes and no at different follow-ups	74	10.3%	39	13.0%	
Total	715	100.0%	301	100.0%	

Patient outcomes

Treatment outcome: overview and chief complaint subgroups

Treatment outcome					
Treatment outcome	**Anthroposophy N=715**		**Conventional N=301**		**Fisher's exact test**
Day 7	N	%	N	%	
Complete recovery	218	30.5%	70	23.3%	p = 0.0221
Major improvement	333	46.6%	129	42.9%	
Slight to moderate improvement	74	10.3%	51	16.9%	
No change	15	2.1%	12	4.0%	
Deterioration	5	0.7%	3	1.0%	
Missing	70	9.8%	36	12.0%	
Total	715	100.0%	301	100.0%	
Day 14, cumulative	N	%	N	%	
Complete recovery	459	64.2%	149	49.5%	p < 0.0001
Major improvement	182	25.5%	105	34.9%	
Slight to moderate improvement	44	6.2%	29	9.6%	
No change	9	1.3%	7	2.3%	
Deterioration	7	1.0%	7	2.3%	
Missing	14	2.0%	4	1.3%	
Total	715	100.0%	301	100.0%	
Day 28, cumulative	N	%	N	%	
Complete recovery	597	83.5%	229	76.1%	p = 0.0064
Major improvement	85	11.9%	57	18.9%	
Slight to moderate improvement	22	3.1%	10	3.3%	
No change	8	1.1%	4	1.3%	
Deterioration	3	0.4%	1	0.3%	
Missing	0	0.0%	0	0.0%	
Total	715	100.0%	301	100.0%	
Response rate (Complete recovery or Major improvement)	N	%	N	%	
Day 7	551/715	77.1%	199/301	66.1%	p = 0.0004
Day 14, cumulative	641/715	89.7%	254/301	84.4%	p = 0.0198
Day 28, cumulative	682/715	95.4%	286/301	95.0%	p = 0.8714
					Test of non-inferiority
Day 14, cumulative	641/715	89.7%	254/301	84.4%	p < 0.00001

Treatment outcome in patients with chief complaint runny nose					
Treatment outcome	**Anthroposophy N=49**		**Conventional N=16**		
	N	%	N	%	**Fisher's exact test**
Day 7					
Complete recovery	18	36.7%	3	18.8%	p = 0.2294
Major improvement	10	20.4%	7	43.8%	
Slight to moderate improvement	11	22.4%	5	31.3%	
No change	4	8.2%	0	0.0%	
Deterioration	1	2.0%	0	0.0%	
No remark	5	10.2%	1	6.3%	
Total	49	10.0%	16	100.0%	
Day 14 cumulative	N	%	N	%	
Complete recovery	28	57.1%	8	50.0%	p = 0.7733
Major improvement	11	22.4%	5	31.3%	
Slight to moderate improvement	6	12.2%	2	12.5%	
No change	2	4.1%	1	6.3%	
Deterioration	2	4.1%	0	0.0%	
Total	49	10.0%	16	100.0%	
Day 28 cumulative	N	%	N	%	
Complete recovery	40	81.6%	13	81.3%	p = 1.0000
Major improvement	5	10.2%	2	12.5%	
Slight to moderate improvement	2	4.1%	1	6.3%	
No change	2	4.1%	0	0.0%	
Total	49	100.0%	16	100.0%	
Response rate (Complete recovery or Major improvement)	N	%	N	%	
Day 7	28	57.1%	10	62.5%	p = 0.7766
Day 14, cumulative	39	79.6%	13	81.3%	p = 1.0000
Day 28, cumulative	45	91.8%	15	93.8%	p = 1.0000

Treatment outcome in patients with chief complaint sore throat					
Treatment outcome	**Anthroposophy N=188**		**Conventional N=70**		
	N	%	N	%	**Fisher's exact test**
Day 7					
Complete recovery	76	40.4%	27	38.6%	p = 0.8865
Major improvement	77	41.0%	24	34.3%	
Slight to moderate improvement	9	4.8%	8	11.4%	
No change	1	0.5%	4	5.7%	
Deterioration	0	0.0%	0	0.0%	
Missing	25	13.3%	7	10.0%	
Total	188	100.0%	70	100.0%	
Day 14, cumulative	N	%	N	%	
Complete recovery	138	73.4%	44	62.9%	p = 0.1242
Major improvement	31	16.5%	19	27.1%	
Slight to moderate improvement	9	4.8%	5	7.1%	
No change	1	0.5%	1	1.4%	
Deterioration	1	0.5%	0	0%	
Missing	8	4.3%	1	1.4%	
Total	188	100.0%	70	100.0%	
Day 28, cumulative	N	%	N	%	
Complete recovery	168	89.4%	55	78.6%	p = 0.0390
Major improvement	13	6.9%	13	18.6%	
Slight to moderate improvement	6	3.2%	1	1.4%	
No change	0	0.0%	1	1.4%	
Deterioration	1	0.5%	0	0.0%	
Total	188	100.0%	70	100.0%	
Response rate (Complete recovery or Major improvement)	N	%	N	%	
Day 7	153	81.4%	51	72.9%	p = 0.1680
Day 14, cumulative	169	89.9%	63	90.0%	p = 1.0000
Day 28, cumulative	181	96.3%	68	97.1%	p = 1.0000

Treatment outcome in patients with chief complaint ear pain					
Treatment outcome	**Anthroposophy N=143**		**Conventional N=57**		
	N	%	N	%	**Fisher's exact test**
Day 7					
Complete recovery	67	46.9%	19	33.3%	p = 0.0850
Major improvement	61	42.7%	17	29.8%	
Slight to moderate improvement	7	4.9%	12	21.1%	
No change	1	0.7%	3	5.3%	
Deterioration	1	0.7%	0	0.0%	
Missing	6	4.2%	6	10.5%	
Total	143	100.0%	57	100.0%	
Day 14 cumulative	N	%	N	%	
Complete recovery	107	74.8%	35	61.4%	p = 0.0835
Major improvement	29	20.3%	13	22.8%	
Slight to moderate improvement	5	3.5%	6	10.5%	
No change	2	1.4%	1	1.8%	
Deterioration	0	0.0%	1	1.8%	
Missing	0	0.0%	1	0.8%	
Total	143	10.0%	57	10.0%	
Day 28 cumulative	N	%	N	%	
Complete recovery	126	88.1%	46	80.7%	p = 0.1815
Major improvement	13	9.1%	8	14.0%	
Slight to moderate improvement	3	2.1%	3	5.3%	
No change	1	0.7%	0	0.0%	
Deterioration	0	0.0%	0	0.0%	
Total	143	100.0%	57	100.0%	
Response rate (Complete recovery or Major improvement)	N	%	N	%	
Day 7	128	89.5%	36	63.2%	p = 0.0001
Day 14, cumulative	136	95.1%	48	84.2%	p = 0.0180
Day 28, cumulative	139	97.2%	54	94.7%	p = 0.4090

Treatment outcome in patients with chief complaint sinus pain					
Treatment outcome	**Anthroposophy N=50**		**Conventional N=56**		
	N	%	N	%	**Fisher's exact test**
Day 7					
Complete recovery	8	16.0%	10	17.9%	p = 1.0000
Major improvement	30	60.0%	25	44.6%	
Slight to moderate improvement	6	12.0%	6	10.7%	
No change	1	2.0%	2	3.6%	
Deterioration	0	0.0%	2	3.6%	
Missing	5	10.0%	11	19.6%	
Total	50	100.0%	56	100.0%	
Day 14 cumulative	N	%	N	%	
Complete recovery	19	38.0%	22	39.3%	p = 1.0000
Major improvement	26	52.0%	25	44.6%	
Slight to moderate improvement	2	4.0%	5	8.9%	
No change	1	2.0%	1	1.8%	
Deterioration	1	2.0%	2	3.6%	
Missing	1	2.0%	1	1.8%	
Total	50	100.0%	56	100.0%	
Day 28 cumulative	N	%	N	%	
Complete recovery	34	68.0%	40	71.4%	p = 0.8325
Major improvement	15	30.0%	13	23.2%	
Slight to moderate improvement	1	2.0%	2	3.6%	
No change	0	0.0%	1	1.8%	
Deterioration	0	0.0%	0	0.0%	
Total	50	100.0%	56	100.0%	
Response rate (Complete recovery or Major improvement)	N	%	N	%	
Day 7	38	76.0%	35	62.5%	p = 0.1475
Day 14, cumulative	45	90.0%	47	83.9%	p = 0.4024
Day 28, cumulative	49	98.0%	53	94.6%	p = 0.6202

Treatment outcome in patients with chief complaint cough					
Treatment outcome	**Anthroposophy N=285**		**Conventional N=102**		
	N	%	N	%	**Fisher's exact test**
Day 7					
Complete recovery	49	17.2%	11	10.8%	p = 0.1516
Major improvement	155	54.4%	56	54.9%	
Slight to moderate improvement	41	14.4%	20	19.6%	
No change	8	2.8%	3	2.9%	
Deterioration	3	1.1%	1	1.0%	
Missing	29	10.2%	11	10.8%	
Total	285	100.0%	102	100.0%	
Day 14 cumulative	N	%	N	%	
Complete recovery	167	58.6%	41	40.2%	p = 0.0017
Major improvement	85	29.8%	42	41.2%	
Slight to moderate improvement	22	7.7%	11	10.8%	
No change	3	1.1%	3	2.9%	
Deterioration	3	1.1%	4	3.9%	
Missing	5	1.8%	1	1.0%	
Total	285	100.0%	102	100.0%	
Day 28 cumulative	N	%	N	%	
Complete recovery	229	80.4%	75	73.5%	p = 0.1610
Major improvement	39	13.7%	21	20.6%	
Slight to moderate improvement	10	3.5%	3	2.9%	
No change	5	1.8%	2	2.0%	
Deterioration	2	0.7%	1	1.0%	
Total	285	100.0%	102	100.0%	
Response rate (Complete recovery or Major improvement)	N	%	N	%	
Day 7	204	71.6%	67	65.7%	p = 0.3137
Day 14, cumulative	252	88.4%	83	81.4%	p = 0.0900
Day 28, cumulative	268	94.0%	96	94.1%	p = 1.0000

Treatment outcome: Subgroup analysis with odds ratios

Response rate of Day 7*: Subgroup analysis with unadjusted odds ratios

	Anthroposophy N		Conventional N		Odds ratio Anthroposophy vs. Conventional		
						95% CI	
	Responders	Patients	Responders	Patients	Value	Lower limit	Upper limit
All patients	551	715	199	301	1.72	1.28	2.31
Country							
Germany	299	362	66	100	2.44	1.49	4.01
Austria	87	101	48	57	1.17	0.47	2.89
Netherlands	108	152	66	104	1.41	0.83	2.40
United Kingdom	26	52	19	40	1.11	0.48	2.52
USA	31	48	0	0			
Gender							
Male	261	333	85	121	1.54	0.96	2.45
Female	290	382	114	180	1.82	1.24	2.68
Age							
< 2 years	87	112	10	17	2.44	0.84	7.05
2-5 years	175	201	26	39	3.37	1.54	7.36
6-17 years	139	174	21	37	3.03	1.43	6.40
18-34 years	62	87	55	81	1.17	0.61	2.26
35-64 years	80	129	77	111	0.72	0.42	1.23
≥ 65 years	7	11	10	16	1.05	0.21	5.16
Chief Complaint							
Runny nose	28	49	10	16	0.80	0.25	2.55
Sore throat	153	188	51	70	1.63	0.86	3.10
Ear pain	128	143	36	57	4.98	2.33	10.63
Sinus pain	38	50	35	56	1.90	0.82	4.42
Cough	204	285	67	102	1.32	0.81	2.13
Duration of chief complaint							
0 to ≤ 24 hours	167	192	24	33	2.51	1.05	6.00
>24 to ≤ 48 hours	134	167	65	93	1.75	0.98	3.14
>2 to ≤ 7 days	249	355	110	175	1.39	0.95	2.03
Chief complaint episode within last 12 months							
Yes	288	376	72	111	1.77	1.12	2.80
No or no remark	263	339	127	190	1.72	1.16	2.55
Symptom Score at Day 0							
0 to <1	178	235	54	88	1.97	1.17	3.32
1 to <2	269	353	120	174	1.44	0.96	2.16
2 to <3	89	111	21	32	2.12	0.89	5.04
3 to 4	14	15	1	1			

* Response = Treatment outcome: complete recovery or major improvement by Day 7

Response rate of Day 7: Adjusted odds ratios			
Response = Treatment outcome: Complete recovery OR Major improvement at Day 7	**Odds ratio Anthroposophy vs. Conventional**		
	Value	**95% Confidence interval**	
		Lower limit	**Upper limit**
All Patients: unadjusted odds ratio	1.72	1.28	2.31
Odds ratio adjusted for			
Country	1.65	1.20	2.26
Gender	1.70	1.27	2.29
Age	1.44	1.05	1.97
Chief Complaint	1.74	1.29	2.36
Duration of chief complaint	1.58	1.17	2.13
Chief complaint episode within last 12 months	1.74	1.29	2.35
Symptom Score at Day 0	1.67	1.23	2.25
Adjustment for all above factors by multiple logistic regression analysis	1.50	1.07	2.11

Response rate of Day 14*: Subgroup analysis with unadjusted odds ratios							
	Anthroposophy		Conventional		Odds ratio Anthroposophy vs. Conventional		
	N		N				
	Respon-ders	Patients	Respon-ders	Patients	Value	95% CI	
						Lower limit	Upper limit
All patients	641	715	254	301	1.60	1.08	2.38
Country							
Germany	338	362	83	100	2.88	1.48	5.62
Austria	94	101	54	57	0.75	0.19	3.01
Netherlands	130	152	87	104	1.15	0.58	2.30
United Kingdom	40	52	30	40	1.11	0.42	2.91
USA	39	48	0	0			
Gender							
Male	296	333	107	121	1.05	0.54	2.01
Female	345	382	147	180	2.09	1.26	3.48
Age							
< 2 years	102	112	13	17	3.14	0.86	11.46
2-5 years	192	201	34	39	3.14	0.99	9.93
6-17 years	159	174	33	37	1.28	0.40	4.12
18-34 years	75	87	74	81	0.59	0.22	1.58
35-64 years	103	129	87	111	1.09	0.59	2.04
≥ 65 years	9	11	13	16	1.04	0.14	7.53
Chief Complaint							
Runny nose	39	49	13	16	0.90	0.21	3.78
Sore throat	169	188	63	70	0.99	0.40	2.46
Ear pain	136	143	48	57	3.64	1.29	10.32
Sinus pain	45	50	47	56	1.72	0.54	5.54
Cough	252	285	83	102	1.75	0.94	3.24
Duration of chief complaint							
0 to ≤ 24 hours	183	192	30	33	2.03	0.52	7.94
>24 to ≤ 48 hours	150	167	81	93	1.31	0.60	2.87
>2 to ≤ 7 days	307	355	143	175	1.43	0.88	2.33
Chief complaint episode within last 12 months							
Yes	341	376	95	111	1.64	0.87	3.09
No or no remark	300	339	159	190	1.50	0.90	2.50
Symptom Score at Day 0							
0 to <1	211	235	68	88	2.59	1.35	4.97
1 to <2	316	353	153	174	1.17	0.66	2.07
2 to <3	99	111	28	32	1.18	0.35	3.94
3 to 4	14	15	1	1			

* Response = Treatment outcome: complete recovery or major improvement by Day 14 (last observation carried forward)

Response rate of Day 14: Adjusted odds ratios			
Response = Treatment outcome: Complete recovery OR Major improvement at Day 14 (last observation carried forward)	**Odds ratio Anthroposophy vs. Conventional**		
	Value	**95% Confidence interval**	
		Lower limit	**Upper limit**
All Patients: unadjusted odds ratio	1.60	1.08	2.38
Odds ratio adjusted for			
Country	1.53	1.01	2.32
Gender	1.59	1.07	2.36
Age	1.20	0.79	1.82
Chief Complaint	1.63	1.09	2.44
Duration of chief complaint	1.44	0.96	2.14
Chief complaint episode within last 12 months	1.55	1.04	2.31
Symptom Score at Day 0	1.57	1.05	2.34
Adjustment for all above factors by multiple logistic regression analysis	1.29	0.82	2.00

Response rate of Day 28*: Subgroup analysis with unadjusted odds ratios							
	Anthroposophy N		Conventional N		Odds ratio Anthroposophy vs. Conventional		
	Respon-ders	Patients	Respon-ders	Patients	Value	95% CI Lower limit	95% CI Upper limit
All Patients	682	715	286	301	1.08	0.58	2.03
Country							
Germany	354	362	96	100	1.84	0.54	6.25
Austria	98	101	56	57	0.58	0.06	5.74
Netherlands	135	152	97	104	0.57	0.23	1.44
United Kingdom	48	52	37	40	0.97	0.21	4.62
USA	47	48	0	0			
Gender							
Male	318	333	115	121	1.11	0.42	2.92
Female	364	382	171	180	1.06	0.47	2.42
Age							
< 2 years	107	112	14	17	4.59	0.99	21.30
2-5 years	196	201	38	39	1.03	0.12	9.08
6-17 years	165	174	34	37	1.62	0.42	6.29
18-34 years	81	87	79	81	0.34	0.07	1.74
35-64 years	121	129	107	111	0.57	0.17	1.93
≥ 65 years	11	11	14	16			
Chief Complaint							
Runny nose	45	49	15	16	0.75	0.08	7.24
Sore throat	181	188	68	70	0.76	0.15	3.75
Ear pain	139	143	54	57	1.93	0.42	8.91
Sinus pain	49	50	53	56	2.77	0.28	27.56
Cough	268	285	96	102	0.99	0.38	2.57
Duration of chief complaint							
0 to ≤ 24 hours	190	192	32	33	2.97	0.26	33.70
>24 to ≤ 48 hours	160	167	90	93	0.76	0.19	3.02
>2 to ≤ 7 days	331	355	164	175	0.93	0.44	1.93
Chief complaint episode within last 12 months							
Yes	357	376	111	111	1.86	0.84	4.13
No or no remark	325	339	190	190	0.63	0.22	1.77
Symptom Score at Day 0							
0 to <1	224	235	88	88	0.97	0.30	3.13
1 to <2	338	353	174	174	1.23	0.53	2.87
2 to <3	104	111	32	32	0.99	0.20	5.02
3 to 4	15	15	1	1			

* Response = Treatment outcome: complete recovery or major improvement by Day 28 (last observation carried forward)

Response rate of Day 28: Adjusted odds ratios			
Response = Treatment outcome: Complete recovery OR Major improvement at Day 28 (last observation carried forward)	**Odds ratio Anthroposophy vs. Conventional**		
	Value	**95% Confidence interval**	
		Lower limit	**Upper limit**
All Patients: unadjusted odds ratio	1.08	0.58	2.03
Odds ratio adjusted for			
Country	0.82	0.43	1.57
Gender	1.08	0.58	2.02
Age	1.00	0.52	1.94
Chief Complaint	1.13	0.60	2.14
Duration of chief complaint	0.94	0.50	1.77
Chief complaint episode within last 12 months	1.18	0.63	2.23
Symptom Score at Day 0	1.11	0.59	2.08
Adjustment for all above factors by multiple logistic regression analysis	0.87	0.45	1.69

Complete recovery rate of Day 7: Subgroup analysis with unadjusted odds ratios							
Recovered = Treatment outcome: Complete recovery rate on Day 7	**Anthroposophy N**		**Conventional N**		**Odds ratio Anthroposophy vs. Conventional**		
						95% CI	
	Re-covered	**Patients**	**Re-covered**	**Patients**	**Value**	**Lower limit**	**Upper limit**
All Patients	218	715	70	301	1.45	1.06	1.98
Country							
Germany	130	362	19	100	2.39	1.39	4.11
Austria	37	101	16	57	1.48	0.73	3.00
Netherlands	23	152	25	104	0.56	0.30	1.06
United Kingdom	15	52	10	40	1.22	0.48	3.09
USA	13	48	0	0			
Gender							
Male	102	333	26	121	1.61	0.99	2.64
Female	116	382	44	180	1.35	0.90	2.02
Age							
< 2 years	29	112	3	17	1.63	0.44	6.08
2-5 years	92	201	15	39	1.35	0.67	2.73
6-17 years	50	174	9	37	1.25	0.55	2.85
18-34 years	24	87	21	81	1.09	0.55	2.16
35-64 years	20	129	19	111	0.89	0.45	1.77
≥ 65 years	3	11	3	16	1.63	0.26	10.10
Chief Complaint							
Runny nose	18	49	3	16	2.52	0.63	10.03
Sore throat	76	188	27	70	1.08	0.62	1.90
Ear pain	67	143	19	57	1.76	0.93	3.35
Sinus pain	8	50	10	56	0.88	0.32	2.43
Cough	49	285	11	102	1.72	0.86	3.45
Duration of chief complaint							
0 to ≤ 24 hours	85	192	15	33	0.95	0.45	2.00
>24 to ≤ 48 hours	54	167	24	93	1.37	0.78	2.42
>2 to ≤ 7 days	79	355	31	175	1.33	0.84	2.11
Chief complaint episode within last 12 months							
Yes	114	376	23	111	1.66	1.00	2.77
No or no remark	104	339	47	190	1.35	0.90	2.01
Symptom Score at Day 0							
0 to <1	75	235	19	88	1.70	0.96	3.03
1 to <2	90	353	41	174	1.11	0.73	1.70
2 to <3	42	111	7	32	2.17	0.86	5.46
3 to 4	11	15	0	1			

Complete Recovery rate of Day 7: Adjusted odds ratios			
Treatment outcome: Complete recovery on Day 7	**Odds ratio Anthroposophy vs. Conventional**		
	Value	**95% Confidence interval**	
		Lower limit	**Upper limit**
All Patients: unadjusted odds ratio	1.45	1.06	1.98
Odds ratio adjusted for			
Country	1.36	0.99	1.88
Gender	1.45	1.06	1.98
Age	1.11	0.80	1.55
Chief Complaint	1.41	1.02	1.96
Duration of chief complaint	1.26	0.92	1.74
Chief complaint episode within last 12 months	1.46	1.07	2.00
Symptom Score at Day 0	1.41	1.02	1.94
Adjustment for all above factors by multiple logistic regression analysis	1.05	0.72	1.54

Complete recovery rate of Day 14*: Subgroup analysis with unadjusted odds ratios							
	Anthroposophy N		Conventional N		Odds ratio Anthroposophy vs. Conventional		
	Re-covered*	Patients	Re-covered*	Patients	Value	95% CI Lower limit	95% CI Upper limit
All Patients	459	715	149	301	1.83	1.39	2.40
Country							
Germany	265	362	40	100	4.10	2.58	6.51
Austria	72	101	37	57	1.45	0.73	2.89
Netherlands	63	152	50	104	0.76	0.46	1.26
United Kingdom	35	52	23	40	1.52	0.65	3.57
USA	24	48	0	0			
Gender							
Male	220	333	65	121	1.68	1.10	2.56
Female	239	382	84	180	1.91	1.33	2.73
Age							
< 2 years	79	112	9	17	2.13	0.76	5.99
2-5 years	154	201	25	39	1.83	0.88	3.81
6-17 years	113	174	18	37	1.96	0.96	4.00
18-34 years	49	87	45	81	1.03	0.56	1.90
35-64 years	58	129	43	111	1.29	0.77	2.16
≥ 65 years	6	11	9	16	0.93	0.20	4.37
Chief Complaint							
Runny nose	28	49	8	16	1.33	0.43	4.13
Sore throat	138	188	44	70	1.63	0.91	2.92
Ear pain	107	143	34	57	2.01	1.05	3.85
Sinus pain	19	50	22	56	0.95	0.43	2.07
Cough	167	285	41	102	2.11	1.33	3.34
Duration of chief complaint							
0 to ≤ 24 hours	152	192	22	33	1.90	0.85	4.24
>24 to ≤ 48 hours	106	167	50	93	1.49	0.89	2.50
>2 to ≤ 7 days	201	355	77	175	1.66	1.15	2.39
Chief complaint episode within last 12 months							
Yes	251	376	48	111	2.64	1.71	4.06
No or no remark	208	339	101	190	1.40	0.98	2.00
Symptom Score at Day 0							
0 to <1	151	235	43	88	1.88	1.15	3.09
1 to <2	223	353	84	174	1.84	1.27	2.65
2 to <3	72	111	17	32	1.63	0.73	3.61
3 to 4	13	15	1	1			

*Recovered = Treatment outcome: Complete recovery at Day 14 (last observation carried forward)

Complete Recovery rate of Day 14: Adjusted odds ratios			
Treatment outcome: Complete recovery at Day 14 (last observation carried forward)	**Odds ratio Anthroposophy vs. Conventional**		
	Value	**95% Confidence interval**	
		Lower limit	**Upper limit**
All Patients: unadjusted odds ratio	1.83	1.39	2.40
Odds ratio adjusted for			
Country	1.79	1.34	2.38
Gender	1.81	1.38	2.38
Age	1.39	1.04	1.86
Chief Complaint	1.72	1.30	2.28
Duration of chief complaint	1.64	1.24	2.16
Chief complaint episode within last 12 months	1.82	1.38	2.39
Symptom Score at Day 0	1.82	1.38	2.40
Adjustment for all above factors by multiple logistic regression analysis	1.35	0.98	1.86

Complete recovery rate of Day 28*: Subgroup analysis with unadjusted odds ratios							
	Anthroposophy N		Conventional N		Odds ratio Anthroposophy vs. Conventional		
	Re-covered*	Patients	Re-covered*	Patients	Value	95% CI Lower limit	95% CI Upper limit
All Patients	597	715	229	301	1.59	1.14	2.21
Country							
Germany	325	362	76	100	2.77	1.57	4.91
Austria	87	101	48	57	1.17	0.47	2.89
Netherlands	102	152	76	104	0.75	0.43	1.30
United Kingdom	43	52	29	40	1.81	0.67	4.92
USA	40	48	0	0			
Gender							
Male	286	333	92	121	1.92	1.14	3.22
Female	311	382	137	180	1.37	0.90	2.11
Age							
< 2 years	97	112	14	17	1.39	0.36	5.40
2-5 years	181	201	31	39	2.34	0.95	5.77
6-17 years	145	174	27	37	1.85	0.81	4.24
18-34 years	71	87	70	81	0.70	0.30	1.61
35-64 years	94	129	76	111	1.24	0.71	2.16
≥ 65 years	9	11	11	16	2.05	0.32	13.16
Chief Complaint							
Runny nose	40	49	13	16	1.03	0.24	4.37
Sore throat	168	188	55	70	2.29	1.10	4.78
Ear pain	126	143	46	57	1.77	0.77	4.07
Sinus pain	34	50	40	56	0.85	0.37	1.95
Cough	229	285	75	102	1.47	0.87	2.50
Duration of chief complaint							
0 to ≤ 24 hours	178	192	27	33	2.83	1.00	7.98
>24 to ≤ 48 hours	145	167	72	93	1.92	0.99	3.72
>2 to ≤ 7 days	274	355	130	175	1.17	0.77	1.78
Chief complaint episode within last 12 months							
Yes	319	376	82	111	1.98	1.19	3.29
No or no remark	278	339	147	190	1.33	0.86	2.07
Symptom Score at Day 0							
0 to <1	195	235	69	88	1.34	0.73	2.47
1 to <2	298	353	132	174	1.72	1.10	2.71
2 to <3	91	111	22	32	2.07	0.85	5.04
3 to 4	13	15	1	1			

*Recovered = Treatment outcome: Complete recovery at Day 28 (last observation carried forward)

Complete Recovery rate of Day 28: Adjusted odds ratios			
Treatment outcome: Complete recovery at Day 28 (last observation carried forward)	**Odds ratio Anthroposophy vs. Conventional**		
	Value	**95% Confidence interval**	
		Lower limit	**Upper limit**
All Patients: unadjusted odds ratio	1.59	1.14	2.21
Odds ratio adjusted for			
Country	1.38	0.98	1.95
Gender	1.57	1.13	2.19
Age	1.25	0.88	1.78
Chief Complaint	1.49	1.06	2.09
Duration of chief complaint	1.44	1.03	2.02
Chief complaint episode within last 12 months	1.57	1.13	2.20
Symptom Score at Day 0	1.63	1.17	2.28
Adjustment for all above factors by multiple logistic regression analysis	1.18	0.82	1.71

Time to first improvement

Time to first improvement					
	Anthroposophy N=715		Conventional N=301		Mann-Whitney U-test
Time to first improvement	N	%	N	%	
≤ 1 day	221	30.9%	50	16.6%	
> 1 day to 2 days	180	25.2%	68	22.6%	
> 2 days to 3 days	122	17.1%	54	17.9%	
> 3 days to 4 days	51	7.1%	31	10.3%	p < 0.0001
> 4 days to 5 days	21	2.9%	17	5.6%	
> 5 days to 6 days	8	1.1%	10	3.3%	
> 6 days to 7 days	9	1.3%	4	1.3%	
> 7 days	2	0.3%	5	1.7%	
No improvement	9	1.3%	8	2.7%	
Missing	92	12.9%	54	17.9%	
Total	715	100.0%	301	100.0%	
					Fisher's exact test
Time to improvement ≤ 1 day	221/715	30.9%	50/301	16.6%	p < 0.0001
Time to improvement ≤ 3 days	523/715	73.1%	172/301	57.1%	p < 0.0001
-excluding missings	N	%	N	%	
<1 day	221	35.5%	50	20.2%	
> 1 day to 2 days	180	28.9%	68	27.5%	
> 2 days to 3 days	122	19.6%	54	21.9%	
> 3 days to 4 days	51	8.2%	31	12.6%	
> 4 days to 5 days	21	3.4%	17	6.9%	
> 5 days to 6 days	8	1.3%	10	4.0%	
> 6 days to 7 days	9	1.4%	4	1.6%	
> 7 days	2	0.3%	5	2.0%	
No improvement	9	1.4%	8	3.2%	
Total	623	100.0%	247	100.0%	
Time to improvement ≤ 1 day	221/623	35.5%	50/247	20.2%	p < 0.0001
Time to improvement ≤ 3 days	523/623	83.9%	172/247	69.6%	p < 0.0001

Time to first improvement ≤ 24 hours: Subgroup analysis with unadjusted odds ratios							
Response = Time to first improvement ≤ 24 hours	**Anthroposophy N**		**Conventional N**		**Odds ratio Anthroposophy vs. Conventional**		
	Respon-ders	**Patients**	**Respon-ders**	**Patients**	**Value**	**95% CI**	
						Lower limit	**Upper limit**
All Patients	221	715	50	301	2.25	1.59	3.16
Country							
Germany	111	362	17	100	2.16	1.22	3.81
Austria	57	101	9	57	6.91	3.06	15.58
Netherlands	25	152	19	104	0.88	0.46	1.70
United Kingdom	10	52	5	40	1.67	0.52	5.34
USA	18	48	0	0			
Gender							
Male	110	333	20	121	2.49	1.46	4.24
Female	111	382	30	180	2.05	1.31	3.21
Age							
< 2 years	30	112	1	17	5.85	0.74	46.07
2-5 years	95	201	14	39	1.60	0.79	3.26
6-17 years	55	174	1	37	16.64	2.22	124.49
18-34 years	21	87	18	81	1.11	0.54	2.28
35-64 years	17	129	15	111	0.97	0.46	2.05
≥ 65 years	2	11	1	16	3.33	0.26	42.21
Chief Complaint							
Runny nose	9	49	5	16	0.50	0.14	1.78
Sore throat	56	188	10	70	2.55	1.22	5.33
Ear pain	77	143	15	57	3.27	1.66	6.42
Sinus pain	12	50	11	56	1.29	0.51	3.26
Cough	67	285	9	102	3.18	1.52	6.64
Duration of chief complaint							
0 to ≤ 24 hours	87	192	10	33	1.91	0.86	4.22
>24 to ≤ 48 hours	55	167	22	93	1.58	0.89	2.82
>2 to ≤ 7 days	79	355	18	175	2.50	1.44	4.32
Chief complaint episode within last 12 months							
Yes	117	376	15	111	2.89	1.61	5.20
No or no remark	104	339	35	190	1.96	1.27	3.02
Symptom Score at Day 0							
0 to <1	71	235	14	88	2.29	1.21	4.32
1 to <2	100	353	31	174	1.82	1.16	2.87
2 to <3	42	111	5	32	3.29	1.18	9.19
3 to 4	8	15	0	1			

Time to first improvement ≤ 24 hours: Adjusted odds ratios			
Time to first improvement ≤ 24 hours	**Odds ratio Anthroposophy vs. Conventional**		
	Value	**95% Confidence interval**	
		Lower limit	**Upper limit**
All Patients: unadjusted odds ratio	2.25	1.59	3.16
Odds ratio adjusted for			
Country	2.17	1.51	3.10
Gender	2.23	1.58	3.14
Age	1.63	1.14	2.35
Chief Complaint	2.36	1.65	3.37
Duration of chief complaint	2.01	1.41	2.85
Chief complaint episode within last 12 months	2.27	1.60	3.20
Symptom Score at Day 0	2.12	1.50	3.00
Adjustment for all above factors by multiple logistic regression analysis	1.54	1.03	2.31

Time to first improvement ≤ 3 days: Subgroup analysis with unadjusted odds ratios							
Response = Time to first improvement ≤ 3 days	**Anthroposophy N**		**Conventional N**		**Odds ratio Anthroposophy vs. Conventional**		
	Respon-ders	**Patients**	**Respon-ders**	**Patients**	**Value**	**95% CI**	
						Lower limit	**Upper limit**
All Patients	523	715	172	301	2.04	1.54	2.71
Country							
Germany	279	362	50	100	3.36	2.12	5.34
Austria	88	101	35	57	4.25	1.93	9.37
Netherlands	96	152	66	104	0.99	0.59	1.66
United Kingdom	26	52	21	40	0.90	0.40	2.06
USA	34	48	0	0			
Gender							
Male	244	333	72	121	1.87	1.21	2.89
Female	279	382	100	180	2.17	1.50	3.14
Age							
< 2 years	82	112	9	17	2.43	0.86	6.87
2-5 years	168	201	28	39	2.00	0.91	4.41
6-17 years	135	174	18	37	3.65	1.75	7.63
18-34 years	59	87	51	81	1.24	0.66	2.34
35-64 years	72	129	56	111	1.24	0.75	2.06
≥ 65 years	6	11	10	16	0.72	0.15	3.43
Chief Complaint							
Runny nose	31	49	10	16	1.03	0.32	3.32
Sore throat	139	188	39	70	2.25	1.27	4.00
Ear pain	118	143	39	57	2.18	1.08	4.41
Sinus pain	32	50	31	56	1.43	0.66	3.13
Cough	203	285	53	102	2.29	1.44	3.65
Duration of chief complaint							
0 to ≤ 24 hours	158	192	23	33	2.02	0.88	4.63
>24 to ≤ 48 hours	131	167	62	93	1.82	1.03	3.21
2 to ≤ 7 days	233	355	87	175	1.93	1.34	2.79
Chief complaint episode within last 12 months							
Yes	287	376	62	111	2.55	1.64	3.97
No or no remark	236	339	110	190	1.67	1.15	2.41
Symptom Score at Day 0							
0 to <1	177	235	48	88	2.54	1.52	4.25
1 to <2	248	353	106	174	1.52	1.04	2.22
>2 to <3	85	111	18	32	2.54	1.11	5.80
3 to 4	12	15	0	1			

Time to first improvement ≤ 3 days: Adjusted odds ratios			
Time to first improvement ≤ 3 days	**Odds ratio Anthroposophy vs. Conventional**		
	Value	**95% Confidence interval**	
		Lower limit	**Upper limit**
All Patients: unadjusted odds ratio	2.04	1.54	2.71
Odds ratio adjusted for			
Country	1.98	1.48	2.66
Gender	2.04	1.53	2.70
Age	1.62	1.20	2.19
Chief Complaint	2.02	1.51	2.70
Duration of chief complaint	1.91	1.43	2.55
Chief complaint episode within last 12 months	1.98	1.49	2.64
Symptom Score at Day 0	1.92	1.44	2.56
Adjustment for all above factors by multiple logistic regression analysis	1.61	1.16	2.22

Time to complete recovery

Time to complete recovery					
	Anthroposophy N=715		**Conventional N=301**		**Mann-Whitney U-test**
≤ 1 day	16	2.2%	0	0.0%	p = 0.1691
> 1 day to 2 days	23	3.2%	10	3.3%	
> 2 days to 3 days	37	5.2%	12	4.0%	
> 3 days to 4 days	50	7.0%	13	4.3%	
> 4 days to 5 days	39	5.5%	17	5.6%	
> 5 days to 6 days	32	4.5%	5	1.7%	
> 6 days to 7 days	13	1.8%	9	3.0%	
> 7 days	505	70.6%	235	78.1%	
Total	715	100.0%	301	100.0%	

Chief complaint remission, Symptom Score, quality of life

Chief Complaint remission rates, Symptom Score outcomes							
	Anthroposophy N=715			Conventional N=301			Fisher's exact test
Chief complaint remission rate	N with CC Rem.*	N with CC** at Day 0	% Remission	N with CC Rem.*	N with CC** at Day 0	% Remission	
-Day 7							
Runny nose	25	49	51.0%	6	16	37.5%	p = 0.3988
Sore throat	121	187	64.7%	36	69	52.2%	p = 0.0826
Ear pain	117	143	81.8%	34	57	59.6%	p = 0.0018
Sinus pain	21	50	42.0%	26	56	46.4%	p = 0.6980
Cough	56	284	19.7%	18	101	17.8%	p = 0.7693
Total	340	713	47.7%	120	299	40.1%	p = 0.0319
-Day 14, cumulative							
Runny nose	31	49	63.3%	13	16	81.3%	p = 0.2294
Sore throat	158	187	84.5%	48	69	69.6%	p = 0.0121
Ear pain	133	143	93.0%	45	57	78.9%	p = 0.0102
Sinus pain	36	50	72.0%	46	56	82.1%	p = 0.2498
Cough	159	284	56.0%	47	101	46.5%	p = 0.1056
Total	517	713	72.5%	199	299	66.6%	p = 0.0588
-Day 28, cumulative							
Runny nose	39	49	79.6%	12	16	75.0%	p = 0.7325
Sore throat	175	187	93.6%	60	69	87.0%	p = 0.1205
Ear pain	139	143	97.2%	50	57	87.7%	p = 0.0137
Sinus pain	44	50	88.0%	48	56	85.7%	p = 0.7809
Cough	214	284	75.4%	73	101	72.3%	p = 0.5950
Total	611	713	85.7%	243	299	81.3%	p = 0.0874
Symptom Score (0-4)	Mean	SD	N	Mean	SD	N	
Day 0	1.3	0.7	714	1.2	0.6	295	
Day 7	0.3	0.4	635	0.5	0.6	262	
Day 14	0.2	0.4	453	0.3	0.5	211	
Day 28	0.2	0.4	225	0.2	0.4	145	
	SRM		N	SRM		N	
Difference: Day 0 – Day 7	1.25		635	1.00		257	
Difference: Day 0 – Day 14	1.43		453	1.29		209	
Difference: Day 0 – Day 28	1.57		225	1.67		143	
	Median (95%-CI)		p	Median (95%-CI)		p	
Difference: Day 0 – Day 7	1.00 (0.90-0.96)		<0.0001	0.70 (0.60-0.78)		<0.0001	
Difference: Day 0 – Day 14	1.09 (0.98-1.02)		<0.0001	0.90 (0.83-1.00)		<0.0001	
Difference: Day 0 – Day 28	1.20 (1.00-1.10)		<0.0001	1.03 (0.92-1.13)		<0.0001	

*N with CC Remission: Chief Complaint severity: not present. **N with CC at Day 0: Chief Complaint severity at Day 0: mild, moderate, severe, or very severe.

Quality of life outcomes							
	Anthroposophy N=715			**Conventional N=301**			
SF-12 Summary Score	Mean	SD	N	Mean	SD	N	
Day 0	32.2	5.8	162	33.5	6.5	165	
Day 7	33.9	5.8	195	35.3	6.5	182	
Day 14	37.7	6.2	156	38.4	6.8	149	
Day 28	38.8	5.2	103	39.5	5.7	108	
	SRM		N	SRM		N	**Mann-Whitney U-test**
Difference: Day 0 – Day 7	0.32		137	0.30		142	
Difference: Day 0 – Day 14	0.97		104	0.89		114	p = 0.6967
Difference: Day 0 – Day 28	1.09		75	0.94		83	
KINDL Summary Score	Mean	SD	N	Mean	SD		
Day 0	44.9	6.9	223	43.4	5.6	57	p = 0.0745
Day 7	45.3	5.8	256	44.9	7.3	58	
Day 14	47.8	4.9	194	47.5	7.3	49	
Day 28	48.5	3.8	87	46.3	7.1	27	
	SRM		N	SRM		N	
Difference: Day 0 – Day 7	0.04		142	0.27		40	
Difference: Day 0 – Day 14	0.48		101	0.74		36	p = 0.2272
Difference: Day 0 – Day 28	0.62		52	0.33		18	

SRM: Standardized Response Mean (47): ($Mean_{pre\text{-}post}$ / $SD_{pre\text{-}post}$)

Patient satisfaction

Patient satisfaction					
	Anthroposophy N=715		Conventional N=301		Mann-Whitney U-test
Satisfaction with treatment, cumulative Day 1-28	N	%	N	%	
Very satisfied	452	63.2%	146	48.5%	
Satisfied	223	31.2%	134	44.5%	
Neutral	25	3.5%	12	4.0%	
Dissatisfied	12	1.7%	7	2.3%	p < 0.0001
Very dissatisfied	0	0.0%	2	0.7%	
No remark	3	0.4%	0	0.0%	
Total	715	100.0%	301	100.0%	
Satisfaction with doctor, cumulative Day 1-28	N	%	N	%	
Very satisfied	500	69.9%	182	60.5%	
Satisfied	196	27.4%	106	35.2%	
Neutral	14	2.0%	8	2.7%	p = 0.0028
Dissatisfied	5	0.7%	3	1.0%	
Very dissatisfied	0	0.0%	2	0.7%	
No remark	0	0.0%	0	0.0%	
Total	715	100.0%	301	100.0%	
Would you choose this therapy again for your problem?	N	%	N	%	**Fisher's exact test**
Yes (continuously during the study)	684	95.7%	251	83.4%	
No (continuously during the study)	16	2.2%	18	6.0%	
Yes and no at different follow-ups	15	2.1%	32	10.6%	
Total	715	100.0%	301	100.0%	
Yes (continuously during the study)	684	95.7%	251	83.4%	
No (continuously during the study) or yes and no at different follow-ups	31	4.3%	50	16.6%	p < 0.0001
Total	715	100.0%	301	100.0%	
Would you choose this health care provider again?					
Yes (continuously during the study)	707	98.9%	290	96.3%	
No (continuously during the study)	4	0.6%	4	1.3%	
Yes and no at different follow-ups	4	0.6%	7	2.3%	
Total	715	100.0%	301	100.0%	
Yes (continuously during the study)	707	98.9%	290	96.3%	
No (continuously during the study) or yes and no at different follow-ups	8	1.1%	11	3.7%	p = 0.0101
Total	715	100.0%	301	100.0%	

Satisfaction with treatment*: Subgroup analysis with unadjusted odds ratios:							
	Anthroposophy N		Conventional N		Odds ratio Anthroposophy vs. Conventional		
	Satisfied patients*	Patients	Satisfied patients*	Patients	Value	95% CI Lower limit	95% CI Upper limit
All Patients	371	715	113	301	1.79	1.36	2.36
Country							
Germany	209	362	51	100	1.31	0.84	2.05
Austria	79	101	34	57	2.43	1.19	4.94
Netherlands	38	152	14	104	2.14	1.09	4.20
United Kingdom	18	52	14	40	0.98	0.41	2.34
USA	27	48	0	0			
Gender							
Male	173	333	46	121	1.76	1.15	2.70
Female	198	382	67	180	1.81	1.26	2.61
Age							
< 2 years	57	112	2	17	7.77	1.70	35.58
2-5 years	133	201	12	39	4.40	2.10	9.22
6-17 years	96	174	11	37	2.91	1.35	6.26
18-34 years	36	87	37	81	0.84	0.46	1.55
35-64 years	45	129	46	111	0.76	0.45	1.28
≥ 65 years	4	11	5	16	1.26	0.25	6.36
Chief Complaint							
Runny nose	23	49	10	16	0.53	0.17	1.69
Sore throat	107	188	28	70	1.98	1.13	3.46
Ear pain	84	143	17	57	3.35	1.74	6.47
Sinus pain	15	50	30	56	0.37	0.17	0.83
Cough	142	285	28	102	2.62	1.60	4.30
Duration of chief complaint							
0 to ≤ 24 hours	128	192	13	33	3.08	1.44	6.58
>24 to ≤ 48 hours	93	167	43	93	1.46	0.88	2.43
>2 to ≤ 7 days	150	355	57	175	1.51	1.04	2.21
Chief complaint episode within last 12 months							
Yes	204	376	41	111	2.02	1.31	3.13
No or no remark	167	339	72	190	1.59	1.11	2.29
Symptom Score at Day 0							
0 to <1	134	235	28	88	2.84	1.69	4.77
1 to <2	168	353	70	174	1.35	0.93	1.95
2 to <3	60	111	13	32	1.72	0.77	3.82
3 to 4	9	15	0	1			

* Satisfied patients: Patient satisfaction with the treatment = very satisfied all evaluable follow-ups (2 missings permitted)

Satisfaction with treatment: Adjusted odds ratios			
Very satisfied with the treatment at all evaluable follow-ups (2 missings permitted)	**Odds ratio Anthroposophy vs. Conventional**		
	Value	**95% Confidence interval**	
		Lower limit	**Upper limit**
All Patients: unadjusted odds ratio	1.79	1.36	2.36
Odds ratio adjusted for			
Country	1.58	1.16	2.14
Gender	1.79	1.36	2.36
Age	1.54	1.15	2.07
Chief Complaint	1.79	1.35	2.37
Duration of chief complaint	1.66	1.25	2.20
Chief complaint episode within last 12 months	1.76	1.33	2.32
Symptom Score at Day 0	1.76	1.33	2.33
Adjustment for all above factors by multiple logistic regression analysis	1.39	0.98	1.95

Would you choose this therapy again for your problem?*: Subgroup analysis with unadjusted odds ratios							
Choose-therapy patients*	Anthroposophy		Conventional		Odds ratio Anthroposophy vs. Conventional		
	N		N				
	Choose-therapy patients*	Patients	Choose-therapy patients*	Patients	Value	95% CI	
						Lower limit	Upper limit
All Patients	684	715	251	301	4.40	2.74	7.04
Country							
Germany	355	362	88	100	6.92	2.65	18.08
Austria	100	101	54	57	5.56	0.56	54.71
Netherlands	135	152	82	104	2.13	1.07	4.25
United Kingdom	47	52	27	40	4.53	1.46	14.08
USA	47	48	0	0			
Gender							
Male	317	333	105	121	3.02	1.46	6.25
Female	367	382	146	180	5.70	3.01	10.77
Age							
< 2 years	110	112	10	17	38.50	7.04	210.66
2-5 years	196	201	34	39	5.76	1.58	20.98
6-17 years	170	174	28	37	13.66	3.94	47.38
18-34 years	79	87	72	81	1.23	0.45	3.37
35-64 years	117	129	95	111	1.64	0.74	3.64
≥ 65 years	11	11	12	16			
Chief Complaint							
Runny nose	46	49	15	16	1.02	0.10	10.58
Sore throat	183	188	60	70	6.10	2.01	18.55
Ear pain	137	143	46	57	5.46	1.91	15.59
Sinus pain	46	50	51	56	1.13	0.29	4.45
Cough	272	285	79	102	6.09	2.95	12.57
Duration of chief complaint							
0 to ≤ 24 hours	191	192	28	33	34.11	3.84	302.74
>24 to ≤ 48 hours	159	167	82	93	2.67	1.03	6.89
>2 to ≤ 7 days	333	355	141	175	3.65	2.06	6.46
Chief complaint episode within last 12 months							
Yes	361	376	94	111	4.35	2.10	9.04
No or no remark	323	339	157	190	4.24	2.27	7.94
Symptom Score at Day 0							
0 to <1	228	235	69	88	8.97	3.62	22.23
1 to <2	335	353	150	174	2.98	1.57	5.65
2 to <3	105	111	26	32	4.04	1.20	13.55
3 to 4	15	15	0	1			

Choose-therapy patients*: Patients responding “yes” to question “Would you choose this therapy again for the problem?” at all evaluable follow-ups (2 missings permitted)

Subgroup analysis: Would you choose this therapy again for your problem? Adjusted odds ratios			
Would you choose this therapy again for the problem: Yes at all evaluable follow-ups (2 missings permitted) -	**Odds ratio Anthroposophy vs. Conventional**		
	Value	**95% Confidence interval**	
		Lower limit	**Upper limit**
All Patients: unadjusted odds ratio	4.40	2.74	7.04
Odds ratio adjusted for			
Country	3.56	2.18	5.82
Gender	4.36	2.72	6.98
Age	3.83	2.33	6.31
Chief Complaint	4.58	2.84	7.40
Duration of chief complaint	3.98	2.47	6.41
Chief complaint episode within last 12 months	4.29	2.66	6.90
Symptom Score at Day 0	4.60	2.86	7.41
Adjustment for all above factors by multiple logistic regression analysis	3.54	2.13	5.90

Summary of adjusted odds ratios for patient outcomes

Summary of adjusted odds ratios after multiple logistic regression			
Adjusted odds ratios (produced by using multiple logistic regression analysis) by country, gender, age, chief complaint, duration of chief complaint, episode of chief complaint within the last 12 months prior start of study and symptom score at day 0	**Odds ratio Anthroposophy vs. Conventional**		
	Value	**95% Confidence interval**	
		Lower limit	**Upper limit**
Time to first improvement ≤ 1 day	1.54	1.03	2.31
Time to first improvement ≤ 3 days	1.61	1.16	2.22
Response rate Day 7	1.50	1.07	2.11
Response rate Day 14	1.29	0.82	2.00
Response rate Day 28	0.87	0.45	1.69
Complete recovery rate Day 7	1.05	0.72	1.54
Complete recovery rate Day 14	1.35	0.98	1.86
Complete recovery rate Day 28	1.18	0.82	1.71
Very satisfied with the treatment at all evaluable follow-ups (2 missings permitted)	1.39	0.98	1.95
Would you choose this therapy again for the problem?: Yes at all evaluable follow-ups (2 missings permitted)	3.54	2.13	5.90

Adverse Events, Adverse Drug Reactions

Adverse Events: relationship with investigational medication				
	Anthroposophy N=715		**Conventional N=301**	
Patients with adverse events				
Probable	9	1.3%	16	5.3%
Possible	10	1.4%	2	0.7%
Improbable	7	1.0%	10	3.0%
Unable to evaluate	13	1.8%	5	1.7%
No relationship	97	13.6%	19	7.0%
Total	136	19.0%	52	16.9%

Adverse Events with no relationship with investigational medication: reported causes				
	Anthroposophy N=97		**Conventional N=19**	
Reports of causes*				
Concomitant illness	97	93.3%	16	88.9%
Concomitant medication	1	1.0%	0	0.0%
Other known cause	6	5.8%	2	11.1%
Total number of reports	104	100.0%	18	100.0%

*Multiple responses at different follow-up interviews possible

Adverse Drug Reactions*					
	Anthroposophy N=715		**Conventional N=301**		**Fisher's exact test**
Patients with Adverse Drug Reactions	19	2.7%	18	6.0%	p = 0.0157
Severity					
Mild (no impairment of the normal daily activities)	17	2.4%	12	4.0%	
Moderate (impairment of the normal daily activities)	1	0.1%	3	1.0%	
Severe (complete impairment of the normal daily activities)	1	0.1%	3	1.0%	p = 0.0805
Total	19	2.7%	18	6.0%	
Necessary actions					
None	8	1.1%	12	4.0%	
Dose reduction of investigational medication	4	0.6%	0	0.0%	
Withdrawal of investigational medication	4	0.6%	4	1.3%	
Temporary withdrawal of investigational medication	0	0.0%	0	0.0%	
Admit to hospital	0	0.0%	0	0.0%	
Therapeutic counteractions	1	0.1%	2	0.7%	
Change of concomitant medication	0	0.0%	0	0.0%	
Others	2	0.3%	0	0.0%	
Total	19	2.7%	18	6.9%	
Outcome					
AE subsided	18	2.5%	12	4.0%	
AE still being treated	0	0.0%	1	0.3%	
Uncertain, AE still under observation	1	0.1%	5	1.7%	
Patient lost to follow-up	0	0.0%	0	0.0%	
Patient alive, but with permanent health damage	0	0.0%	0	0.0%	
Patient died	0	0.0%	0	0.0%	
Total	19	2.7%	18	6.9%	
Occurrence in adults and children					
Children aged 0-17 years	10/487	2.1%	2/91	2.2%	p = 1.0000
Adults aged ≥ 18 years	9/227	4.0%	16/192	7.7%	p = 0.0654

* Adverse Drug Reaction: Adverse Event with Relationship with study medication = probable or possible, according to patient response

Adverse Drug Reaction*: Subgroup analysis with unadjusted odds ratios							
	Anthroposophy		Conventional		Odds ratio Anthroposophy vs. Conventional		
	N		N				
	Patients without ADR*	Patients	Patients without ADR*	Patients	Value	95% CI	
						Lower limit	Upper limit
All Patients	696	715	283	301	2.33	1.21	4.50
Country							
Germany	353	362	88	100	5.35	2.18	13.09
Austria	96	101	54	57	1.07	0.25	4.64
Netherlands	151	152	102	104	2.96	0.26	33.08
United Kingdom	50	52	39	40	0.64	0.06	7.33
USA	46	48	0	0			
Gender							
Male	325	333	116	121	1.75	0.56	5.46
Female	371	382	167	180	2.63	1.15	5.98
Age							
< 2 years	108	112	17	17			
2-5 years	199	201	39	39			
6-17 years	170	174	35	37	2.43	0.43	13.78
18-34 years	83	87	77	81	1.08	0.26	4.46
35-64 years	124	129	103	111	1.93	0.61	6.07
≥ 65 years	11	11	12	16			
Chief Complaint							
Runny nose	48	49	15	16	3.20	0.19	54.32
Sore throat	180	188	67	70	1.01	0.26	3.91
Ear pain	141	143	56	57	1.26	0.11	14.16
Sinus pain	49	50	52	56	3.77	0.41	34.91
Cough	278	285	93	102	3.84	1.39	10.61
Duration of chief complaint							
0 to ≤ 24 hours	186	192	31	33	2.00	0.39	10.36
>24 to ≤ 48 hours	162	167	90	93	1.08	0.25	4.62
>2 to ≤ 7 days	347	355	162	175	3.48	1.41	8.56
Chief complaint episode within last 12 months							
Yes	367	376	103	111	3.17	1.19	8.41
No or no remark	329	339	180	190	1.83	0.75	4.47
Symptom Score at Day 0							
0 to <1	233	235	85	88	4.11	0.68	25.03
1 to <2	341	353	164	174	1.73	0.73	4.09
2 to <3	106	111	27	32	3.93	1.06	14.54
3 to 4	15	15	1	1			

Patients without ADR = No Adverse Drug Reaction (Adverse Event with Relationship with study medication = probable or possible, according to patient response) reported on Day 0-28

Adverse Drug Reactions* in Anthroposophy Group: details						
Pat. no.**	**Decode of adverse event**	**Intensity**	**Duration in days**	**Relationship with invest. medication**	**Necessary actions**	**Outcome**
1	Nasal congestion	Mild	<1	Probable	Others	AE subsided
2	Condition aggravated	Mild	1	Possible	None	AE subsided
2	Fever	Mild	1	Possible	None	AE subsided
3	Self-criticism	Mild	2	Possible	None	AE subsided
4	Nausea	Mild	4	Probable	Withdrawal of investigational medication	AE subsided
5	Cramp abdominal	Mild	<1	Possible	Dose reduction of investigational medication	AE subsided
5	Vomiting	Mild	<1	Possible	Dose reduction of investigational medication	AE subsided
6	Diarrhoea	Mild	1	Possible	Withdrawal of investigational medication	AE subsided
7	Eyelid oedema	Mild	3	Probable	Withdrawal of investigational medication	AE subsided
8	Restlessness marked	Mild	8	Possible	Withdrawal of investigational medication	AE subsided
9	Rash	Mild	>7	Possible	None	Uncertain, AE still under observation
10	Gastro-intestinal disorder NOS	Mild	8	Probable	None	AE subsided
11	Restlessness marked	Mild	8	Possible	None	AE subsided
12	Rash	Mild	4	Possible	Therapeutic counteractions	AE subsided
13	Mouth dry	Mild	4	Possible	Others	AE subsided
14	Abdominal pain upper	Mild	<1	Probable	None	AE subsided
15	Sleep difficult	Severe	2	Probable	Dose reduction of investigational medication	AE subsided
16	Injection site reaction	Mild	1	Probable	Dose reduction of investigational medication	AE subsided
17	Dry lips	Mild	4	Possible	None	AE subsided
18	Concentration impaired	Moderate	5	Probable	Dose reduction of investigational medication	AE subsided
18	Feeling bad	Moderate	5	Probable	Dose reduction of investigational medication	AE subsided
18	Urine abnormal	Moderate	5	Probable	Dose reduction of investigational medication	AE subsided
19	Change in bowel habits	Mild	11	Probable	None	AE subsided

* Adverse Drug Reaction: Adverse Event with Relationship with study medication = probable or possible, according to patient response. **Each patient with a an Adverse Drug Reaction is allocated a number.

Adverse Drug Reactions* in Conventional Group: details						
Pat. no.**	**Decode of adverse event**	**Intensity**	**Duration in days**	**Relationship with invest. Medication (name if stated)**	**Necessary actions**	**Outcome**
1	Diarrhoea	Moderate	?	Probable	None	AE subsided
1	Vaginitis	Mild	15 d	Probable	Therapeutic counteractions	AE still being treated
1	Itching	Mild	?	Probable	None	AE subsided
2	Appetite Decreased	Severe	6 d	Probable	None	AE subsided
3	Tremor	Mild	4 d	Probable	None	AE subsided
4	Gastro-Intestinal Disorder NOS	Mild	On-going	Probable (Doxycycline)	None	Uncertain, AE still under observation
5	Nausea	Severe	1 d	Probable	Withdrawal of investigational medication	AE subsided
5	Tooth Ache	Severe	1 d	Probable	Withdrawal of investigational medication	AE subsided
5	Vomiting	Severe	1 d	Probable	Withdrawal of investigational medication	AE subsided
6	Diarrhoea	Mild	4d	Probable	Withdrawal of investigational medication	AE subsided
7	Diarrhoea	Severe	On-going	Probable	None	Uncertain, AE still under observation
8	Diarrhoea	Mild	On-going	Probable (Optipect)	None	Uncertain, AE still under observation
9	Taste Bitter	Mild	On-going	Probable	None	Uncertain, AE still under observation
10	Taste Bitter	Mild	On-going	Probable	None	Uncertain, AE still under observation
11	Restlessness marked	Moderate	1 d	Probable (Optipect)	Withdrawal of investigational medication	AE subsided
11	Nausea	Moderate	1 d	Probable (Optipect)	Withdrawal of investigational medication	AE subsided
12	Gastro-Intestinal Disorder NOS	Mild	<1 d	Probable	None	AE subsided
13	Diarrhoea	Mild	1 d	Probable	None	AE subsided
14	Hoarseness	Mild	?	Probable	None	AE subsided
15	Diarrhoea	Mild	6 d	Probable	Therapeutic counteractions	AE subsided
16	Nasal congestion	Moderate	1 d	Possible (Spasmalgine)	Withdrawal of investigational medication	AE subsided
17	Acne	Mild	3 d	Possible (Ibuprofen)	None	AE subsided
18	Diarrhoea	Mild	1 d	Probable	None	AE subsided

*Adverse Drug Reaction: Adverse Event with Relationship with study medication = probable or possible, according to patient response. **Each patient with a an Adverse Drug Reaction is allocated a number.

Serious Adverse Events

Serious Adverse Events: relationship with investigational medication				
Patients with serious Adverse Events	**Anthroposophy N=715**		**Conventional N=301**	
Probable	0	0.0%	0	0.0%
Possible	0	0.0%	0	0.0%
Improbable	2	0.3%	0	0.0%
Unable to evaluate	0	0.0%	0	0.0%
No relationship	2	0.3%	3	1.0%
Total	4	0.6%	3	1.0%

Serious Adverse Events: details						
Patient No*	**Decode of adverse event**	**Intensity**	**Relationship with investigational medication**	**Cause**	**Necessary actions**	**Outcome**
	Anthroposophy Group					
1	Fracture of patella	Severe	No relationship	Concomitant illness	Admit to hospital	AE still being treated
2	Asthma	Severe	Improbable	Other known cause	Admit to hospital	AE subsided
2	Mesenteric adenitis	Severe	Improbable	Other known cause	Admit to hospital	AE subsided
3	Gastroenteritis	Severe	No relationship	Concomitant illness	Admit to hospital	AE subsided
3	Hypovolaemia	Severe	No relationship	Concomitant illness	Admit to hospital	AE subsided
3	Vomiting	Severe	No relationship	Concomitant illness	Admit to hospital	AE subsided
3	Fever	Severe	No relationship	Concomitant illness	Admit to hospital	AE subsided
4	Meningitis**	Severe	No relationship	Concomitant illness	Admit to hospital	AE subsided
	Conventional group					
5	Arthroscopy of knee	Severe	No relationship	Concomitant illness	Admit to hospital	AE subsided
6	Emotional lability	Severe	No relationship	Concomitant illness	Admit to hospital	AE still being treated
7	Tonsillectomy	Severe	No relationship	Concomitant illness	Admit to hospital	AE subsided

*Each patient with a Serious Adverse Events is allocated a number.
** Name: suspected meningitis (German: Verdacht auf Meningitis). Comments: Suspicion of meningitis not confirmed.