Annals of Internal Medicine | ORIGINAL RESEARCH

Acupuncture in Patients With Seasonal Allergic Rhinitis

A Randomized Trial

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Background: Acupuncture is frequently used to treat seasonal allergic rhinitis (SAR) despite limited scientific evidence.

Objective: To evaluate the effects of acupuncture in patients with SAR.

Design: Randomized, controlled multicenter trial. (ClinicalTrials.gov: NCT00610584)

Setting: 46 specialized physicians in 6 hospital clinics and 32 private outpatient clinics.

Patients: 422 persons with SAR and IgE sensitization to birch and grass pollen.

Intervention: Acupuncture plus rescue medication (RM) (cetirizine) (n = 212), sham acupuncture plus RM (n = 102), or RM alone (n = 108). Twelve treatments were provided over 8 weeks in the first year.

Measurements: Changes in the Rhinitis Quality of Life Questionnaire (RQLQ) overall score and the RM score (RMS) from baseline to weeks 7 and 8 and week 16 in the first year and week 8 in the second year after randomization, with predefined noninferiority margins of −0.5 point (RQLQ) and −1.5 points (RMS).

Results: Compared with sham acupuncture and with RM, acupuncture was associated with improvement in RQLQ score (sham vs. acupuncture mean difference, 0.5 point [97.5% CI, 0.2 to 0.8 point; $P < 0.001$]; RM vs. acupuncture mean difference, 0.7 point [97.5% CI, 0.4 to 1.0 point; $P < 0.001$]) and RMS (sham vs. acupuncture mean difference, 1.1 points [97.5% CI, 0.4 to 1.9 points; $P < 0.001$]; RM vs. acupuncture mean difference, 1.5 points [97.5% CI, 0.8 to 2.2 points; $P < 0.001$]). There were no differences after 16 weeks in the first year. After the 8-week follow-up phase in the second year, small improvements favoring real acupuncture over the sham procedure were noted (RQLQ mean difference, 0.3 point [95% CI, 0.03 to 0.6 point; $P = 0.032$]; RMS mean difference, 1.0 point [95% CI, 0.2 to 1.9 points; $P = 0.018$]).

Limitation: The study was not powered to detect rare adverse events, and the RQLQ and RMS values were low at baseline.

Conclusion: Acupuncture led to statistically significant improvements in disease-specific quality of life and antihistamine use measures after 8 weeks of treatment compared with sham acupuncture and with RM alone, but the improvements may not be clinically significant.

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Allergic rhinitis (AR) affects an estimated 16% of U.S. children (1), and $1.2 billion is spent annually in the United States on medication and preventive measures (2). Despite advances in treatment and consensus guidelines for management of the condition (3), many patients seek complementary and alternative therapies for their symptoms. The estimated lifetime prevalence of complementary and alternative medicine (CAM) use among patients with AR ranges from 27% to 46% (4, 5), and acupuncture is used by about 18% of patients with AR (4, 5).

Evidence for the efficacy of acupuncture for AR is limited. A pilot study suggested that a combination of acupuncture and Chinese herbal medicine was superior to sham acupuncture and placebo herbal medicine for AR (6), and a large pragmatic trial showed that adjunctive acupuncture therapy was associated with clinically relevant benefits in patients with AR (7). However, whether acupuncture has any apparent effect on AR remains unclear (8, 9).

We designed a trial to assess the short-, mid-, and long-term effects of acupuncture on disease-specific quality of life and the need for antihistamine medication in patients with seasonal AR (SAR). We hypothesized that, compared with sham acupuncture and rescue medication (RM) (cetirizine) and with RM alone, acupuncture with RM would lead to improved disease-specific quality of life and reduce the overall need for antihistamines.

METHODS

Design Overview

Details of the study protocol have been described previously (10). We designed a multicenter trial that randomly assigned patients to 8 weeks of acupuncture plus RM, penetrating sham acupuncture plus RM, or RM alone (**Figure 1**), and we assessed SAR outcomes at the end of treatment (7 to 8 weeks), 8 weeks after treatment (at 16 weeks), and after an 8-week period starting at the onset of birch pollen flow in the year after randomization. Patients initially randomly assigned to RM alone received 12 sessions of real acupuncture between weeks 8 and 16 so that

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Context

Many patients with seasonal allergic rhinitis seek nonallopathic treatment for symptom relief.

Contribution

This trial shows small improvements in measures of rhinitis-specific quality of life and antihistamine use after 8 weeks of acupuncture.

Caution

The improvements were statistically significant but may not be clinically significant.

Implication

Acupuncture seemed useful for patients with seasonal allergic rhinitis, but the observed improvements may not be clinically significant and the mechanism of any possible effect is not yet known.

—The Editors

all trial groups would receive some form of acupuncture (real or sham). Rescue medication was added to acupuncture and sham acupuncture to provide patients a therapeutic option if acupuncture failed. We measured outcomes at 16 weeks to assess maintenance of any effect of acupuncture after the end of treatment, and we measured outcomes in the allergy season of the year after the intervention to test the claim that acupuncture can have long-term effects on SAR rather than just temporarily alleviating symptoms (11).

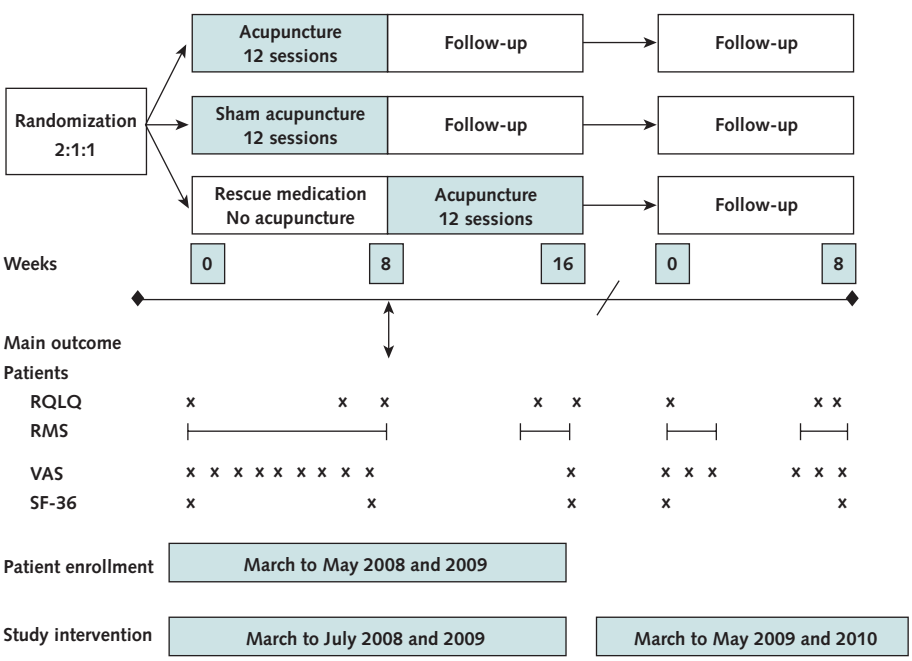
The randomization schedule was generated using DatInf RandList, version 1.2 (DatInf, Tübingen, Germany), at the University of Hamburg, Hamburg, Germany. We stratified randomization by center in blocks of 8 by using a 2:1:1 allocation ratio (acupuncture, sham acupuncture, and RM, respectively) to enhance recruitment and patient adherence by allowing more patients to receive acupuncture. An independent clinical trials unit (KKS Charité) implemented the allocation schedule using a centralized telephone randomization procedure. Patients, trial statisticians, outcome assessors, data entry personnel, and the funder were blinded to treatment assignment throughout the study.

This study followed the Declaration of Helsinki Good Clinical Practice guidelines for trial conduct and included an external audit. All study participants provided written informed consent and were not reimbursed for participating in the study. The study protocol was approved by the appropriate ethical review boards. No amendments were made after trial commencement.

Patients

About 80% of participants were recruited at the start of birch pollen season via newspaper articles about the use of acupuncture or CAM for AR; the remaining 20% were patients recruited by physicians from the trial centers. Patients were primarily screened over the telephone by mem-

Figure 1. **Study design.**



Baseline in the second-year follow-up started at birch pollen flow onset. RMS = rescue medication score; RQLQ = Rhinitis Quality of Life Questionnaire; SF-36 = Short Form-36 Health Survey; VAS = visual analog scale.

bers of the study team and were then referred to the study physicians to complete enrollment.

Inclusion criteria were SAR diagnosed by an allergologist; IgE positivity to grass and birch pollen (by either a result of at least a 3-mm wheal on a skin-prick test or specific IgE level of at least 0.7 kU/L [fluorescent enzyme immunoassay; Phadia, Freiburg, Germany]); age 16 to 45 years; moderate to severe SAR of at least 2 years' duration; moderate SAR symptoms during the previous year, defined as symptoms rated between 40 and 80 mm on a visual analog scale (VAS); no contraindications to cetirizine as antiallergic medication; and ability to complete a symptom diary, including recording RM use. Exclusion criteria were perennial AR, allergic asthma, moderate to severe atopic dermatitis, autoimmune disorders, severe chronic inflammatory diseases, history of anaphylactic reactions, hypersensitivity to cetirizine or related drugs, specific immunotherapy during the past 3 years or planned in the next 2 years, pregnancy or breastfeeding, previous acupuncture treatment for SAR, and any CAM use.

Interventions

We developed the trial interventions in a consensus process using a Delphi approach with experienced acupuncture experts. Acupuncture was administered in outpatient clinics by conventionally trained physicians (67% with postgraduate specialization, such as internal or family medicine) with additional extensive acupuncture training (median, 500 hours [interquartile range, 350 to 1000 hours]) and experience (mean, 14 years in practice) who were also trained in sham acupuncture and were instructed to deliver both in the same context and with the same behaviors. Treatments (real and sham) were administered in 12 sessions over 8 weeks (2 sessions in each of the first 4 weeks and 1 each in weeks 5 through 8), with needle retention time between 20 and 30 minutes in each session. No other Chinese medicine interventions were applied.

Technical details of real acupuncture are provided in **Appendix 1** (available at www.annals.org). We instructed physicians to achieve "de qi" (an irradiating feeling considered to indicate effective needling), if possible. Needles were manually stimulated at least once each session. Needle type, length, and diameter were not predefined. Patients randomly assigned to sham acupuncture were needled in at least 5 of 7 predefined nonacupuncture points bilaterally, with only superficial insertion of needles (maximum 20 mm in length). Needle type and diameter were not defined (10). De qi and manual stimulation of the needles were avoided. We did not assess crossover in acupuncture type (that is, failure to achieve manual stimulation or de qi in real acupuncture participants). Both interventions used sterile, disposable, single-use needles.

All patients could receive up to 2 doses of cetirizine per day. If SAR symptoms were not adequately controlled with cetirizine, participants could be treated with an oral corticosteroid. The use of other antiallergic medication was prohibited. Patients were instructed to precisely document the use of all antiallergic medications in their diaries.

We assessed patient beliefs about assigned treatment after the third real or sham acupuncture intervention (**Appendix 1**).

Outcome Measurements

Primary trial outcomes were change in symptoms and change in need for medication between baseline and the end of treatment. We assessed symptoms by using the Rhinitis Quality of Life Questionnaire (RQLQ), which has 28 questions in 7 domains (activity limitation, sleep problems, nose symptoms, eye symptoms, other symptoms, practical problems, and emotional function) ranked from 0 (no impairment) to 6 (severe impairment) (12). Medication need was measured using an RM score (RMS), comprising the weekly sum of daily assessments (cetirizine, 10 mg/d, or equivalent [1 point]; cetirizine, 20 mg/d, or equivalent [2 points]; and any form of systemic steroids for SAR [3 points]) (daily range, 0 to 3; weekly range, 0 to 21) (13). Secondary outcomes included proportion of responders, defined as patients with a decrease in RQLQ score (mean scores at weeks 7 and 8) of at least 0.5 point compared with baseline; change in symptoms, assessed using a VAS (0 to 100 mm) for overall SAR symptom severity and for nasal, eye, pharyngeal, and common symptoms; and health-related quality of life, assessed with a German version of the Short Form-36 Health Survey (SF-36) (14, 15).

We evaluated primary and secondary outcomes by using patient questionnaires (RQLQ, VAS, and SF-36) and diaries (RMS). The first questionnaire and diary were given to patients by study physicians; patients completed the baseline questionnaire before randomization and mailed the symptom diary in a sealed envelope at the completion of the 8-week observation period. Questionnaires and diaries for additional observation periods were mailed by the study office and returned by participants in sealed envelopes.

Adverse events (AEs) were actively assessed by trial physicians using a list at each session and were also reported by patients at the end of week 8.

Statistical Analysis

We based our sample size calculation on RQLQ data from our previous trial (7); no previous data on RMS were available for trial planning purposes. Using nQuery Advisor, version 4.0 (16), and assuming a power of 80% and a common SD of 1.1 (data from previous trial [7]), we calculated that a sample of 328 patients (164 in the acupuncture group, 82 in the sham acupuncture group, and 82 in the RM group) would enable detection of a difference in RQLQ score at or beyond a noninferiority threshold of 0.5 point (a previously reported minimum clinically important difference [12]) in a 1-sided test with a 2.5% significance level. Assuming a dropout rate of approximately 20%, we sought to enroll 400 patients.

Primary analyses were done on the data of all randomly assigned patients. For each of the 2 primary outcomes, we performed a multilevel analysis of covariance with baseline value, region, and year of randomization as covariates (fixed effects) and study center as the random effect. We based end-of-treatment values for RQLQ score on the mean scores at 7 and 8 weeks after randomization.

Study nurses contacted patients directly to obtain missing data from questionnaires and diaries. We imputed isolated missing baseline RQLQ items on the basis of the other items of the same question complex. Missing values of the primary outcome were multiply imputed (**Appendix 1**).

Our analyses were hierarchical (17, 18). We designed the analysis to prove superiority of acupuncture in at least 1 of the 2 primary outcome measures. If acupuncture was superior in one of the primary end points, it was necessary to show at least noninferiority in the other end point because RQLQ score and RMS were not independent (RM might decrease SAR scores, and vice versa). We therefore started with noninferiority tests of change in RQLQ score and concluded that real acupuncture was noninferior if the left limit of the covariance-based, 2-sided 95% CI surrounding the between-group difference between real and sham acupuncture was greater than the noninferiority margin of −0.5 point (12). If we showed noninferiority, we repeated the analysis for the RMS outcome using a noninferiority margin of −1.5 points. This threshold was chosen on the basis of a review that we performed of unpublished RQLQ and RMS data suggesting a rough equivalence of scales at a ratio of 1:3, so the RQLQ threshold of 0.5 point translated to an RMS threshold of 1.5 points. If this procedure also showed noninferiority, we tested for superiority and concluded that real acupuncture was superior to sham acupuncture if at least one of the Bonferroni-adjusted, analyses of covariance–based, 2-sided 97.5% CIs surrounding the between-group difference in RQLQ score and RMS was completely greater than zero. Finally, we repeated these procedures for comparisons of acupuncture with RM. Logistic regression was used to compare the proportion of responders between groups. We also performed sensitivity analyses using different methods of modeling (**Appendix 1**).

Exploratory analyses for all secondary outcomes and for the comparison of sham acupuncture with RM were done using similar models. We used the baseline in year 1 to calculate changes in outcomes at 8 weeks in year 2. All analyses were done using PASW Statistics 18 (SPSS, Chicago, Illinois) and SAS, version 9.2 (SAS Institute, Cary, North Carolina).

Role of the Funding Source

The study was funded by a grant from the German Research Foundation, which had requested a randomized trial that included a sham control group and a hierarchical test procedure with a noninferiority and superiority procedure for the comparisons of acupuncture with sham acupuncture and acupuncture with RM alone. All other decisions on design; data collection, analysis, and interpretation; and publication were the complete responsibility of the authors.

RESULTS

Between March and May in 2008 and 2009, 1588 patients with SAR were contacted by telephone, 559 were assessed for eligibility, and 422 were randomly assigned (212 to the acupuncture group, 102 to the sham acupuncture group, and 108 to the RM group) and treated between March and July of both years (**Figure 2**). Six patients had missing follow-up RQLQ values, and 14 had missing follow-up RQLQ and RMS values that we multiply imputed. Fifteen patients (9 in the acupuncture group, 4 in the sham acupuncture group, and 2 in the RM group) received acupuncture after week 16 in the first year and before the 8-week follow-up in the second year.

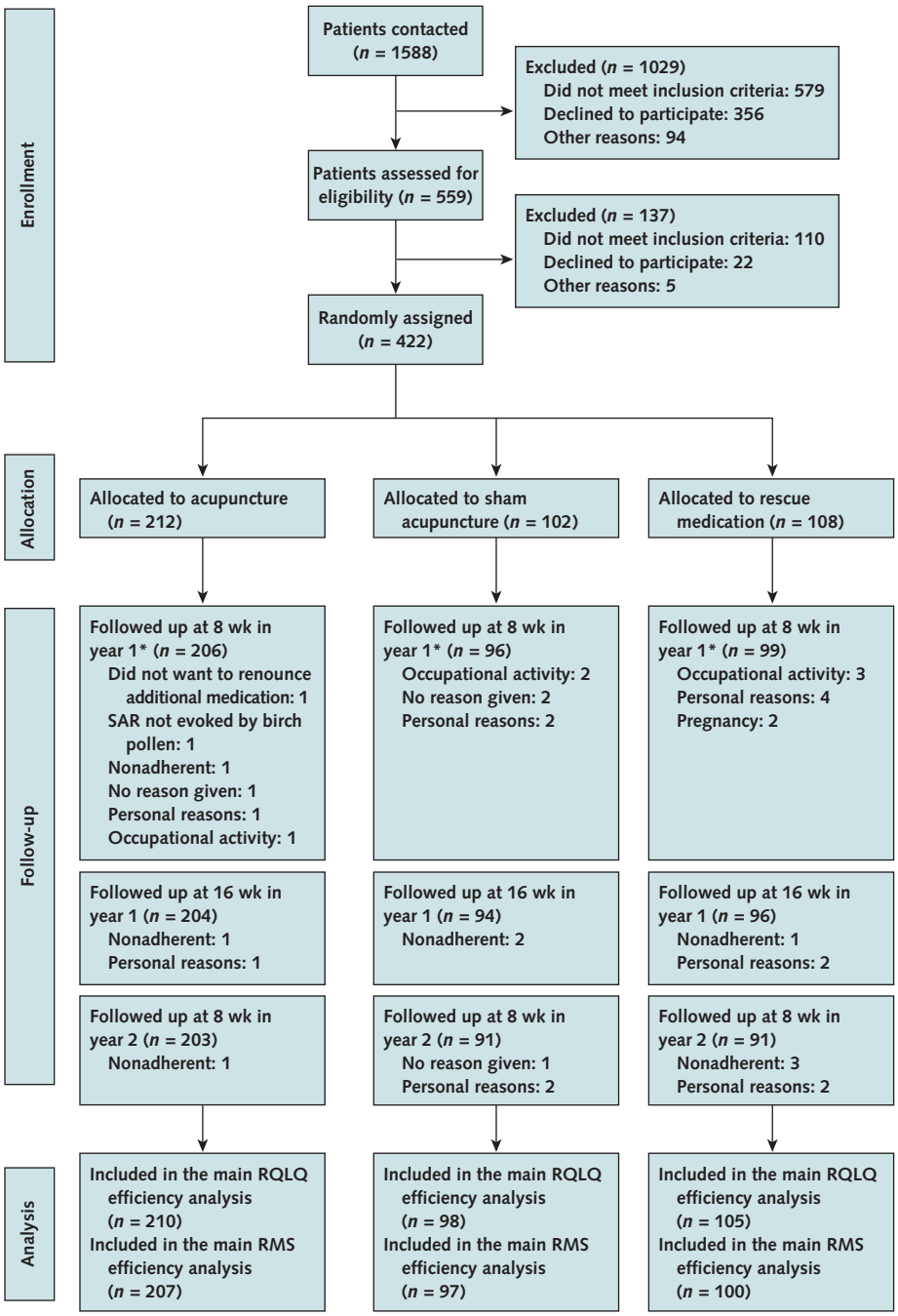
Overall, baseline characteristics were similar among the 3 study groups (**Table 1**). Patients in the acupuncture group started with slightly higher mean RQLQ and lower mean RMS values, and a lower proportion of patients in the sham acupuncture group had high expectations that the intervention would be effective (**Table 1** and **Figure 3**).

Forty-six physicians in 6 hospitals and 32 private outpatient clinics each treated a median of 8 patients (range, 2 to 30 patients). In the acupuncture group, 94% of patients received 12 sessions and 5% received fewer than 10 sessions. In the sham acupuncture group, 91% of patients received 12 sessions and 8% received fewer than 10 sessions. Patients receiving real acupuncture were treated with a mean of 16 needles (range, 9 to 25 needles), and patients receiving sham acupuncture were treated with a mean of 10 needles (range, 4 to 14 needles). Mean needle retention time was 24 minutes in both acupuncture groups. In the first 8 weeks, the proportion of patients who used any cetirizine was 71% in the real acupuncture group, 76% in the sham acupuncture group, and 83% in the RM group. Oral steroids were used by 3 patients (1 in each group). Twenty-seven patients (16 in the acupuncture group, 4 in the sham acupuncture group, and 7 in the RM group) used antiallergic medication (mostly topical steroids and cromoglicic acid on fewer than 12 days) not permitted in the trial.

Beliefs about treatment in the real and sham acupuncture groups were generally high and similar (**Appendix 1**), but recipients of real acupuncture rated the question, "How confident do you feel that acupuncture can alleviate your complaint?," higher than did recipients of sham acupuncture ($P = 0.016$).

After 7 to 8 weeks, RQLQ score decreased by 0.5 point (97.5% CI, 0.2 to 0.8 point) more and RMS decreased by 1.1 points (97.5% CI, 0.4 to 1.9 points) more with real acupuncture than with sham acupuncture; RQLQ score decreased by 0.7 point (97.5% CI, 0.4 to 1.0 point) more and RMS decreased by 1.5 points (97.5% CI,

Figure 2. **Study flow diagram.**



All patients with available baseline data were included in the analyses. RMS = rescue medication score; RQLQ = Rhinitis Quality of Life Questionnaire; SAR = seasonal allergic rhinitis.

* Missing outcome values were imputed on the basis of baseline values. No patient is excluded because of missing outcome values.

0.8 to 2.2 points) more with real acupuncture than with RM (**Table 2**). Findings were similar in a longitudinal analysis with all available data and in all other sensitivity analyses. Interaction tests did not reveal any relationship between study outcome and baseline data or between study outcome and belief in treatment (**Appendix 1**). The proportion of treatment responders was 71% for acupuncture, 56% for sham acupuncture ($P = 0.006$), and 44% for RM ($P < 0.001$). Patients also had greater improvements in VAS symptom scores and the SF-36 physical component scale (but not the mental component scale) with real acupuncture than with sham acupuncture and with RM.

Table 1. **Baseline Characteristics**

Characteristic	All Patients (n = 422)	Acupuncture (n = 212)	Sham Acupuncture (n = 102)	Rescue Medication (n = 108)
Female, *n (%)*	251 (59.5)	130 (61.3)	65 (63.7)	56 (51.9)
Mean age (SD), *y*	33.0 (7.8)	33.4 (7.5)	33.0 (8.2)	32.2 (8.1)
Mean BMI (SD), *kg/m²*	23.7 (3.4)	23.4 (3.2)	24.2 (3.9)	23.8 (3.3)
Mean duration of SAR (SD), *y*	17.9 (9.3)	18.4 (8.9)	18.1 (10.2)	16.8 (9.2)
Duration of SAR in previous year, *n (%)*				
2–5 mo	265 (62.8)	133 (62.7)	59 (57.8)	73 (67.6)
6–8 mo	157 (37.2)	79 (37.3)	43 (42.2)	35 (32.4)
CAM treatment in past 12 mo, *n (%)*	30 (7.3)	15 (7.1)	5 (5.1)	10 (9.4)
Prior acupuncture treatment, *n (%)*	89 (21.1)	50 (23.6)	17 (16.7)	22 (20.4)
Prior specific immunotherapy, *n (%)*	33 (7.8)	15 (7.1)	14 (13.7)	4 (3.7)
Mean RQLQ overall score (SD)*	2.5 (1.2)	2.7 (1.2)	2.3 (1.1)	2.5 (1.2)
Mean RMS (SD)*	2.6 (3.3)	2.3 (3.3)	2.6 (3.3)	3.2 (3.3)
Mean VAS score (SD), *mm**				
Overall symptoms	46.5 (26.5)	48.9 (26.5)	43.6 (26.1)	44.2 (26.5)
Eye symptoms	38.5 (28.5)	41.6 (29.6)	34.8 (25.4)	35.6 (28.6)
Nasal symptoms	49.4 (28.9)	51.4 (28.8)	45.6 (28.2)	48.9 (29.7)
Pulmonary symptoms	21.1 (25.1)	19.7 (23.6)	23.8 (25.8)	21.5 (27.2)
Pharyngeal symptoms	24.5 (26.7)	24.1 (25.5)	25.3 (28.6)	24.3 (27.5)
Mean SF-36 score (SD)†				
Physical health	50.2 (6.9)	49.9 (7.5)	50.5 (6.1)	50.3 (6.4)
Mental health	46.1 (9.2)	46.1 (9.3)	45.7 (9.1)	46.4 (9.3)
High expectations for acupuncture efficacy, *n (%)*	340 (82.1)	178 (84.8)	71 (72.5)	91 (85.9)
Year of recruitment, *n (%)*				
2008	165 (39.1)	84 (39.6)	39 (38.2)	42 (38.9)
2009	257 (60.9)	128 (60.4)	63 (61.8)	66 (61.1)
Study center region, *n (%)*				
Bavaria	146 (34.6)	71 (33.5)	36 (35.3)	39 (36.1)
Berlin/Brandenburg	239 (56.6)	123 (58.0)	56 (54.9)	60 (55.6)
North Rhine-Westphalia	8 (1.9)	4 (1.9)	2 (2.0)	2 (1.9)
Saxony	29 (6.9)	14 (6.6)	8 (7.8)	7 (6.5)

BMI = body mass index; CAM = complementary and alternative medicine; RMS = rescue medication score; RQLQ = Rhinitis Quality of Life Questionnaire; SAR = seasonal allergic rhinitis; SF-36 = Short Form-36 Health Survey; VAS = visual analog scale.
* Lower value indicates better status.
† Higher value indicates better status.

Between-group differences in change were generally smaller and no longer statistically significant at 16 weeks (**Table 2**). Patients in the RM group who received acupuncture between weeks 9 and 16 showed improvements after treatment that were similar to those in the real and sham acupuncture groups at week 16, with no demonstrable between-group differences (**Figure 3**).

Compared with first-year baseline, we saw statistically significantly greater improvements in RQLQ score (mean difference, 0.3 point [95% CI, 0.03 to 0.6 point]; P = 0.032) and RMS (mean difference, 1.0 point [95% CI, 0.2 to 1.9 points]; P = 0.018) in the acupuncture group than in the sham acupuncture group (but not the RM group) 8 weeks after the onset of birch pollen season in the postrandomization year, with no further treatment after the first year (**Table 2** and **Figure 3**). Changes within each domain of RQLQ and VAS score are shown in **Appendix Tables 1** to **3** (available at www.annals.org).

There were 157 AEs among 133 patients during weeks 1 to 16 in the first year (39% in the acupuncture group, 37% in the sham acupuncture group, and 23% in the RM group). Most (67%) were hematoma or inconsequential bleeding (62%, 77%, and 68% of all AEs in the acupuncture, sham acupuncture, and RM groups, respectively) or pain (24% [29%, 13%, and 14% of all AEs in the acupuncture, sham acupuncture, and RM groups, respectively]). None of the AEs led to clinically relevant disease or was treated in the hospital. Five serious AEs occurred among 5 patients (adnexal tumor and appendicitis in a patient in the acupuncture group and Bartholin gland abscess, tibia and fibula fracture, and vertebral fracture among patients in the RM group); none was related to the study intervention.

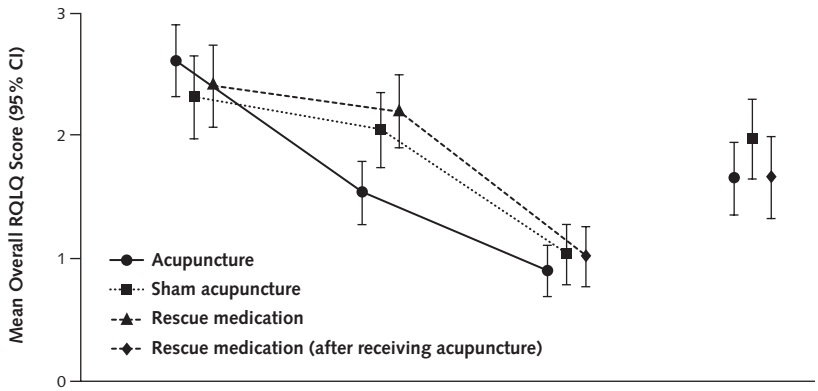
DISCUSSION

In this randomized trial of acupuncture for SAR, acupuncture led to improvements in disease-specific quality of life and antihistamine use after 8 weeks of treatment compared with sham acupuncture. However, the CIs surrounding the estimates of improvement included values that were less than predefined thresholds for clinically important differences, so the clinical significance of the findings is uncertain. There were no between-group differences in responses at 16 weeks, and acupuncture led to greater improvements than sham acupuncture (but not RM) after the 8-week follow-up phase in the second year, with CIs

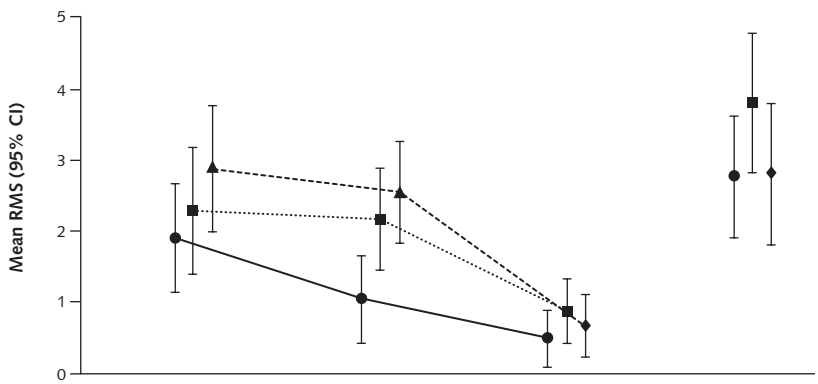
that again included differences of uncertain clinical significance.

We searched MEDLINE, the Cochrane Library, EMBASE, and CAMbase through March 2012 using the term *acupuncture and seasonal allergic rhinitis* to identify all trials evaluating the use of acupuncture for SAR. Five trials (6, 7, 19–21) were identified, but none compared real acupuncture with both sham acupuncture and RM and they were characterized by important differences—namely, lack of a consensus-based definition of intervention, a semistandardization of intervention, and a clearly defined RM. To date, 3 trials have been published comparing acupuncture and sham acupuncture interventions in SAR (19–21). In 1 trial, there was a significant difference favoring acupuncture (21), whereas in the 2 other trials there were no significant differences between the intervention groups. In contrast to our trial, none of the previous trials reported a significant difference in medication scores. Another pragmatic trial reported that acupuncture in addition to routine care was beneficial and cost-effective for treating AR (22). Because of a current lack of a validated standard RMS in SAR, we preferred an RMS that has previously been used successfully (13). None of the previous studies used the RQLQ as the main outcome measure. Study de-

Figure 3. **RQLQ and RMS values at baseline, in weeks 7 and 8 of the first year, in weeks 15 and 16 of the first year, and in weeks 7 and 8 of the second year.**



Patients, *n*	Baseline, Year 1	Weeks 7 and 8, Year 1	Weeks 15 and 16, Year 1	Weeks 7 and 8, Year 2
Acupuncture	210	210	189	177
Sham acupuncture	98	98	88	83
Rescue medication	105	105	90	83



Patients, *n*	Baseline, Year 1	Weeks 7 and 8, Year 1	Weeks 15 and 16, Year 1	Weeks 7 and 8, Year 2
Acupuncture	207	207	192	184
Sham acupuncture	97	97	90	83
Rescue medication	100	100	93	84

Means and 95% CIs are adjusted for baseline value, study center, region, and year of randomization. Baseline means are not adjusted for baseline values. RMS = rescue medication score; RQLQ = Rhinitis Quality of Life Questionnaire.

Table 2. **Primary and Secondary Outcomes***

Outcome	Mean Change From Baseline (95% CI)			Acupuncture vs. Sham Acupuncture		Acupuncture vs. Rescue Medication	
	Acupuncture† (*n* = 212)‡	Sham Acupuncture§ (*n* = 102)‡	Rescue Medication and Acupuncture‖ (*n* = 108)‡	Difference (95% CI)	*P* Value	Difference (95% CI)	*P* Value
RQLQ score¶**							
Year 1, weeks 7 to 8††	−1.0 (−1.3 to −0.7)	−0.5 (−0.8 to −0.2)	−0.3 (−0.6 to −0.02)	−0.5 (−0.8 to −0.2)	<0.001	−0.7 (−1.0 to −0.4)	<0.001
Year 1, weeks 15 to 16	−1.6 (−1.8 to −1.4)	−1.5 (−1.7 to −1.2)	−1.5 (−1.7 to −1.3)	−0.1 (−0.4 to 0.1)	0.25	−0.1 (−0.3 to 0.1)	0.31
Year 2, weeks 7 to 8	−0.8 (−1.1 to −0.5)	−0.5 (−0.8 to −0.2)	−0.8 (−1.2 to −0.5)	−0.3 (−0.6 to −0.03)	0.032	−0.01 (−0.3 to 0.3)	0.95
RMS¶‡‡							
Year 1, weeks 7 to 8††	−1.5 (−2.2 to −0.9)	−0.4 (−1.1 to 0.3)	−0.05 (−0.8 to 0.7)	−1.1 (−1.9 to −0.4)	<0.001	−1.5 (−2.2 to −0.8)	<0.001
Year 1, weeks 15 to 16	−2.0 (−2.4 to −1.6)	−1.6 (−2.0 to −1.1)	−1.9 (−2.3 to −1.4)	−0.4 (−0.8 to −0.03)	0.035	−0.2 (−0.6 to 0.3)	0.46
Year 2, weeks 7 to 8	0.3 (−0.5 to 1.2)	1.4 (0.4 to 2.3)	0.4 (−0.6 to 1.3)	−1.0 (−1.9 to −0.2)	0.018	−0.04 (−0.9 to 0.8)	0.93
VAS score, *mm* (overall symptoms)§§							
Year 1, weeks 7 to 8	−21.8 (−27.5 to −16.1)	−9.6 (−16.3 to −2.8)	−4.7 (−11.2 to 1.9)	−12.2 (−18.2 to −6.3)	<0.001	−17.2 (−23.0 to −11.3)	<0.001
Year 1, weeks 15 to 16	−33.6 (−38.1 to −29.1)	−29.4 (−34.6 to −24.2)	−31.9 (−37.0 to −26.7)	−4.2 (−8.7 to 0.3)	0.067	−1.8 (−6.2 to 2.7)	0.44
Year 2, weeks 7 to 8	−14.5 (−21.8 to −7.3)	−6.8 (−15.0 to 1.4)	−13.9 (−22.1 to −5.6)	−7.7 (−14.5 to −0.9)	0.026	−0.7 (−7.5 to 6.1)	0.85
SF-36 score§§							
Physical component‖ ‖							
Year 1, weeks 7 to 8	2.1 (0.7 to 3.5)	0.6 (−1.1 to 2.2)	−0.6 (−2.2 to 1.1)	1.6 (0.1 to 3.0)	0.037	2.7 (1.3 to 4.1)	<0.001
Year 1, weeks 15 to 16	3.5 (2.2 to 4.7)	3.4 (1.9 to 4.9)	3.7 (2.2 to 5.2)	0.1 (−1.3 to 1.4)	0.92	−0.3 (−1.6 to 1.1)	0.70
Year 2, weeks 7 to 8	3.2 (1.6 to 4.7)	2.5 (0.7 to 4.2)	4.1 (2.3 to 5.8)	0.7 (−0.8 to 2.2)	0.35	−0.9 (−2.4 to 0.6)	0.24
Mental component‖ ‖							
Year 1, weeks 7 to 8	2.7 (0.9 to 4.6)	1.6 (−0.6 to 3.7)	1.3 (−0.8 to 3.4)	1.2 (−0.8 to 3.1)	0.24	1.5 (−0.4 to 3.3)	0.120
Year 1, weeks 15 to 16	4.3 (2.5 to 6.1)	3.2 (1.0 to 5.3)	4.8 (2.7 to 6.9)	1.1 (−0.8 to 3.1)	0.25	−0.5 (−2.4 to 1.4)	0.60
Year 2, weeks 7 to 8	3.0 (1.0 to 5.0)	1.9 (−0.4 to 4.2)	3.4 (1.1 to 5.7)	1.1 (−1.0 to 3.1)	0.30	−0.4 (−2.4 to 1.6)	0.69

RMS = rescue medication score; RQLQ = Rhinitis Quality of Life Questionnaire; SF-36 = Short Form-36; VAS = visual analog scale.
* Results are adjusted for baseline value, study center, region, and year of randomization.
† Real acupuncture only in weeks 0 to 8 in year 1.
‡ Number shown is the number of randomly assigned patients. The number of patients in the analyses varies (RQLQ, *n* = 414; RMS, *n* = 404). See **Figure 2** for details.
§ Sham acupuncture only in weeks 0 to 8 in year 1.
‖ No acupuncture in weeks 0 to 8 followed by real acupuncture in weeks 9 to 16 in year 1.
¶ RQLQ score and RMS are primary end points. Lower values indicate better improvement.
** Assessed in the diary and questionnaire.
†† CIs shown are 2-sided, Bonferroni-adjusted 97.5% CIs.
‡‡ Assessed in the diary.
§§ Assessed in the questionnaire.
‖ ‖ Higher values indicate better improvement.

signs and methodology, including sample size and acupuncture interventions, showed great heterogeneity in all 3 trials, which may be the reason for the different outcomes. In contrast to both negative trials, a more individualized acupuncture intervention that was based on a Chinese syndrome diagnosis was used in our trial and in the other positive trial (21). This approach is more consistent with the theory of Chinese medicine.

In general, acupuncture is a relatively safe treatment (23–25) but its mechanisms of effect in AR remain speculative. A few basic studies have investigated the effect of acupuncture on itching (the main symptom of AR), and all suggest point-specific effects (26–30). Two of these studies (29, 30) evaluated the effect of acupuncture on allergen-induced and clinically relevant itching and showed point-specific effects. Further studies have shown a potential effect of acupuncture on atopic diseases via different mechanisms, including changes of the endogenous opioid peptides in the central nervous system; reduction of prostaglandin E2 levels in the brain and serum; suppression of IgE production and modulation of Th1/Th2 cell response; central influence of acupuncture stimulation with specific

activation of brain regions, including the influence of neuronal structures containing encephalin or β-endorphin (27, 31); and reduction of allergen-induced basophil activation (32).

Our study has limitations. Participants were recruited primarily through media and may not be representative of all patients with SAR. The results in 1 of the 4 questions assessing treatment beliefs showed differences between acupuncture groups. Although some degree of unblinding might have influenced the overall result (33), a major bias seems unlikely because we informed patients that 2 types of acupuncture treatment were being compared without mentioning such terms as "placebo" or "sham," because similar strategies of informed consent have been used in most previous acupuncture trials (34–38), and because post hoc analyses suggested that differences in study outcomes could not be explained by patient beliefs about treatment or other baseline differences.

The sham procedure was not an inert placebo intervention (39); however, the concepts of placebo and its specific and nonspecific effects in relation to such complex physical interventions as acupuncture are unclear (40), and no sham treatment or other sham control treatment represents a clear placebo.

Improvements in disease severity measured by the RQLQ cannot be extrapolated to duration of symptoms. However, we used several outcome variables that accurately reflect clinical changes, including overall and single–SAR symptom VAS score, and results for these secondary outcomes were congruent with those of the primary outcome.

The discontinuous nature of SAR symptoms also makes the evaluation of clinical effects difficult. We chose inclusion criteria that involved positive results on grass and birch pollen tests covering a SAR symptom phase of about 5 months. In addition, pollen exposure varies slightly at the study sites, and the pollen season in both enrollment years was over before our 16-week outcome assessment, which may explain the absence of effect of intervention at that time. We also could not control for each patient's SAR symptoms individually. However, because of the large randomization size trial, potential differences in exposure of patients between groups should have balanced out.

Finally, RM consisting of oral, second-generation, nonsedating antihistamines and oral steroids is not standard guideline treatment (3), but we chose antihistamines because they are the most widely used medication for SAR in Germany, are available over the counter, and are primarily taken on an as-needed basis.

In summary, we found that acupuncture led to statistically significant improvements in disease-specific quality of life and antihistamine use after 8 weeks of treatment compared with sham acupuncture and with RM alone, but the clinical significance of the findings remains uncertain. The effectiveness of acupuncture for SAR compared with other antiallergic interventions and the possible underlying mechanisms of any effect, including context effects, need to be addressed in further research. Because the effects of acupuncture compared with RM in this study might have been affected by patient beliefs about acupuncture (41), the effect of patient expectation should also be further investigated.

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Reproducible Research Statement: *Study protocol:* Available at http://epidemiologie.charite.de. The protocol and the predefined data analysis plan of this trial are available on request. Details of the protocol were published in reference 10. *Statistical code:* Available from Dr. Roll (e-mail, stephanie.roll@charite.de). *Data set:* Certain portions of the analytic data set are available to approved individuals through written agreements with the author or research sponsor.

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Appendix 1: Technical Details of the Trial

Real Acupuncture

All patients randomly assigned to real acupuncture were treated at 4 obligatory basic Chinese medicine acupuncture points (LI 4, LI 11, LI 20 bilaterally, and Ex-HN 3 [Yintang]), at least 3 of 8 facultative basic points (EX-HN 8 [Bitong], Gb 20, LIV 3, LU 7, ST 36, SP 6, SJ 17, or BL 13), and at least 3 additional points (10).

Assessment of Treatment Beliefs

After the third intervention, we used a tested questionnaire from previous acupuncture trials to assess treatment beliefs among patients in the acupuncture and sham acupuncture groups. The questionnaire comprises the following 4 questions, each rated on a 5-point Likert scale (42): How confident do you feel that acupuncture can alleviate your complaint? How confident would you be in recommending acupuncture to a friend suffering from similar complaints? How logical does this treatment seem to you? How successful do you think this treatment will be in alleviating other complaints? We used the information to assess whether participants correctly guessed the identity of the assigned intervention and whether outcome differences between sham and real acupuncture could be explained by those beliefs. We assessed the latter using 4 post hoc interaction tests with the actual treatment (for both RQLQ and RMS) (43). The *P* values of the interaction tests were always greater than 0.05, suggesting that the treatment effect was independent of personal appraisal of the study treatment.

Statistical Analysis

Missing Values

Missing values of the primary outcome were multiply imputed using Markov-chain Monte Carlo procedures, stratified by treatment group on the basis of the available baseline information and RQLQ and RMS follow-up scores. We performed 5000 iterations before the first imputation and 5000 iterations between successive imputations. One hundred data sets were imputed. We performed all analyses using PROC MI and PROC MIANALYZE in SAS, version 9.2.

Sensitivity Analysis

We performed different types of sensitivity analysis on the robustness of our primary results applying direct maximum likelihood method, complete case analysis, and control of additional covariates. Rescue medication use and VAS score were recorded daily and weekly, respectively, during the first 8 weeks of the study. We performed constrained longitudinal data analyses (44, 45) with all available data. When modeling longitudinal data, we applied an unstructured covariance matrix (46).

We also performed extended analyses of covariance in which we adjusted for baseline SAR severity (measured by overall VAS score) and for some variables with slight imbalances at baseline (sex, prior acupuncture treatment, and prior immunotherapy). All analyses were performed using SAS, version 9.2 (PROC MIXED), and showed effects similar to those of the primary analysis.

Appendix 2: Acknowledgment

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Participating Trial Centers and Trial Physicians

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Generation of Randomization List

We thank the Department of Medical Biometry and Epidemiology, University Medical Center Eppendorf, Hamburg, Germany.

Randomization Center and Monitoring

We thank both monitoring centers: the Coordinating Center for Clinical Studies of the Charité University Medical Center of Berlin and the Center for Clinical Studies at the Technical University of Munich.

Appendix Table 1. **Primary and Secondary Outcomes at Week 7 and 8 in the First Year***

Outcome	Mean Change From Baseline (95% CI)			Acupuncture vs. Sham Acupuncture		Acupuncture vs. Rescue Medication	
	Acupuncture† (*n* = 212)‡	Sham Acupuncture§ (*n* = 102)‡	Rescue Medication‖ (*n* = 108)‡	Difference (95% CI)	*P* Value	Difference (95% CI)	*P* Value
RQLQ score¶ ** †† ‡‡	−1.0 (−1.3 to −0.7)	−0.5 (−0.8 to −0.2)	−0.3 (−0.6 to −0.02)	−0.5 (−0.8 to −0.2)	<0.001	−0.7 (−1.0 to −0.4)	<0.001
Sleep domain	−0.6 (−0.9 to −0.4)	−0.3 (−0.6 to 0.04)	−0.2 (−0.5 to 0.1)	−0.4 (−0.6 to −0.1)	0.016	−0.4 (−0.7 to −0.2)	0.003
Non–hay fever domain	−0.6 (−0.8 to −0.3)	−0.2 (−0.5 to 0.1)	0.1 (−0.2 to 0.4)	−0.4 (−0.7 to −0.1)	0.003	−0.7 (−1.0 to −0.5)	<0.001
Practical problems domain	−1.7 (−2.1 to −1.3)	−1.2 (−1.7 to −0.7)	−0.8 (−1.2 to −0.3)	−0.5 (−0.9 to −0.1)	0.014	−0.9 (−1.3 to −0.5)	<0.001
Nasal symptoms domain	−1.1 (−1.4 to −0.8)	−0.6 (−1.0 to −0.2)	−0.3 (−0.7 to 0.1)	−0.5 (−0.8 to −0.1)	0.007	−0.8 (−1.1 to −0.5)	<0.001
Eye symptoms domain	−0.9 (−1.2 to −0.7)	−0.4 (−0.7 to −0.1)	−0.4 (−0.7 to −0.04)	−0.5 (−0.8 to −0.2)	<0.001	−0.6 (−0.9 to −0.3)	<0.001
Activities domain	−1.3 (−1.7 to −1.0)	−0.7 (−1.1 to −0.2)	−0.6 (−1.0 to −0.1)	−0.7 (−1.1 to −0.3)	<0.001	−0.8 (−1.2 to −0.4)	<0.001
RMS¶ †† ‡‡ §§	−1.5 (−2.2 to −0.9)	−0.4 (−1.1 to 0.3)	−0.05 (−0.8 to 0.7)	−1.1 (−1.9 to −0.4)	<0.001	−1.5 (−2.2 to −0.8)	<0.001
VAS score, *mm*¶ ‖‖							
Overall symptoms	−21.8 (−27.5 to −16.1)	−9.6 (−16.3 to −2.8)	−4.7 (−11.2 to 1.9)	−12.2 (−18.2 to −6.3)	<0.001	−17.2 (−23.0 to −11.3)	<0.001
Eye symptoms	−18.7 (−24.3 to −13.2)	−7.0 (−13.5 to −0.5)	−6.8 (−13.1 to −0.4)	−11.7 (−17.5 to −5.9)	<0.001	−12.0 (−17.6 to −6.3)	<0.001
Nasal symptoms	−21.5 (−27.8 to −15.1)	−10.3 (−17.8 to −2.9)	−3.7 (−11.0 to 3.6)	−11.1 (−17.7 to −4.5)	0.001	−17.8 (−24.2 to −11.4)	<0.001
Pulmonary symptoms	−6.4 (−11.2 to −1.5)	2.8 (−2.9 to 8.5)	4.3 (−1.2 to 9.9)	−9.2 (−14.1 to −4.2)	<0.001	−10.7 (−15.5 to −5.9)	<0.001
Pharyngeal symptoms	−8.6 (−13.8 to −3.5)	−1.7 (−7.7 to 4.4)	4.1 (−1.8 to 10.0)	−7.0 (−12.3 to −1.6)	0.011	−12.8 (−18.0 to −7.5)	<0.001
SF-36 score‖‖¶¶							
Physical component scale	2.1 (0.7 to 3.5)	0.6 (−1.1 to 2.2)	−0.6 (−2.2 to 1.1)	1.6 (0.1 to 3.0)	0.037	2.7 (1.3 to 4.1)	<0.001
Mental component scale	2.7 (0.9 to 4.6)	1.6 (−0.6 to 3.7)	1.3 (−0.8 to 3.4)	1.2 (−0.8 to 3.1)	0.24	1.5 (−0.4 to 3.3)	0.120

RMS = rescue medication score; RQLQ = Rhinitis Quality of Life Questionnaire; SF-36 = Short Form-36 Health Survey; VAS = visual analog scale.
* Results are adjusted for baseline value, study center, region, and year of randomization.
† Real acupuncture only in weeks 0 to 8 in year 1.
‡ Number shown is the number of randomly assigned patients. The number of patients in the analyses varies (RQLQ, *n* = 414; RMS, *n* = 404). See **Figure 2** for details.
§ Sham acupuncture only in weeks 0 to 8 in year 1.
‖ No acupuncture in weeks 0 to 8.
¶ Lower values indicate better improvement.
** Assessed in the diary and questionnaire.
†† Primary end points.
‡‡ CIs shown are 2-sided, Bonferroni-adjusted 97.5% CIs.
§§ Assessed in the diary.
‖‖ Assessed in the questionnaire in week 8.
¶¶ Higher values indicate better improvement.

Appendix Table 2. Secondary Outcomes at Week 15 and 16 in the First Year*

Outcome	Mean Change From Baseline (95% CI)			Acupuncture vs. Sham Acupuncture		Acupuncture vs. Rescue Medication	
	Acupuncture† (*n* = 212)‡	Sham Acupuncture§ (*n* = 102)‡	Rescue Medication and Acupuncture‖ (*n* = 108)‡	Difference (95% CI)	*P* Value	Difference (95% CI)	*P* Value
RQLQ score¶ **	−1.6 (−1.8 to −1.4)	−1.5 (−1.7 to −1.2)	−1.5 (−1.7 to −1.3)	−0.1 (−0.4 to 0.1)	0.25	−0.1 (−0.3 to 0.1)	0.31
Sleep domain	−1.1 (−1.3 to −0.8)	−1.1 (−1.3 to −0.8)	−1.1 (−1.4 to −0.8)	0.0 (−0.2 to 0.2)	0.97	0.03 (−0.2 to 0.3)	0.82
Non–hay fever domain	−1.2 (−1.4 to −0.9)	−1.0 (−1.3 to −0.7)	−1.0 (−1.3 to −0.7)	−0.2 (−0.4 to 0.1)	0.156	−0.1 (−0.4 to 0.1)	0.31
Practical problems domain	−2.6 (−2.9 to −2.2)	−2.5 (−2.9 to −2.1)	−2.2 (−2.6 to −1.8)	−0.1 (−0.5 to 0.3)	0.67	−0.4 (−0.8 to −0.03)	0.033
Nasal symptoms domain	−1.9 (−2.1 to −1.6)	−1.6 (−2.0 to −1.3)	−1.7 (−2.1 to −1.4)	−0.2 (−0.5 to 0.1)	0.164	−0.1 (−0.4 to 0.2)	0.41
Eye symptoms domain	−1.5 (−1.7 to −1.3)	−1.2 (−1.5 to −1.0)	−1.4 (−1.7 to −1.2)	−0.2 (−0.5 to 0.0)	0.052	−0.04 (−0.3 to 0.2)	0.75
Activities domain	−2.0 (−2.2 to −1.7)	−1.8 (−2.2 to −1.5)	−1.8 (−2.1 to −1.5)	−0.1 (−0.4 to 0.2)	0.36	−0.2 (−0.4 to 0.1)	0.30
RMS¶ ††	−2.0 (−2.4 to −1.6)	−1.6 (−2.0 to −1.1)	−1.9 (−2.3 to −1.4)	−0.4 (−0.8 to 0.01)	0.056	−0.2 (−0.6 to 0.2)	0.39
VAS score, *mm*¶ ‡‡							
Overall symptoms	−33.6 (−38.1 to −29.1)	−29.4 (−34.6 to −24.2)	−31.9 (−37.0 to −26.7)	−4.2 (−8.7 to 0.3)	0.067	−1.8 (−6.2 to 2.7)	0.44
Eye symptoms	−31.2 (−35.0 to −27.5)	−26.5 (−30.9 to −22.1)	−29.8 (−34.2 to −25.5)	−4.7 (−8.6 to −0.7)	0.020	−1.4 (−5.3 to 2.5)	0.49
Nasal symptoms	−38.0 (−42.4 to −33.6)	−32.7 (−37.9 to −27.6)	−34.9 (−40.0 to −29.8)	−5.3 (−9.9 to −0.7)	0.025	−3.1 (−7.7 to 1.5)	0.185
Pulmonary symptoms	−14.2 (−17.9 to −11.2)	−11.1 (−14.5 to −7.6)	−13.4 (−16.9 to −10.0)	−3.1 (−6.1 to −0.1)	0.041	−0.8 (−3.7 to 2.2)	0.61
Pharyngeal symptoms	−17.7 (−20.8 to −14.5)	−16.8 (−20.5 to −13.1)	−17.4 (−21.1 to −13.7)	−0.8 (−4.2 to 2.5)	0.63	−0.3 (−3.6 to 3.1)	0.88
SF-36 score‡‡ §§							
Physical component scale	3.5 (2.2 to 4.7)	3.4 (1.9 to 4.9)	3.7 (2.2 to 5.2)	0.1 (−1.3 to 1.4)	0.92	−0.3 (−1.6 to 1.1)	0.70
Mental component scale	4.3 (2.5 to 6.1)	3.2 (1.0 to 5.3)	4.8 (2.7 to 6.9)	−1.1 (−0.8 to 3.1)	0.25	−0.5 (−2.4 to 1.4)	0.60

RMS = rescue medication score; RQLQ = Rhinitis Quality of Life Questionnaire; SF-36 = Short Form-36 Health Survey; VAS = visual analog scale.
* Results are adjusted for baseline value, study center, region, and year of randomization.
† Real acupuncture only in weeks 0 to 8 in year 1.
‡ Number shown is the number of randomly assigned patients. The number of patients in the analyses varies.
§ Sham acupuncture only in weeks 0 to 8 in year 1.
‖ No acupuncture in weeks 0 to 8 followed by real acupuncture in weeks 9 to 16 in year 1.
¶ Lower values indicate better improvement.
** Assessed in the diary and questionnaire.
†† Assessed in the diary.
‡‡ Assessed in the questionnaire on week 16.
§§ Higher values indicate better improvement.

Appendix Table 3. **Secondary Outcomes at Week 7 and 8 in the Second Year***

Outcome	Mean Change From Baseline (95% CI)			Acupuncture vs. Sham Acupuncture		Acupuncture vs. Rescue Medication	
	Acupuncture† (*n* = 212)‡	Sham Acupuncture§ (*n* = 102)‡	Rescue Medication and Acupuncture‖ (*n* = 108)‡	Difference (95% CI)	*P* Value	Difference (95% CI)	*P* Value
RQLQ score¶ **	−0.8 (−1.1 to −0.5)	−0.5 (−0.8 to −0.2)	−0.8 (−1.2 to −0.5)	−0.3 (−0.6 to −0.03)	0.032	−0.01 (0.3 to −0.3)	0.95
Sleep domain	−0.4 (−0.7 to −0.1)	−0.1 (−0.5 to 0.2)	−0.4 (−0.7 to −0.04)	−0.2 (−0.5 to 0.1)	0.162	0.03 (−0.3 to 0.3)	0.84
Non–hay fever domain	−0.6 (−0.9 to −0.3)	−0.3 (−0.7 to 0.0)	−0.7 (−1.0 to −0.3)	−0.3 (−0.6 to 0.04)	0.090	0.1 (−0.2 to 0.4)	0.57
Practical problems domain	−1.6 (−2.0 to −1.2)	−1.2 (−1.7 to −0.7)	−1.4 (−1.9 to −0.9)	−0.4 (−0.8 to 0.03)	0.069	−0.2 (−0.6 to 0.3)	0.43
Nasal symptoms domain	−0.7 (−1.1 to −0.4)	−0.3 (−0.7 to 0.1)	−0.6 (−1.0 to −0.2)	−0.4 (−0.8 to −0.1)	0.019	−0.1 (−0.5 to 0.2)	0.55
Eye symptoms domain	−0.6 (−1.0 to −0.3)	−0.3 (−0.7 to 0.1)	−0.7 (−1.0 to −0.3)	−0.3 (−0.7 to 0.0)	0.049	0.02 (−0.3 to 0.4)	0.91
Activities domain	−1.3 (−1.7 to −0.9)	−1.0 (−1.4 to −0.5)	−1.3 (−1.7 to −0.8)	−0.4 (−0.8 to 0.04)	0.078	−0.1 (−0.5 to 0.3)	0.76
RMS¶ ††	0.3 (−0.5 to 1.2)	1.4 (0.4 to 2.3)	0.4 (−0.6 to 1.3)	−1.0 (−1.9 to −0.2)	0.018	−0.04 (−0.9 to 0.8)	0.93
VAS score, *mm*¶ ‡‡							
Overall symptoms	−14.5 (−21.8 to −7.3)	−6.8 (−15.0 to 1.4)	−13.9 (−22.1 to −5.6)	−7.7 (−14.5 to −0.9)	0.026	−0.7 (−7.5 to 6.1)	0.85
Eye symptoms	−13.7 (−20.4 to −7.1)	−8.1 (−15.7 to −0.5)	−14.0 (−21.6 to −6.3)	−5.7 (−12.2 to 0.9)	0.092	0.2 (−6.4 to 6.8)	0.95
Nasal symptoms	−13.4 (−20.6 to −6.2)	−4.7 (−13.0 to 3.6)	−11.1 (−19.5 to −2.8)	−8.7 (−16.0 to −1.4)	0.020	−2.3 (−9.6 to 5.0)	0.54
Pulmonary symptoms	−2.5 (−8.2 to 3.2)	2.9 (−3.6 to 9.4)	−1.2 (−7.7 to 5.3)	−5.4 (−11.0 to 0.1)	0.055	−1.3 (−6.8 to 4.3)	0.65
Pharyngeal symptoms	−5.5 (−11.1 to 0.04)	0.4 (−6.0 to 6.8)	−5.4 (−11.8 to 1.1)	6.0 (−11.6 to −0.3)	0.039	−0.2 (−5.8 to 5.5)	0.95
SF-36 score‡‡ §§							
Physical component scale	3.2 (1.6 to 4.7)	2.5 (0.7 to 4.2)	4.1 (2.3 to 5.8)	0.7 (−0.8 to 2.2)	0.35	−0.9 (−2.4 to 0.6)	0.24
Mental component scale§	3.0 (1.0 to 5.0)	1.9 (−0.4 to 4.2)	3.4 (1.1 to 5.7)	1.1 (−1.0 to 3.1)	0.30	0.4 (−2.4 to 1.6)	0.69

RMS = rescue medication score; RQLQ = Rhinitis Quality of Life Questionnaire, SF-36 = Short Form-36 Health Survey; VAS = visual analog scale.
* Results are adjusted for baseline value, study center, region, and year of randomization.
† Real acupuncture only in weeks 0 to 8 in year 1.
‡ Number shown is the number of randomly assigned patients. The number of patients in the analyses varies.
§ Sham acupuncture only in weeks 0 to 8 in year 1.
‖ No acupuncture in weeks 0 to 8 followed by real acupuncture in weeks 9 to 16 in year 1.
¶ Lower values indicate better improvement.
** Assessed in the diary and questionnaire.
†† Assessed in the diary.
‡‡ Assessed in the questionnaire in week 8 in the second year.
§§ Higher values indicate better improvement.