

Cost-effectiveness for acupuncture in seasonal allergic rhinitis: economic results of the ACUSAR trial

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ABSTRACT

Background: Allergic rhinitis (AR) is a frequent allergic disorder with a significant economic effect on health care costs and productivity.

Objective: To assess the cost-effectiveness of acupuncture for patients with seasonal AR (SAR) in Germany. **Methods:** The present analysis was part of the Acupuncture in Seasonal Allergic Rhinitis (ACUSAR) trial, a 3-arm randomized, controlled, multicenter trial in patients with SAR, comparing acupuncture plus rescue medication (RM), penetrating sham acupuncture plus RM, and a control group receiving RM alone. Measures for health economic analyses were costs and health-related quality of life. Incremental cost-effectiveness ratio was calculated for different scenarios on the duration of acupuncture effects and was expressed as costs per quality-adjusted life-year gained. The study was conducted from society's and from a third-party payer's perspective.

Results: From 422 initially randomized patients, a total of 364 patients with complete data on costs and quality of life were included in the health economic evaluation. Patients receiving acupuncture or sham acupuncture caused higher costs than patients in the RM group. Patients in the acupuncture group gained significantly more quality-adjusted life-years compared with the RM group. Depending on different scenarios, the incremental cost-effectiveness ratio for acupuncture patients was between €31,241 (approximately US \$38,569) and €118,889 (approximately US \$146,777) from society's perspective and between €20,807 (approximately US \$25,688) and €74,585 (approximately US \$92,080) from a third-party payer's perspective. **Conclusion:** Acupuncture is an effective intervention that results in improved quality of life in patients with SAR. However, in times of limited resources for health care, acupuncture for AR may not be a cost-effective intervention.

Trial Registration: clinicaltrials.gov Identifier: NCT00610584

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Introduction

Allergic rhinitis (AR) belongs to the most frequent allergic disorders and is associated with a number of symptoms that reduce the patient's quality of life (QOL).¹ The prevalence of patients with AR is up to 25% in adults.^{2,3}

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Besides the epidemiologic burden of disease, AR is further associated with a significant economic effect on health care costs and social productivity. A study published in 2003 reports annual mean total costs of €1,089 per affected child or adolescent and €1,543 per adult.⁴ Depending on the age group, the proportion of indirect costs range from 22% in children and adolescents to 58% in adult patients.⁴

Despite advances in pharmacotherapy for grass pollen allergy, including allergen immunotherapy and clearly defined guidelines,⁵ the lifetime prevalence of complementary and alternative medicine use in patients with AR ranges from 27% to 46%. Acupuncture, one kind of alternative treatment option, is used by 17% to 19% of patients with AR.^{6,7} A previous large, pragmatic, partly randomized trial by our group found that treating patients with AR with adjunctive acupuncture is associated with clinically relevant benefits and is a cost-effective option in treating AR.^{8,9} A review published in 2009 suggested that acupuncture is effective primarily in patient with persistent AR.¹⁰ However, it is unclear whether this result is similar in patients with only seasonal AR (SAR).

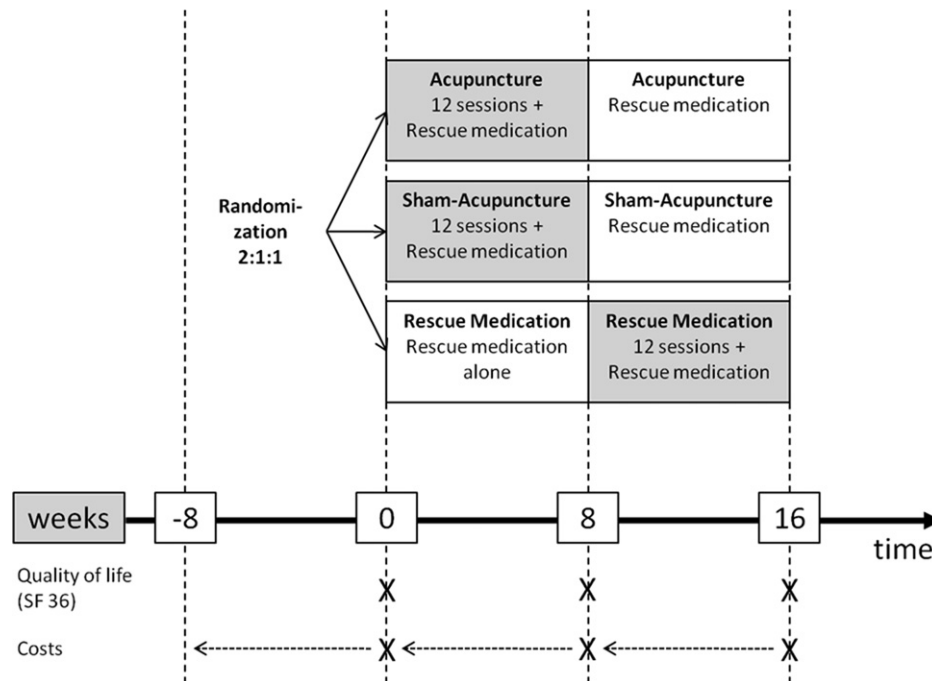


Figure 1. Study design and time points for health economic outcome measurement. SF-36 indicates Medical Outcomes Study 36-Item Short Form Health Survey.

Because the main clinical outcomes of the Acupuncture in Seasonal Allergic Rhinitis (ACUSAR) trial have been previously published elsewhere,¹¹ the objective of the economic evaluation was (1) to compare costs of the 3 groups and, in case of better outcome and higher costs in the acupuncture groups, (2) to determine the cost-effectiveness of acupuncture compared with patients without such an intervention.

Methods

Study Design and Patients

The present analyses are based on data from the ACUSAR trial (ClinicalTrials.gov registration: NCT00610584). The ACUSAR study was a 3-arm, randomized, multicenter trial comparing acupuncture plus rescue medication (RM) (acupuncture group), penetrating sham acupuncture (sham acupuncture group) plus RM, and a waiting-list control group receiving RM alone (RM group). If required, patients of all 3 groups were allowed to take up to 2 doses of second-generation oral antihistamines per day (cetirizine) as RM, which was provided by the study centers. In case the clinical symptom(s) of SAR could not be controlled sufficiently by the antihistamine treatment, medication with an oral steroid was allowed but not the use of any other antiallergic medication. All patients were instructed to precisely document the applied RM on a daily basis in a special diary. Further details of the trial protocol have been described elsewhere.¹² The first part of the study took 8 weeks, followed by an additional 8 weeks of observation during which the control patients also received acupuncture. Patients received a mean of 12 acupuncture sessions (respectively sham acupuncture sessions in the sham acupuncture group).

Patients were randomized in a 2:1:1 (acupuncture, sham acupuncture, and RM) ratio using a centralized telephone randomization procedure. A randomization list was generated with nMaster 2.0 Sample Size software (Department of Biostatistics, Christian Medical College, Tamil Nadu, India) by an independent statistician. Patients who were randomized to acupuncture and sham acupuncture arms were masked to their intervention.

The study was performed according to guidelines for clinical trials (Declaration of Helsinki, International Conference on

Harmonisation—Good Clinical Practice), including an external audit. All study participants provided written, informed consent. The study protocol was approved by the appropriate ethics review boards.

Patients between 16 and 45 years of age were included after having been clinically diagnosed as having moderate to severe SAR for at least 2 years. The main exclusion criteria were perennial AR, allergic asthma, and/or moderate to severe atopic dermatitis, autoimmune disorders, severe chronic inflammatory diseases, history of anaphylactic reactions, hypersensitivity to cetirizine or related drugs used in study, specific immunotherapy during the last 3 years or planned in the next 2 years, pregnancy or breastfeeding, previous acupuncture treatment for SAR, or any use of complementary or alternative treatment.

The relevant measures for health economic analyses and cost-effectiveness assessment, costs, and health-related QOL were documented in patient questionnaires at several time points (Fig 1).

Cost Determination

All disease-specific costs were analyzed from society's perspective, including direct and indirect costs, and from a third-party payer's perspective, restricted to direct costs. Costs were not discounted and were only considered if they were associated with SAR.

The number of acupuncture sessions were taken from physician's study case report forms. Acupuncture costs from society's perspective were €35 per session as defined in the ACUSAR investigator contract. For the third-party payer's perspective, we used the amount of €21 per acupuncture session, which is the regular reimbursement.¹³ The overall acupuncture costs were calculated by multiplying the number of acupuncture sessions with the unit costs.

Additional data on resource consumption and related cost data were taken from patient questionnaires that were completed at baseline and after 8 and 16 weeks. Outpatient costs were calculated by multiplying the documented number of physician contacts with the mean costs per visit as recommended and published by Krauth et al.¹⁴

Hospital admission costs were considered, depending on the number of hospital days. We assumed a mean diagnosis related

group base case of €2,800 in 2010¹⁵ and a mean inpatient duration of 8.1 days. The resulting daily costs of €345 were multiplied with the documented number of inpatient days.

Medication costs were valued using prices for daily defined dosages provided by the *Drug Prescription Report 2009*.¹⁶ Overall medication costs resulted by multiplying daily defined dosage prices with the number of days with drug intake. We used the same costs for both society's and a third-party payer's perspective.

Private expenditures were taken as reported by the patients but were not considered from a third-party payer's perspective. Indirect cost measurement was based on the human capital approach.¹⁷ The mean labor costs, including employers' payment to social insurances, were assumed to be €47,129 per year¹⁸; the mean number of working days per year was 230 days. Overall costs were calculated by multiplying patients' self-reported number of days off from work with €205.

Effectiveness Measurement

Effectiveness was measured in terms of health-related QOL using the Medical Outcomes Study 36-Item Short Form Health Survey.¹⁹ Patients were asked to complete this questionnaire at baseline and after 8 and 16 weeks. The QOL data were converted to health state utilities using the algorithm developed by Brazier et al.²⁰ A utility of 1 represents the perfect QOL, whereas a utility of 0 represents the absence of full QOL, often handled as equal to death. Because the analysis is based on utilities at several different time points, we used the common assumption of a linear change over time.²¹ For cost-effectiveness analysis these utilities were used to generate quality-adjusted life-years (QALYs) by adopting the area under the curve method.^{21,22}

Cost-effectiveness Assessment

The cost-effectiveness measurement was performed as a cost-utility analysis. In case of superior QOL in acupuncture or in the sham acupuncture group compared with patients in the RM group, cost-effectiveness was calculated as the relation of between-group differences in costs and differences in QALYs, the so-called incremental cost-effectiveness ratio (ICER):

The ICER can be interpreted as the additional costs for gaining one additional QALY due to the intervention compared with the control strategy. Knowing well that such a threshold does not exist in German health care decision-making as of yet, we used a threshold of €50,000 per QALY gained to reach better compar-

bootstrapped 1,000 times to obtain 1,000 means for cost and effect differences and the resulting ICERs. These bootstrapped results were transformed into net benefit values under varying threshold values and then plotted in a cost-effectiveness acceptability curve. The cost-effectiveness acceptability curve shows the probability that an intervention is cost-effective against different values of λ .²⁴

Cost-effectiveness Scenarios

Because the RM group also received acupuncture after their initial waiting time of 8 weeks, it was not possible to perform a direct group comparison after 16 weeks. For that reason we assumed 3 different scenarios:

- Base case scenario: In this most conservative scenario, we compared costs and QALYs between the groups only for the period from baseline to week 8, where a direct comparison was possible.
- Scenario 1: In this scenario it was specified that patients in the RM group did not receive acupuncture between week 8 and week 16. Therefore, we assumed that the utility trend in the RM group between baseline and 8 weeks would continue in the same way between week 8 and 16 (linear extrapolation). According to this assumption, we modeled a new utility value at 16 weeks for the RM group, whereas the 16-week utilities in the acupuncture and the sham acupuncture group were taken as reported. For costs, a comparable assumption was made. For the RM group, we modeled costs from week 8 to week 16 that are based on cost trends within that group between baseline and week 8. The costs in acupuncture and sham acupuncture patients were taken as reported. For cost-utility analysis, the group differences in costs and QALYs were thus compared during the total study duration of 16 weeks.
- Scenario 2: In this scenario it was also assumed that the RM group did not get acupuncture between week 8 and week 16. However, compared with scenario 1 we now assumed that the utility trend in RM group between 8 weeks and 16 weeks will be the same as in respective comparison groups (acupuncture respectively sham acupuncture group). On the basis of this assumption, a new utility for the time point of 16 weeks was modeled for the RM group. Again, the utilities in the acupuncture and sham acupuncture patients were taken as reported. Regarding the costs of control patients between weeks 8 and 16, we took the costs as reported subtracted by the costs of acupuncture sessions. The costs in acupuncture and sham acupuncture patients were taken as reported. For cost-utility

$$ICER = \frac{\text{mean total costs}_{\text{acupuncture OR sham-acupuncture}} - \text{mean total costs}_{\text{recue medication}}}{\text{mean QALYs}_{\text{acupuncture OR sham-acupuncture}} - \text{mean QALYs}_{\text{recue medication}}}$$

bility with other international study results. In addition, the net benefit approach was used to measure the incremental cost-effectiveness against different societal threshold values λ .²³ For a given threshold value λ , an intervention would be considered to be cost-effective if its net benefit is greater than zero.²⁴ The net benefit is defined by following relation:

$$\text{Net benefit} = \left(\lambda * \text{QALYs}_{\text{gained for acupuncture}} \right) - (\text{mean costs}_{\text{acupuncture}} - \text{mean costs}_{\text{controls}})$$

To derive cost-effectiveness acceptability curves, we used nonparametric bootstrapping.²⁵ The original sample was

analysis, the group differences in costs and QALYs were compared during the total study duration of 16 weeks.

Statistical Analysis

Initially, all health economic data were analyzed descriptively and summarized as raw means and SDs, with 95% confidence intervals (CIs). For measuring cost-effectiveness, exploratory analyses were performed by generalized linear mixed models (without the hierarchical testing procedure used for the primary medical analyses).¹² Scenario-based values on costs and QALYs used for cost-effectiveness evaluation were adjusted for center (random

Table 1
Baseline characteristics

Characteristic	Acupuncture (n = 188)	Sham acupuncture (n = 86)	Control (n = 90)
Age, mean (SD), y	33.9 (7.3)	32.5 (8.3)	32.9 (8.0)
Female, No. (%)	124 (66.0)	57 (66.3)	46 (51.1)
Total costs during 8 weeks before randomization, mean (SD), €			
Society's perspective	162.0 (1,335.7)	205.5 (829.5)	62.0 (204.5)
Third-party payer's perspective	30.9 (111.0)	18.0 (27.8)	15.3 (25.0)
Health state utility, mean (SD)	0.750 (0.118)	0.744 (0.101)	0.762 (0.117)
Recruitment region, No. (%)			
Bavaria	68 (36.2)	32 (37.2)	35 (38.9)
Berlin	103 (54.8)	46 (53.5)	47 (52.2)
Saxonia	14 (7.4)	6 (7.0)	6 (6.7)
Northrhine-Westfalia	3 (1.6)	2 (2.3)	2 (2.2)

effect), region (fixed), year (fixed), and baseline value. We used PASW statistics version 18.0.0 (SPSS Inc, Chicago, Illinois) and SAS for Windows, version 9.2 (SAS Institute Inc, Cary, North Carolina). Bootstrap analyses (as described in the "Cost-effectiveness Assessment" section) were performed in MS EXCEL 2007 (Microsoft Inc, Redmond, Washington). The significance level was predefined at $\alpha = .05$ without correction for multiple testing.

Results

Baseline Characteristics

Between March and May in both 2008 and 2009, a total of 1,588 SAR patients were contacted by telephone and 599 were assessed for eligibility to participate in the study.¹¹ A total of 422 patients were randomized into the 3 treatment arms. Complete information on resource consumption, costs, and QOL were available for 364 patients. These patients were considered in the following cost-effectiveness analyses. The proportion of female patients (62.4%) was higher compared with male patients. The mean (SD) age of all patients was 33.3 (7.7) years, with no differences between the groups.

Baseline costs between groups differed and were the lowest in the RM group (society's perspective, €62.0 [€204.5]; third party payer's perspective, €15.3 [€25.0]), followed by patients randomized to acupuncture (society's perspective, €162.0 [€1,335.7]; third party payer's perspective, €30.9 [€111.0]) and sham acupuncture (society's perspective, €205.5 [€829.5]; third party payer's perspective, €18.0 [€27.8]). This difference was primarily caused by a higher number of outpatient visits and more days of work loss in patients allocated to the acupuncture or sham acupuncture group.

Health state utility values were comparable between groups at baseline (acupuncture, 0.750 [0.118]; sham acupuncture, 0.744 [0.101]; RM, 0.762 [0.117]; Table 1).

Resource Consumption and Costs

Between baseline and week 8, nearly all patients (95.4%) allocated to the acupuncture group or to the sham acupuncture group received the intended number of 12 acupuncture or sham acupuncture sessions (mean, 11.84; 95% CI, 11.76–11.99). Within the same period, a comparable proportion of patients had outpatient visits (beside study intervention) because of their SAR in the acupuncture group (4.3%) and in sham acupuncture group (4.7%). In the RM group this proportion was larger (16.7%). No relevant differences were detected with regard to further resource consumption areas, such as medication intake, private expenditures, or SAR-related absence from work (Table 2). During the total

study duration, no hospital stays have been reported in relation to SAR.

The disease-related total costs per patient during the first 8 weeks were €427.3 (95% CI, €419.5–€435.1) in the acupuncture group, €564.2 (95% CI, €422.1–€706.3) in the sham acupuncture group, and €58.1 (95% CI, €0.0–€121.6) in the RM group from society's perspective. From a third-party payer's perspective, we found mean costs of €245.9 (95% CI, €240.8–€251.0) in the acupuncture group, €248.2 (95% CI, €246.0–€250.4) in the sham acupuncture group, and €15.5 (95% CI, €11.6–€19.4) in the RM group.

During the 8 to 16 weeks after study onset, the patients in the RM group received a mean number of 11.33 (95% CI, 10.82–11.84) acupuncture sessions. Because the acupuncture was the most relevant cost driver, RM patients, who were the only patients receiving acupuncture in this period, had the highest overall costs (society's perspective, €435.7 [95% CI, €384.0–€487.4]; third party payer's perspective, €232.4 [95% CI, 221.2–€243.6]) compared with patients originally assigned to the acupuncture or sham acupuncture group (Table 2).

Effectiveness

Eight weeks after the study onset we measured a raw health state utility of 0.798 (95% CI, 0.782–0.813) for acupuncture, 0.770 (95% CI, 0.747–0.793) for sham acupuncture, and 0.768 (95% CI, 0.747–0.789) for RM. Compared with baseline, the unadjusted utility values improved in the acupuncture group (from 0.750 to 0.798) and in the sham acupuncture group (from 0.744 to 0.770), whereas for control patients nearly no change was observed (from 0.762 to 0.768).

From weeks 8 to 16 patients allocated to the RM group also received acupuncture, resulting in a utility of 0.832 (95% CI, 0.813–0.850) in week 16. Although the acupuncture and sham acupuncture patients did not get further interventions during that time, their QOL still shows further improvement. The utilities in week 16 were 0.821 (95% CI, 0.806–0.836) for acupuncture and 0.800 (95% CI, 0.777–0.823) for sham acupuncture.

Cost-effectiveness Analyses

As described above, the unadjusted results on costs and effects were used to calculate cost-effectiveness scenarios that were adjusted for potential group differences (Table 3). Between baseline and week 8 (base case analysis) the acupuncture group had significant higher QALYs than the RM group ($P = .001$), whereas no significant differences between sham acupuncture and waiting list were observed ($P = .40$). Equal observations were made for scenario 1 and 2, in which the observational time was extended to week 16. Nevertheless, in all 3 scenarios patients receiving acupuncture or sham acupuncture accrued higher costs than control patients who received no acupuncture. These cost differences could be mainly explained by the costs for the acupuncture and sham acupuncture intervention itself.

Depending on the scenario, the ICER for acupuncture was between €31,241 (95% CI, €12,049–€96,013) and €118,889 (95% CI, €55,658–€378,600) from society's perspective and between €20,807 (95% CI, €12,856–€47,624) and €74,585 (95% CI, €45,273–€195,142) from a third-party payer's perspective (Table 4). On the basis of the most conservative base case scenario (which was restricted to an 8-week comparison) and a threshold value of €50,000 per QALY gained, the probability that additional acupuncture is worth its money is only 1.3% from society's perspective and 22.2% from a third-party payer's perspective (Figure 2). Taking into account a longer comparison period up to week 16 leads to an increase of cost-effectiveness probability. So the resulting cost-effectiveness probability range of 81.8% (scenario

Table 2

Overall and specific use and unadjusted costs from society's perspective and a third-party payer's perspective per treatment group

Variable	Acupuncture (n = 188)			Sham acupuncture (n = 86)			Rescue medication (n = 90)		
	Costs relative to all patients, mean (95% CI), €	Actual use by patients, No. (%)	Costs relative to actual use by patients, mean (95% CI), €	Costs relative to all patients, mean (95% CI), €	Actual use by patients, No. (%)	Costs relative to actual use by patients, mean (95% CI), €	Costs relative to all patients, mean (95% CI), €	Actual use by patients, No. (%)	Costs relative to actual use by patients, mean (95% CI), €
Society's Perspective									
Baseline to 8 weeks									
Acupuncture	414.2 (408.5–419.9)	188 (100)	414.2 (408.5–419.9)	418.8 (416.4–421.2)	86 (100)	418.8 (416.4–421.2)			
Outpatient visits	3.5 (0–7.4)	8 (4.3)	81.8 (4.8–158.8)	1.2 (0.0–2.4)	4 (4.7)	26.2 (19.0–34.0)	6.4 (2.9–9.9)	15 (16.7)	38.3 (26.3–50.3)
Medication	6.1 (4.3–7.9)	115 (61.2)	10.0 (7.5–12.5)	7.8 (6.0–9.6)	64 (74.4)	10.42 (8.7–12.2)	10.2 (8.2–12.2)	73 (81.1)	12.6 (10.4–14.8)
Private expenditures	2.4 (0.8–4.0)	24 (12.8)	18.9 (9.3–28.5)	1.5 (0.3–2.7)	9 (10.5)	14.6 (7.3–21.8)	2.7 (0.9–4.5)	14 (15.6)	17.6 (10.2–25.0)
Indirect costs	1.1 (0–3.3)	1 (0.5)	205.0 (205.0–205.0)	134.9 (0–275.8)	5 (5.8)	2320.6 (774.7–3866.5)	38.7 (0–101.8)	3 (3.3)	1161.7 (0–2839.9)
Total	427.3 (419.5–435.1)	188 (100)	427.3 (419.5–435.1)	564.2 (122.1–406.3)	86 (100)	564.2 (0–1985.2)	58.1 (0–121.6)	75 (83.3)	69.7 (0–145.7)
8 to 16 Weeks									
Acupuncture							396.7 (379.1–414.3)	87 (96.7)	410.3 (401.3–419.3)
Outpatient visits	2.8 (0.3–5.3)	9 (4.8)	58.3 (16.0–100.6)	0.2 (0–0.6)	1 (1.2)	16.8 (16.8–16.8)	2.6 (0–6.9)	3 (3.3)	78.2 (0–198.7)
Medication	1.4 (0.8–2.0)	48 (25.5)	5.6 (3.8–7.4)	3.4 (2.0–4.8)	34 (39.5)	8.5 (5.6–11.4)	3.3 (1.9–4.7)	40 (44.4)	7.5 (4.8–10.2)
Private expenditures	1.5 (0.5–2.5)	15 (8.0)	18.4 (8.4–28.4)	1.3 (0.3–2.3)	7 (8.1)	15.4 (9.5–21.3)	3.1 (0–7.0)	7 (7.8)	39.4 (0–85.9)
Indirect costs	10.2 (0–30.2)	1 (0.5)	1913.3 (1913.3–1913.3)				30.1 (0–80.9)	2 (2.2)	1353.0 (0–3201.3)
Total	15.9 (0–38.6)	57 (30.3)	52.4 (0–127.1)	4.8 (2.6–7.0)	34 (39.5)	12.2 (7.5–16.9)	435.7 (384.0–487.4)	88 (97.8)	445.7 (394.7–496.7)
Third-Party Payer's Perspective									
Baseline to 8 weeks									
Acupuncture	236.7 (233.4–240.0)	188 (100)	236.7 (233.4–240.0)	239.3 (237.9–240.7)	86 (100)	239.3 (237.9–240.7)			
Outpatient visits	3.1 (0–6.7)	8 (4.3)	73.6 (4.4–142.8)	1.1 (0–2.3)	4 (4.7)	23.6 (22.4–24.8)	5.3 (2.2–8.4)	14 (15.6)	33.8 (22.2–45.4)
Medication	6.1 (4.3–7.9)	115 (61.2)	10.0 (7.5–12.5)	7.8 (6.0–9.6)	64 (74.4)	10.4 (8.6–12.2)	10.2 (8.2–12.2)	73 (81.1)	12.6 (10.4–14.8)
Total	245.9 (240.8–251.0)	188 (100)	245.9 (240.8–251.0)	248.2 (246.0–250.4)	86 (100)	248.2 (246.0–250.4)	15.5 (11.6–19.4)	75 (83.3)	18.6 (13.7–23.5)
8 to 16 Weeks									
Acupuncture							226.7 (216.7–236.7)	87 (96.7)	234.5 (229.2–239.8)
Outpatient visits	1.6 (0.0–3.2)	8 (4.3)	37.4 (10.2–64.6)	0.2 (0–0.6)	1 (1.2)	15.1 (15.1–15.1)	2.4 (0–6.7)	3 (3.3)	70.4 (0–178.8)
Medication	1.4 (0.8–2.0)	48 (25.5)	5.6 (3.8–7.4)	3.4 (2.0–4.8)	34 (39.5)	8.5 (5.6–11.4)	3.3 (1.9–4.7)	40 (44.4)	7.5 (4.8–10.2)
Total	3.0 (1.2–4.8)	50 (26.6)	11.4 (5.3–17.5)	3.5 (1.9–5.1)	34 (39.5)	8.9 (5.8–12.0)	232.4 (221.2–243.6)	88 (97.8)	237.6 (228.8–246.4)

Abbreviation: CI, confidence interval.

Table 3Adjusted results used for cost-utility analyses^a

	Mean (95% CI)			P value	
	Acupuncture	Sham acupuncture	Rescue medication	Acupuncture vs control ^b	Sham acupuncture vs control ^c
Adjusted QALYs					
Base case	0.129 (0.127–0.131)	0.127 (0.125–0.129)	0.126 (0.124–0.128)	.001	.40
Scenario 1	0.265 (0.259–0.270)	0.259 (0.252–0.265)	0.254 (0.248–0.261)	<.001	.18
Scenario 2a ^d			0.255 (0.249–0.261)	.001	.29
Scenario 2b ^e			0.256 (0.250–0.261)	.001	.38
Adjusted Costs From Society's Perspective, €					
Base case	416.7 (329.9–503.5)	552.1 (449.7–654.5)	52.9 (0–154.1)	<.001	<.001
Scenario 1	425.2 (292.6–557.8)	547.9 (393.7–702.2)	101.8 (0–254.3)	<.001	<.001
Scenario 2			85.7 (0–197.4)	<.001	<.001
Adjusted Costs From a Third-Party Payer's Perspective, €					
Base case	244.2 (237.0–251.4)	248.3 (240.3–256.4)	16.0 (8.0–24.0)	<.001	<.001
Scenario 1	244.9 (235.1–254.6)	249.7 (238.3–261.2)	29.5 (18.2–40.8)	<.001	<.001
Scenario 2			22.0 (13.4–30.6)	<.001	<.001

Abbreviations: CI, confidence interval; QALY, quality-adjusted life-year.

^aAdjusted for center (random effect), region (fixed), year (fixed), and baseline value.^bP value for pairwise comparison of acupuncture vs control patients.^cP value for pairwise comparison of sham acupuncture vs control patients.^dScenario 2a is extrapolation according to acupuncture group trend.^eScenario 2b is extrapolation according to sham acupuncture group trend.

1) to 70.5% (scenario 2) from society's perspective and from 93.5 (scenario 1) to 88.7 (scenario 2) from a third-party payer's perspective.

The lowest ICER calculated for sham acupuncture was €49,161 (95% CI, €18,795–€108,245) for a 16-week time horizon in scenario 1; all other results lay clearly outside the cost-effective threshold of €50,000 per QALY, and the results were not included in the cost-effectiveness acceptability curves.

Discussion

In this study, acupuncture, in contrast to sham acupuncture, was more effective in improving QOL compared with RM patients with SAR, but in all 3 scenarios patients receiving acupuncture or sham acupuncture accrued higher costs than patients in the RM group. For the short-term observation period from baseline to week 8,

costs per QALY were far over the threshold used (threshold €50,000 per QALY gained²⁶). The findings on effectiveness, based on general health-related QOL measurements, are in concordance with the results from the main outcomes of the study (disease-specific QOL and medication intake).¹¹

The most important strengths of our study are the relatively large number of participants, the randomized design, and high-quality data due to monitoring. Although this was a randomized study, the multicenter treatment setting in outpatient practices is naturalistic for a randomized controlled trial. Limitations of the study include that the RM group also received acupuncture between weeks 8 and 16. As a result we were able to conduct a direct comparison between both intervention groups and the controls only for the period of baseline to 8 weeks. For that reason the base case scenario is the most conservative approach to our analysis. Otherwise, the approach of base case scenario assumed that all group differences in effects completely disappeared after 8 weeks. However, this assumption would not reflect the reality because after collecting the QOL data at week 16, we saw that the improvement in the acupuncture group still progresses, maybe because the end of the SAR season was reached. To get a picture about midterm effects respectively the mid-term cost-effectiveness, we decided to assume a longer comparison period as stated in our scenarios 1 and 2. Analyzing a longer-time horizon leads to another more improved interpretation of acupuncture's cost-effectiveness; however, these scenarios are also associated with a higher level of uncertainty.

Only a few studies reported cost-effectiveness data for acupuncture in AR patients. Our previous study assessed the cost-effectiveness of additional acupuncture in a usual care setting for a period of 3 months and found an ICER of €17,377 per QALY gained.⁹ That is clearly less than in our most conservative base case scenario but more comparable to the main results found in our scenarios 1 and 2 (€20,807 in third party payers perspective to €37,438 Euro in society's perspective). However, this economic evaluation included both patients with SAR and perennial AR. We assume that in SAR acupuncture effects are not so substantial because the natural course of disease will lead to a complete symptom recovery after the pollen season is finished. For Germany a recently published article reports the highest pollen concentration between March and July.²⁷ The assumption that acupuncture might be more cost-effective in treating chronic conditions is supported by a number of studies.^{28–30}

Table 4Cost differences, effect differences, and resulting ICERs^a

Variable	Mean (95% CI)	
	Acupuncture vs rescue medication	Sham acupuncture vs rescue medication
QALY Differences		
Base case	0.00306 (0.00491 to 0.0012)	0.00094 (0.00312 to –0.00124)
Scenario 1	0.01035 (0.01598 to 0.00473)	0.00448 (0.0111 to –0.00214)
Scenario 2	0.00905 (0.01414 to 0.00395)	0.00265 (0.00864 to –0.00334)
Cost Differences From Society's Perspective, €		
Base case	363.8 (454.3 to 273.3)	499.17 (605.7 to 392.7)
Scenario 1	323.3 (454.1 to 192.5)	446.11 (600.0 to 292.2)
Scenario 2	338.8 (438.8 to 238.8)	462.81 (580.4 to 345.2)
Resulting ICER From Society's Perspective per QALY Gained, €		
Base case	118,889 (55,658 to 378,600)	531,032 (12,5856 to –488,058)
Scenario 1	31,241 (12,049 to 96,013)	99,578 (26,323 to –280,126)
Scenario 2	37,438 (16,891 to 111,081)	174,645 (39,953 to –173,784)
Cost Differences From a Third-Party Payer's Perspective, €		
Base case	228.2 (234.2 to 222.3)	232.3 (239.3 to 225.4)
Scenario 1	215.4 (225.3 to 205.4)	220.2 (231.9 to 208.6)
Scenario 2	224.9 (232.6 to 217.2)	230.1 (239.1 to 221.1)
Resulting ICER From a Third-Party Payer's Perspective per QALY Gained, €		
Base case	74,585 (45,273 to 195,142)	247,149 (72,228 to –192,812)
Scenario 1	20,807 (12,856 to 47,624)	49,161 (18,795 to –108,245)
Scenario 2	24,850 (15,361 to 58,881)	86,830 (25,589 to –71,590)

Abbreviations: CI, confidence interval; ICER, incremental cost effectiveness ratio; QALY, quality-adjusted life-year.

^aNegative values result from additional costs for sham acupuncture and worse results on QALYs compared with controls.

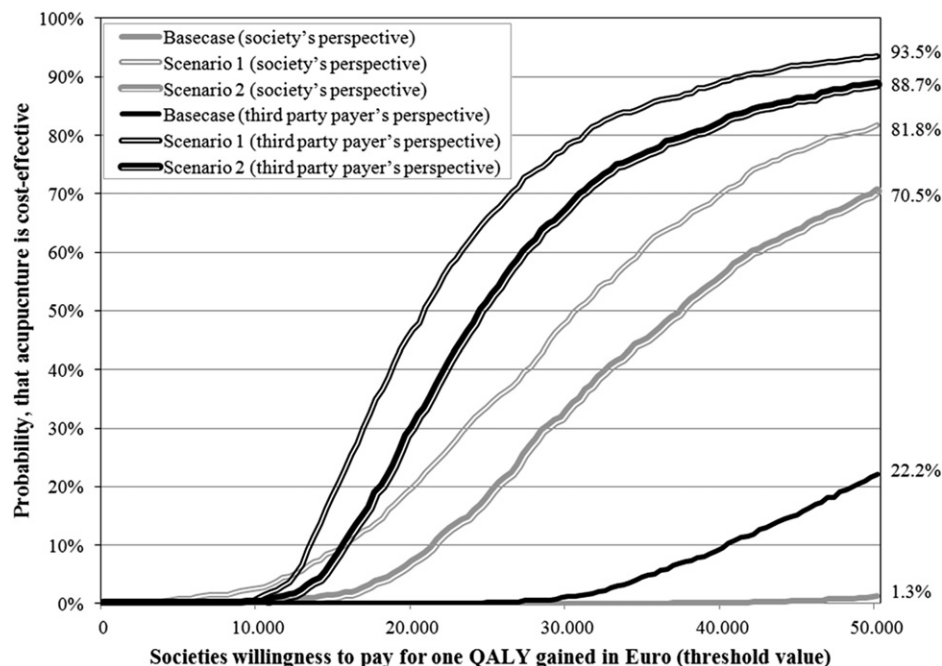


Figure 2. Cost-effectiveness acceptability curves of acupuncture vs rescue medication group. QALY indicates quality-adjusted life-year.

In our analysis we further found that the cost-effectiveness level was mainly driven by the costs of acupuncture itself. Assuming that a more widely used acupuncture would also be associated with decreasing treatment costs respectively prices, cost-effectiveness would be improved. However, this applies only if a reduced price per acupuncture session does not lead to reduced effects, which might be not the case because there is evidence from placebo research that a higher price can induce a higher placebo response³¹ and acupuncture is known to have nonspecific effects of relevant size.³²

The transferability of effectiveness results from one country to another may be subject to certain restrictions, but it is generally possible. However, the transferability of cost-effectiveness results is limited but not only in the present study.³³ The main factors for this limited transferability were found in country-specific differences in resource consumption and the resulting costs. These differences are affected by a number of influencing cofactors (demography, epidemiology, and individual patient's factors) and the overall health care system structures (eg, payment systems and health care professional incentives).

In conclusion, acupuncture is, in contrast to sham acupuncture, an effective add-on intervention that results in improved QOL in patients with SAR. However, acupuncture was not a cost-effective intervention for SAR patients, and therefore its value in times of limited health care resources remains unclear. Only under consideration of longer time horizons it might be possible that the additional acupuncture reach the international accepted cost-effectiveness criteria of €50,000 per QALY gained. Proving this assumption could be an objective for further studies.

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