GENERAL GYNECOLOGY

Acupuncture in patients with dysmenorrhea: a randomized study on clinical effectiveness and cost-effectiveness in usual care

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OBJECTIVE: To investigate the clinical effectiveness and cost-effectiveness of acupuncture in patients with dysmenorrhea.

STUDY DESIGN: In a randomized controlled trial plus non-randomized cohort, patients with dysmenorrhea were randomized to acupuncture (15 sessions over three months) or to a control group (no acupuncture). Patients who declined randomization received acupuncture treatment. All subjects were allowed to receive usual medical care.

RESULTS: Of 649 women (mean age 36.1 ± 7.1 years), 201 were randomized. After three months, the average pain intensity (NRS 0-10) was lower in the acupuncture compared to the control group: 3.1 (95% CI 2.7; 3.6) vs. 5.4 (4.9; 5.9), difference −2.3 (−2.9; −1.6); $P<.001$. The acupuncture group had better quality of life and higher costs. (overall ICER €3,011 per QALY).

CONCLUSION: Additional acupuncture in patients with dysmenorrhea was associated with improvements in pain and quality of life as compared to treatment with usual care alone and was cost-effective within usual thresholds.

Key words: acupuncture, complementary medicine, cost-effectiveness, dysmenorrhea, randomized controlled trial

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Dysmenorrhea is the leading cause of recurrent short term school absence in adolescent girls and a common problem in women of reproductive age.[1] The prevalence rates ranged from 18-81% depending on the measurement method used.[2] Chronic diseases such as dysmenorrhea that affect the working population can cause losses in productivity.[3] Nonsteroidal anti-inflammatory drugs are the initial therapy of choice in patients with primary dysmenorrhea.[1] Nevertheless, the anti-inflammatory medications are associated with a number of side effects.[4] Apart from pharmacological treatment several techniques including acupressure and acupuncture have been used.[1,5] There is some evidence that acupuncture is effective in the treatment of pain conditions like osteoarthritis of the knee or low back pain.[6,7] However, the evidence for acupuncture treatment in women with dysmenorrhea is unclear.

In Germany, acupuncture is mainly administered by physicians. Before the year 2000, acupuncture was partly paid by some health insurance companies. Under the increasing budgetary pressure the Federal Committee of Physicians and Health Insurers recommended in 2000 that large research initiatives on acupuncture should be conducted for pain syndromes.[8] Subsequently, acupuncture could only be reimbursed by insurance companies if the patients participated in 1 of the studies.

The primary objective of the present study was to investigate effectiveness and cost-effectiveness of acupuncture in addition to routine care compared to routine care alone in patients with pain due to dysmenorrhea. In addition, we investigated whether the effects of acupuncture differ in randomized and nonrandomized patients and whether treatment effects last over a longer period of time.

Materials and Methods

Design

The Acupuncture in Routine Care (ARC) Study was a multicenter randomized controlled trial plus a nonrandomized cohort. Patients who agreed to randomization were allocated to an acupuncture group that received immediate acupuncture treatment for 3 months or to a control group that received delayed acupuncture treatment after 3 months. Patients who declined to

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be randomized were included in a third arm and also received immediate acupuncture treatment (nonrandomized acupuncture group) for 3 months. The study period per patient was 6 months. The Acupuncture in Routine Care study is part of a large acupuncture research initiative of a group of social health insurance funds who provide coverage to approximately 10% of the German population. The protocol of this study was approved by the local ethics review boards, and the study itself was conducted according to common standard guidelines (Declaration of Helsinki, Good Epidemiological Practice: http://www.dundee.ac.uk/iea/GoodPract.htm). All study participants provided written, informed consent.

Patients

Patients insured by 1 of the participating social health insurance funds were recruited after contacting a participating physician due to dysmenorrhea. If a patient requested acupuncture or if the physician considered acupuncture to be a suitable treatment option the patient was informed about the study. Patients who met inclusion criteria and provided informed consent were randomized using a central telephone randomization procedure (in blocks of 10; random list generated with SAS). Patients were included in the study only if we received both the physicians' baseline questionnaire and the patients' consent form following randomization.

For inclusion in this study, the female patients had to meet the following criteria: age $\geq$ 18 years (age between menarche and menopause), primary dysmenorrhea from the start of the menarche on or secondary dysmenorrhea (for at least 12 months) with cramping pain during menstruation, written informed consent. Exclusion criteria were pain caused by inflammatory or malignant diseases.

Interventions

For participation in this study the physicians were required to hold at least an "A-diploma," a German diploma representing 140 hours of certified acupuncture education. This education and further trainings include wide variations in styles and acupuncture technique. Each patient received a maximum of 15 acupuncture sessions. To assess the effectiveness of acupuncture in general medical practice, the number of needles and the acupuncture points used were chosen at the physicians' discretion. Only needle acupuncture (with disposable 1-time needles and manual stimulation) was allowed; other forms of acupuncture treatment such as laser acupuncture were not permitted. In all 3 treatment groups, the patients were allowed to use any additional conventional treatments as needed.

In accordance with German federal regulations, the social health insurance funds covered 100% of the acupuncture costs for the patients who agreed to randomization and 90% cost for patients who participated in the study but did not agree to randomization.

Outcome measurements

Patients completed standardized questionnaires which included sociodemographic characteristics, at baseline and after 3 and 6 months. The main outcome parameter was the average pain intensity during the last menstruation before assessment measured on a numeric rating using numbers from 0 to 10 (0 described as no pain and 10 as maximal pain).[9]

As a secondary analysis we calculate responder rates. A patient with a reduction of at least 33% was considered to be a treatment responder. All patients without data were counted as nonresponders.

Secondary outcome parameters included the worst pain intensity (numeric rating scale)[9] during last menstruation and the SF-36[10] component scales and its subscores to assess health-related quality of life. Side effects were evaluated using patient and physician questionnaires after 3 months.

Statistics

A sample size of 86 patients per group will have at least 90% power to detect a difference of 1 point in the pain intensity scale between the acupuncture and the control group with an assumed common standard deviation of 2 points using a 2-sided t test with significance level .05. Sample size estimation was done in nQuery Advisor version 6.01 (Statistical Solutions, Saugees, MA).

Results of descriptive analyses at baseline are reported as means and standard deviations or frequencies and percentages. Differences at baseline between groups were examined using t test or χ^2 test. Confirmatory testing of the primary outcome was done using an analysis of covariance (ANCOVA, adjusted for baseline value) to test the null hypothesis of equal means in pain intensity scores after 3 months between the randomized groups of acupuncture versus control. The same analysis was done for all secondary outcomes (worst pain intensity and quality of life) between acupuncture and control group.

Comparison in pain intensity and QoL between randomized acupuncture group and nonrandomized acupuncture group was done using covariance analysis (adjusted for baseline value) and additional sensitivity analysis (adjustments for any baseline differences between the 2 groups). Sensitivity analysis was performed for the primary outcome by replacing missing data using last value carried forward imputation. This is seen as an adequate approach since dysmenorrhea should not show a progressive change within 3 months.

All reported P values are from 2-sided tests. All analyses were based on the intention to treat (ITT) population using the maximal available data set, performed in SAS version 9.1 (SAS Institute, Cary, NC).

For derivation of cost effectiveness acceptability curves nonparametric bootstrapping was used. Therefore, the original sample was bootstrapped 1000 times in order to obtain 1000 means for costs and effect differences as well as the resulting incremental cost-effectiveness ratio (ICER). For inferential statistics, SPSS version 11.0 (Chicago, IL) was used and for the cost effectiveness acceptability curves MS EXCEL 2000 (Redmond, WA) was used.

Economic analyses

The cost perspective was societal. Data analysis included 1) the overall costs during the 3 months after randomization (including costs not related to dysmenorrhea) and 2) only diagnosis-specific costs using ICD-10 codes to identify costs due to dysmenorrhea and related conditions. Direct health-related costs for physician visits, hospital stays, medication, acupuncture treatment, and the number of sick leave days were provided by the participating health insurance companies and valued using the human-capital approach. Cost per acupuncture session was €35.

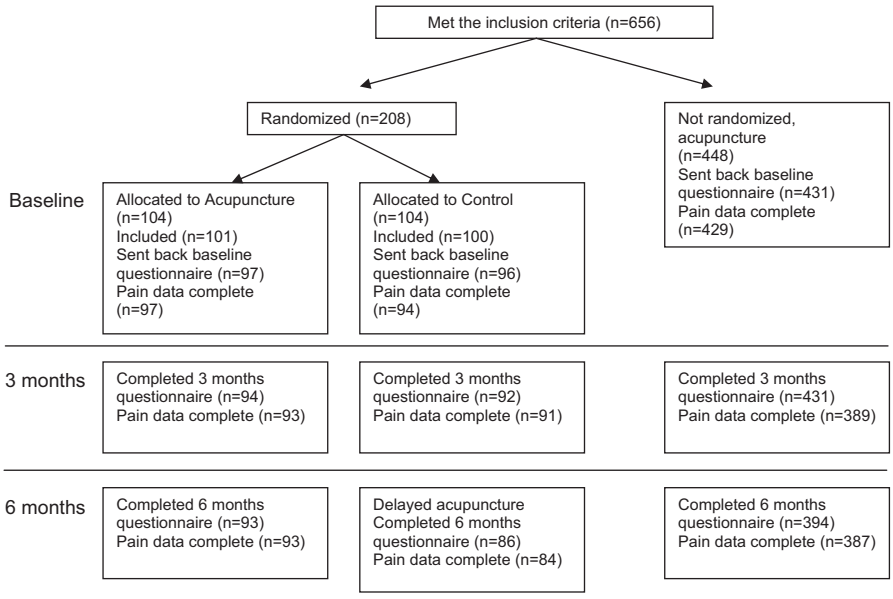
Because the observation period was only 6 months in length, there was no need to discount any costs or effects. We compared costs between the 2 randomized groups and performed a cost-effectiveness analysis based on QALYs (cost-benefit analysis). The SF-36[10] data at baseline and after 3 months were transformed to the SF-6D using the algorithm developed by Brazier.[11] Only patients with complete SF-36 data were included in the cost-effectiveness analysis. Quality adjusted life years (QALY) gained were calculated by adopting the area under the curve method[12,13] using the following formula:

$$\text{QALY utility}_{\text{gained}} = \left(\frac{\alpha_{\text{Acupuncture}} + \beta_{\text{Acupuncture}}}{2}\right) - \left(\frac{\alpha_{\text{Control}} + \beta_{\text{Control}}}{2}\right)$$

The analysis was based on the utility values at each time point (α = baseline utility, β = utility after 3 months) using the common assumption of a linear change over time.[12] As the health economic section of our study was designed to focus on estimation rather than on hypothesis testing, we calculated the ICER as a measure for additional costs which are necessary to realize an additional QALY as follows[14]:

$$\text{ICER} = \frac{\text{mean costs}_{\text{Acupuncture}} - \text{mean costs}_{\text{Control}}}{\text{mean QALY}_{\text{Acupuncture}} - \text{mean QALY}_{\text{Control}}}$$

FIGURE 1
Trial flow chart



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RESULTS

Patient inclusion, baseline characteristics, and treatment

Between January 2001 and August 2001 a total of 656 patients with pain due to dysmenorrhea were recruited for the study by 456 study physicians (see Figure 1 for patient selection). A total of 208 patients accepted randomization and were allocated to the acupuncture or the control group. Seven patients (3 acupuncture, 4 control) could not be included in the analysis because the study office did not receive the consent form or the patients did not receive the study intervention. The remaining 649 patients (101 acupuncture, 100 control, 448 nonrandomized acupuncture) were included in the analysis. After 3 months, data were available for 88.3% of the patients (acupuncture 93, control 91, nonrandomized acupuncture 389).

The randomized groups were comparable with regard to most baseline characteristics (see Table 1) except of physical functioning, bodily pain, and the physical component score of the SF-36. Between the randomized and the nonrandomized acupuncture groups, there were some significant differences as well: Nonrandomized patients had, on average, more pain due to dysmenorrhea, and reduced quality of life on the physical component score, the bodily pain, and physical functioning subscales compared to randomized patients. Patients in the acupuncture groups received 10.5 ± 3.1 acupuncture sessions (randomized acupuncture 10.6 ± 2.9; nonrandomized acupuncture 10.5 ± 3.2; P = .960). Most patients (68.8%) received 5-10 sessions, whereas 27.0% received more than 10 sessions and 4.2% less than 5 sessions.

Randomized comparisons

The course of pain intensity in both randomized groups is depicted in Figure 2. In the primary analysis after 3 months, the average pain intensity was lower in the acupuncture group compared to the control group 3.1 (95% CI 2.7, 3.6) versus 5.4 (4.9, 5.9), difference −2.3 (−2.9, −1.6), $P < .001$, after adjustment for baseline differences. This improvement was robust in the sensitivity analyses for missing data (difference between acupuncture and control group of −2.2 (−2.8, −1.5), $P < .001$). Furthermore, adjusting for all baseline differences did not change the results. The proportion of responder was 63.4% in the acupuncture group compared to 24.0% in the control group ($P < .001$).

TABLE 1
Baseline characteristics of study population

Parameter	Randomized			Acupuncture			
	Acupuncture n = 101 mean ± SD/ n (%)	Control n = 100 mean ± SD/ n (%)	*P* value	Randomized n = 101 mean ± SD/ n (%)	Nonrandomized n = 448 mean ± SD/n (%)	*P* value	Total n = 649 mean ± SD/ n (%)
Age (y)	35.4 ± 7.8	36.3 ± 6.5	.374	35.4 ± 7.8	36.3 ± 7.1	.251	36.1 ± 7.1
> 10 years of school	55 (57.9%)	55 (57.3%)	.933	55 (57.9%)	287 (67.7%)	.069	397 (64.6%)
Duration of disease (y)	9.4 ± 8.7	10.4 ± 8.7	.441	9.4 ± 8.7	9.3 ± 7.7	.936	9.5 ± 8.0
Pain intensity (NRS)	6.0 ± 2.0	6.3 ± 2.1	.283	6.0 ± 2.0	6.7 ± 2.1	.004	6.5 ± 2.1
Worst pain intensity (NRS)*	8.1 ± 1.9	8.2 ± 2.2	.793	8.1 ± 1.9	8.4 ± 1.8	.107	8.4 ± 1.9
Quality of life (SF-36)							
Physical functioning	89.0 ± 12.7	82.9 ± 21.0	.015	89.0 ± 12.7	83.1 ± 19.5	.000	84.0 ± 18.9
Role physical	70.7 ± 36.8	62.2 ± 38.2	.119	70.7 ± 36.8	62.7 ± 39.0	.070	63.8 ± 38.6
Bodily pain	72.9 ± 31.9	61.7 ± 32.9	.018	72.9 ± 31.9	63.2 ± 33.2	.010	64.5 ± 33.1
General health perceptions	64.3 ± 18.4	64.0 ± 18.9	.892	64.3 ± 18.4	61.8 ± 20.2	.257	62.5 ± 19.7
Vitality	47.9 ± 17.8	43.8 ± 20.2	.138	47.9 ± 17.8	44.0 ± 18.4	.057	44.6 ± 18.6
Social functioning	69.7 ± 26.5	66.1 ± 27.5	.368	69.7 ± 26.5	66.6 ± 27.1	.310	67.0 ± 27.0
Role emotional	64.9 ± 40.7	64.5 ± 38.4	.951	64.9 ± 40.7	63.4 ± 40.5	.751	63.8 ± 40.2
Mental health	60.8 ± 20.6	60.3 ± 18.8	.868	60.8 ± 20.6	58.3 ± 20.2	.283	59.0 ± 20.1
Physical Component Score	50.9 ± 9.0	47.5 ± 9.6	.014	50.9 ± 9.0	47.9 ± 9.6	.007	48.3 ± 9.6
Mental Component Score	41.0 ± 12.3	41.3 ± 11.3	.859	41.0 ± 12.3	40.6 ± 12.0	.780	40.8 ± 11.9

* Lower values indicate less pain. Exploratory *P* values from 2-sided *t* tests or χ^2 tests.

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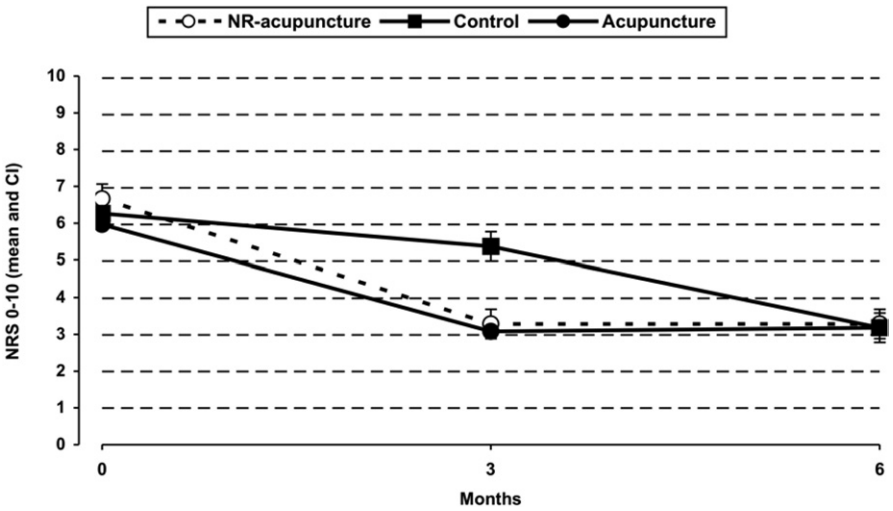
FIGURE 2
Development of pain intensity in the 3 treatment groups (means and 95% confidence intervals)



NRS = numeric rating scale, NR-acupuncture = nonrandomized acupuncture group.

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For quality of life (on all SF-36 subscales and both component scores with the exception of the subscale general health perception), the 3-month improvement was significantly more pronounced in the acupuncture than in the control group; see Table 2).

Following delayed acupuncture between 3 and 6 months, control patients showed similar improvements compared to the patients randomized to immediate acupuncture therapy (Table 2).

Nonrandomized comparisons

The comparison of the randomized and the nonrandomized acupuncture groups (Table 3) after 3 months revealed that the acupuncture effect was similar in both groups. The proportion of responder was 63.4% in the acupuncture group and 60.9% in the nonrandomized acupuncture group ($P = .651$). In addition both groups were comparable after 6 months.

TABLE 2
Pain intensity and secondary outcomes for both randomized groups after 3 and 6 months (adjusted means from ANCOVA adjusted for baseline values)

	3 months				6 months			
			Acupuncture vs control				Acupuncture vs control	
	Acupuncture Mean [95% CI]	Control Mean [95% CI]	Δ [95% CI]	*P* value	Acupuncture Mean [95% CI]	Control[b] Mean [95% CI]	Δ [95% CI]	*P* value
Pain intensity (NRS)[a]	3.1 [2.7, 3.6]	5.4 [4.9, 5.9]	−2.3 [−2.9, −1.6]	< .001	3.2 [2.7, 3.6]	3.2 [2.7, 3.6]	−0.0 [−0.6, 0.6]	.963
Worst pain intensity (NRS)[a]	4.4 [3.9, 4.9]	7.1 [6.6, 7.6]	−2.7 [−3.4, −2.0]	< .001	4.7 [4.1, 5.2]	4.7 [4.2, 5.3]	−0.0 [−0.8, 0.7]	.933
Quality of life (SF-36)								
Physical functioning	90.5 [87.6, 93.4]	85.6 [82.7, 88.5]	4.9 [0.7, 9.0]	.021	91.4 [89.0, 93.7]	91.7 [89.3, 94.0]	−0.3 [−3.7, 3.1]	.866
Role physical	86.8 [80.6, 92.9]	69.7 [63.7, 75.7]	17.1 [8.4, 25.7]	< .001	82.7 [76.8, 88.7]	85.1 [79.1, 91.1]	−2.3 [−11.0, 6.1]	.585
Bodily pain	84.0 [78.5, 89.5]	63.7 [58.2, 69.2]	20.3 [12.5, 28.2]	< .001	81.5 [76.6, 86.4]	78.7 [73.7, 83.7]	2.8 [−4.2, 9.9]	.427
General health perceptions	71.4 [68.9, 73.9]	68.2 [65.7, 70.6]	3.2 [−0.3, 6.8]	.071	69.3 [66.3, 72.2]	69.5 [66.5, 72.5]	−0.2 [−4.5, 4.0]	.913
Vitality	60.2 [57.1, 63.3]	48.0 [44.9, 51.2]	12.2 [7.8, 16.6]	< .001	57.9 [54.8, 61.1]	58.7 [55.4, 61.9]	−0.7 [−5.2, 3.8]	.751
Social functioning	84.3 [80.0, 88.7]	69.3 [65.0, 73.6]	15.0 [8.9, 21.2]	< .001	84.1 [80.6, 87.6]	83.8 [80.2, 87.5]	0.3 [−4.8, 5.3]	.922
Role emotional	83.5 [77.2, 89.9]	70.2 [63.9, 76.5]	13.3 [4.4, 22.3]	.004	84.1 [78.5, 89.7]	85.9 [80.2, 91.7]	−1.8 [−9.9, 6.2]	.651
Mental health	70.5 [67.6, 73.5]	61.1 [58.1, 64.0]	9.5 [5.3, 13.7]	< .001	70.6 [67.8, 73.4]	68.5 [65.6, 71.4]	2.1 [−2.0, 6.1]	.312
Physical Component Score	53.1 [51.5, 54.7]	49.1 [47.5, 50.6]	4.1 [1.9, 6.3]	< .001	52.2 [50.8, 53.6]	52.3 [51.0, 53.7]	−0.1 [−2.1, 1.9]	.908
Mental Component Score	47.6 [45.6, 49.5]	42.5 [40.6, 44.4]	5.0 [2.3, 7.7]	< .001	48.0 [46.3, 49.7]	47.7 [46.0, 49.4]	0.3 [−2.1, 2.7]	.829

NRS, numeric rating scale.

[a] Lower values indicate less pain.

[b] Control group also received acupuncture.

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Side effects

In 11.8% of patients (n = 59) a total of 70 side effects were reported after receiving acupuncture (74.3% minor local bleeding or hematoma, 10% pain [eg, needling pain], 4.3% vegetative symptoms, and 11.4% other). No life-threatening side effects were reported.

Economic analyses

For all randomized patients (n = 201), we observed significant differences between the acupuncture and control group for the period between baseline to 3 months in overall costs (€666.66 [SD: 739.95] vs €407.40 [SD: 1179.71], $P <$ .001) and diagnosis-specific costs (€467.62 [SD: 401.20] vs €29.95 [SD 76.05], $P <$ .001). The mean difference between the 2 treatment groups during the 3 months intervention phase (overall: €259.26, 95% CI €−14.37, 532.89; diagnosis-specific: €437.67, 95% CI €357.16, 518.18) was essentially due to the costs of acupuncture (€365.59 [SD: 98.56]) in the acupuncture group.

Complete data on quality adjusted life years were available for 177 of the 201 randomized patients (88%; 88 acupuncture, 89 control). As a result, only these 177 patients were included in the cost-effectiveness analysis. Table 4 shows the QALY utility values at baseline and after 3 months. There were no significant differences between the 2 randomized groups at baseline (P = .085). Three months after randomization, QALY utility values were higher in the acupuncture group than in the control group (0.79 [SD: 0.11] vs 0.69 [SD: 0.13], $P <$ .001). The cost difference between both groups was €195.40 (SD: 152.33) for the overall costs and €426.11 (SD: 43.39) for diagnosis-specific costs. The incremental cost effectiveness ratio was estimated to be €3011 per additional QALY gained (bootstrapped mean €3296, 95% CI: €−1705, 9025) in the overall cost perspective and €6567 (bootstrapped mean €7104, 95% CI €4207, 12,679) in the diagnosis-specific cost perspective.

COMMENT

Patients with pain due to dysmenorrhea chronic treated with acupuncture in addition to routine care showed significant improvements in pain intensity and quality of life compared to patients who received routine care alone. In patients who consented to randomization, treatment outcomes after acupuncture were similar to those who declined randomization. Acupuncture treatment was associated with better quality of life as well as higher costs. This increase in costs was

TABLE 3
Pain intensity and secondary outcomes for the nonrandomized acupuncture patients compared to the randomized acupuncture patients after 3 and 6 months (adjusted means from ANCOVA adjusted for baseline values)

	3 months				6 months			
	Randomized Mean (95% CI)	Nonrandomized Mean (95% CI)	Δ (95%CI)	*P* value	Randomized Mean (95% CI)	Nonrandomized Mean (95% CI)	Δ (95%CI)	*P* value
Pain intensity (NRS)[a]	3.2 [2.8, 3.7]	3.3 [3.1, 3.6]	−0.1 [−0.6, 0.4]	.726	3.3 [2.8, 3.7]	3.3 [3.1, 3.5]	−0.0 [−0.5, 0.5]	.914
Worst pain intensity (NRS)[a]	4.5 [4.0, 5.1]	4.9 [4.6, 5.1]	−0.3 [−0.9, 0.3]	.302	4.7 [4.2, 5.3]	4.9 [4.6, 5.2]	−0.2 [−0.8, 0.4]	.565
Quality of life (SF-36)								
Physical functioning	90.6 [88.3, 92.9]	91.5 [90.4, 92.6]	−0.9 [−3.5, 1.6]	.473	90.9 [88.2, 93.6]	91.7 [90.5, 93.0]	−0.8 [−3.8, 2.2]	.582
Role physical	86.8 [81.3, 92.3]	84.8 [82.2, 87.4]	2.0 [−4.1, 8.1]	.510	82.4 [76.3, 88.4]	82.9 [80.0, 85.7]	−0.5 [−7.2, 6.2]	.891
Bodily pain	83.2 [78.6, 87.8]	79.0 [76.8, 81.3]	4.2 [−1.0, 9.3]	.113	80.8 [75.9, 85.8]	78.8 [76.4, 81.2]	2.1 [−3.5, 7.6]	.464
General health perceptions	70.1 [67.4, 72.8]	68.9 [67.6, 70.2]	1.2 [−1.8, 4.2]	.430	68.8 [65.7, 71.9]	68.5 [67.0, 70.0]	0.2 [−3.2, 3.7]	.886
Vitality	60.2 [57.0, 63.5]	58.5 [56.9, 60.1]	1.7 [−1.9, 5.3]	.348	57.6 [54.1, 61.1]	56.2 [54.5, 57.8]	1.4 [−2.5, 5.3]	.476
Social functioning	84.2 [80.2, 88.1]	82.5 [80.6, 84.4]	1.7 [−2.8, 6.1]	.460	83.8 [79.7, 88.0]	81.5 [79.5, 83.5]	2.3 [−2.2, 6.9]	.316
Role emotional	83.3 [77.7, 89.0]	83.0 [80.3, 85.7]	0.3 [−5.9, 6.6]	.913	83.7 [77.4, 90.0]	81.0 [77.9, 84.0]	2.7 [−4.3, 9.7]	.444
Mental health	70.0 [67.0, 73.0]	69.3 [67.9, 70.7]	0.7 [−2.6, 4.0]	.685	70.1 [66.7, 73.4]	68.7 [67.1, 70.3]	1.4 [−2.3, 5.0]	.466
Physical Component Score	52.9 [51.6, 54.2]	52.4 [51.8, 53.0]	0.5 [−1.0, 2.0]	.495	52.0 [50.5, 53.4]	52.5 [51.8, 53.1]	−0.5 [−2.1, 1.1]	.565
Mental Component Score	47.4 [45.5, 49.2]	47.2 [46.4, 48.1]	0.1 [−1.9, 2.2]	.899	47.8 [45.7, 49.8]	46.6 [45.6, 47.6]	1.2 [−1.1, 3.5]	.301

NRS, numeric rating scale.

[a] Lower values indicate less pain.

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essentially due to acupuncture costs and was not compensated for by savings in other health care components during the study period.

The study took a pragmatic approach, aiming to evaluate acupuncture in a manner that would reflect as closely as possible the conditions of daily medical practice and maximize external validity. Although the study had high follow-up rates we used conservative methods to deal with missing data. The additional inclusion of patients who declined randomization allowed us to investigate any potential selection effects. The present study includes, to our knowledge, the first calculation of ICERs for acupuncture treatment in patients with dysmenorrhea.

TABLE 4
QALY-utilities at different time points and means

	Acupuncture mean (SD) n = 88	Control mean (SD) n = 89	*P* value[a]
QALY utility at baseline (α)	0.72 (0.14)	0.69 (0.13)	.085
QALY utility at 3 months (β)	0.79 (0.11)	0.69 (0.13)	< .001
QALY utility over study duration: $\frac{\alpha+\beta}{2}$	0.75 (0.11)	0.69 (0.12)	< .001

[a] *P* values from 2-sided *t* tests.

Witt. Acupuncture in patients with dysmenorrhea. Am J Obstet Gynecol 2008.

Obviously, such an approach also has its methodological limitations. In this study, neither providers nor patients were blinded to treatment. Therefore, a bias due to unblinding cannot be ruled out. To minimize social acceptability bias, all questionnaires were sent directly from and to the coordinating research institute. Because both the specifics of acupuncture treatment as well as of any cointerventions were left to the discretion of the physicians, the treatment regimens of patients in our study were highly variable. Inclusion criteria were broad, which resulted in a heterogeneous patient sample with high comorbidity and possibly some diagnostic misclassification. While these issues might be considered limitations from an experimental perspective, the study design was chosen to reflect general medical practice. Another limitation arises from the

duration of the study. The cost and effectiveness data were compared between the 2 groups for 3 months after baseline since subsequently patients in the waiting list control group were also offered acupuncture. Therefore, possible long-term health economic effects could not be investigated in the present study. The projection of the 3 months' therapy effect in our base-case-scenario up to 1 year was supported by findings of other acupuncture trials, which showed that the improvement in quality of life maintained up to 1 year.[15,16]

Patient's self-selection in randomized studies of complementary and alternative medicine could be a relevant problem.[17] A variety of designs such as comprehensive cohort studies have been recommended for including both randomized and nonrandomized patients, although only few studies have actually employed them to date.[18] In our study, approximately two thirds of eligible patients refused randomization in spite of a (minor) financial incentive and the slight disadvantage of having a 50% chance of a 3 month delay before starting acupuncture treatment. Those patients had a slightly higher pain intensity and lower quality of life on the more physical oriented subscales of the SF-36. When comparing a verum treatment with a placebo, selection bias may play a more prominent role than in our study. An interesting finding of our study is that the results in randomized and nonrandomized patients were comparable. This finding is supported by a review from Concato who observed that observational studies and randomized controlled studies can have similar results.[19]

Another important finding of our study is that improvements seen immediately after completion of 3 months of treatment continued for at least another 3 months.

To date, there are only a few studies on acupuncture treatment in patients with dysmenorrhea.[20] An observational study[21] included 48 women with dysmenorrhea. After 5 acupuncture sessions satisfactory results were found in more than 80% of cases after 6 and 12 months. In an older RCT with 91 patients comparing acupuncture with sham acupuncture 90% of the patients in the acupuncture group had pain relief compared to 36% of control patients.[22] A more recent study including 57 patients found a reduction in medication in women with acupuncture compared to sham acupuncture.[23] However, all these studies had a small sample size. Our pragmatic study cannot answer the question as to whether the effects observed may be due, at least in part, to "placebo." Nevertheless, our study showed that acupuncture was beneficial for women if offered as part of the health insurance system.

There is some evidence that naproxen reduces absenteeism from work or school in women with primary dysmenorrhea[3] but no cost analysis was found. In our study acupuncture treatment resulted in additional costs but taking the size of the treatment effect into account it was highly cost-effective.

Our study provides further evidence that acupuncture is a safe intervention. This is in agreement with large, previously published surveys.[24,25] When interpreting these findings, however, it must be kept in mind that all acupuncture in this study was administered by physicians.

Acupuncture is a relatively resource-intensive intervention due to the time involved for physicians and patients alike. To date, acupuncture was shown to be cost-effective for chronic headache,[26] low back pain,[27,28] and neck pain.[29] As in these studies the present study showed that acupuncture was associated with additional costs but was highly cost effective according to international threshold values of GBP 30,000 or $50,000 per QALY gained.[30,31]

In conclusion, our study shows that acupuncture, in addition to routine care, resulted in a clinically relevant benefit and was cost effective in patients with dysmenorrhea in primary care practices in Germany. As a result, acupuncture should be considered as a viable option in the management of these patients. ■

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