

Homoeopathic versus Conventional Therapy for Atopic Eczema in Children: Medical and Economic Results

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Key Words

Homoeopathy • Complementary therapies • Atopic dermatitis • Atopic eczema • Cost-effectiveness

Abstract

Background: One of five children visiting a homoeopathic physician is suffering from atopic eczema. **Objective:** To examine the effectiveness, safety and costs of homoeopathic versus conventional treatment in usual care. **Methods:** In a prospective multicentre comparative observational non-randomised study, 135 children (homoeopathy $n = 48$ vs. conventional $n = 87$) with mild to moderate atopic eczema were included. The primary outcome was the SCORAD (Scoring Atopic Dermatitis) at 6 months. Further outcomes at 6 and 12 months also included quality of life of parents and children, use of conventional medicine, treatment safety and disease-related costs. **Results:** The adjusted SCORAD showed no significant differences between the groups at both 6 months (homoeopathy 22.49 ± 3.02 [mean $\pm$ SE] vs. conventional 18.20 ± 2.31 , $p = 0.290$) and 12 months (17.41 ± 3.01 vs. 17.29 ± 2.31 , $p = 0.974$). Adjusted costs were higher in the homoeopathic than in the conventional group: for the first 6 months EUR 935.02 vs. EUR 514.44, $p = 0.026$,

and for 12 months EUR 1,524.23 vs. EUR 721.21, $p = 0.001$. Quality of life was not significantly different between both groups. **Conclusion:** Taking patient preferences into account, homoeopathic treatment was not superior to conventional treatment for children with mild to moderate atopic eczema.

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Introduction

Atopic eczema is a chronic inflammatory skin condition and the most common childhood skin disorder in developed countries affecting about up to 15% of children of school age and 1–3% of adults with annual costs of 1.1 [1] to 3.6 billion EUR [2, 3] in Germany alone. The reported prevalence is higher in Australasia and Northern Europe, and lower in Eastern and Central Europe and Asia [4, 5]. Children with higher socioeconomic status are more affected than children from poorer families [6]. Clinical findings of atopic eczema are variable and often age-specific, but pruritus can be especially burdensome [7]. Other disease characteristics like sleep disturbance, the requirement for special clothing, the avoidance of

certain activities (e.g. swimming), the need for frequent medication, or loss of working time have also great impact on the quality of life of both the affected children and their parents [7, 8]. Nevertheless, prognosis is usually favourable because children commonly outgrow the condition by early adolescence [4].

Until now the causes of atopic eczema are not clear. It is a complex multifactorial disease with many possible contributing factors like immunological, genetic, metabolic and neuroendocrine ones, which interact with each other and the environment. Atopic eczema is related to an abnormal barrier function of the skin and early immunoglobulin E production with later allergen/immunoglobulin E reactivity [4, 9–12]. Exposure to allergens, irritants and bacteria [4, 9] as well as psychological factors [13] also have an impact on skin conditions.

Today different treatment options are available [4, 14, 15]. Persistent use of emollients is the cornerstone of maintenance therapy, topical corticosteroids are the mainstay of treatment for flare-ups and are the standard to which other treatments are compared. In the last few years, topical calcineurin inhibitors became popular among patients because they lack the typical side effects of corticosteroids. However, with conventional treatment often only symptomatic relief is possible [4, 9].

There has been growing public demand for the application of alternative or complementary medicine to atopic eczema and other allergic complaints [8, 16–18]. In Germany, homoeopathy is widely used for atopic eczema, although official guidelines do not recommend it. According to an earlier study, one child in five who attends a homoeopathic practice suffers from atopic eczema [19].

Homoeopathy is based on the ‘principle of similars’, whereby substances that cause symptoms in healthy individuals are used to stimulate healing in patients who have similar symptoms when ill [20]. Usually these substances are used in extremely high dilutions, which makes homoeopathy a controversially debated system. When a single homoeopathic remedy is selected based on a patient’s total symptom picture, it is called ‘classical’ homoeopathy [21]. A prior study demonstrated that disease severity and quality of life can show marked and sustained improvements under homoeopathic care [22]. However, the evidence for the effectiveness of homoeopathy remains unclear. The aim of this trial was to assess whether effectiveness of homoeopathic treatment is superior to conventional therapy for patients with atopic eczema in usual care while taking patient preferences into account.

Methods

This prospective multicentre comparative observational study was carried out from January 2005 to January 2007 in Berlin, Germany, with an observation period of 12 months per patient. The study was planned as an observational, open and non-randomised investigation. The children and their parents were recruited at the homoeopathic or conventional doctor’s practice and had thus already made their own choice of therapy. The study was compliant with Good Epidemiological Practice, Good Clinical Practice and official data protection laws. It was approved by the Ethics Committee of the Charité University Medical Centre, Berlin, Germany.

Participants

To be included into the study, children (1–14 years) with atopic eczema had to have a disease duration of at least 6 months and had to fulfill 3 of 4 Williams’ criteria [23, 24]. The Three-Item Severity (TIS) score had to be between 2 and 7 [25]. Major exclusion criteria were another dermal disease, severe medical or psychological disease, oral or intravenous corticosteroids during the last 3 months before study entry, psychotherapy, allergy desensitisation or additional complementary therapy during the last 3 months before study entry or planned for the study period.

Patients in the conventional group were recruited by physicians practising conventional medicine, and patients in the homoeopathic group were recruited by physicians with specialisation in homoeopathy. In contrast to conventional physicians, whose costs were covered by health insurance funds, homoeopaths were mainly paid out of pocket. Only conventional physicians who had at least 5 years experience in treating atopic eczema, who knew the treatment guidelines for atopic eczema, and who had at least 20% children in their clinics were included in the study. Homoeopathic physicians had to have completed a training for classical homoeopaths, at least 5 years experience in homoeopathic treatment, more than 50% homoeopathy in their treatment activities, experience in the treatment of atopic eczema, and at least 20% children in their outpatient clinics.

Homoeopathic doctors were recruited by the organisation of homoeopathic doctors in Berlin (Berliner Verein Homöopathischer Ärzte). Doctors for conventional treatment (paediatricians or dermatologists) were chosen from address lists or via recommendation.

Intervention

Children in the homoeopathic group were treated according to classical homoeopathy defined as a homoeopathic case taking and a prescription of a single remedy according to the simile law. Emollient creams were recommended. Corticosteroids were reserved for rescue medication only. Therapy in the conventional group should be applied according to the German guidelines [14].

Outcome Measurements

Primary outcome measure was the SCORAD (Scoring Atopic Dermatitis) [26, 27], a well-evaluated and internationally accepted outcome measure for atopic eczema [28], at 6 months. Secondary outcome measures included SCORAD at 12 months, quality of life of parents [29, 30] and children (Children’s Dermatology Life Quality Index validated for ages 3–16 years [31]), use of conventional medicine, disease-related costs, response rates and safety of treatment at 6 and 12 months.

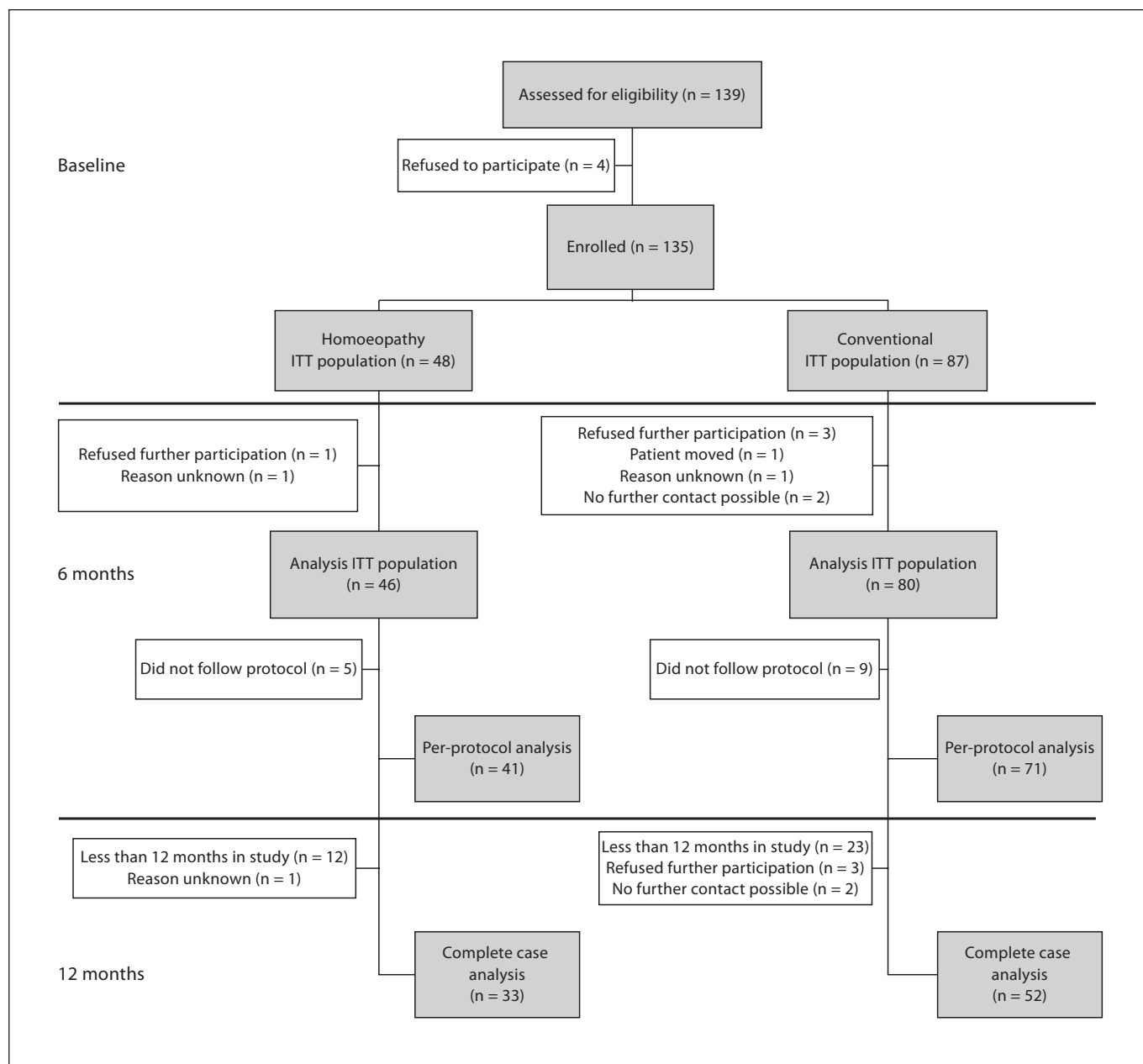


Fig. 1. Trial flow chart; questionnaire and SCORAD rating at baseline, 6 months and 12 months. ITT = Intention to treat.

After conventional case taking, screening and recruitment, patients were enrolled into the study (fig. 1). The baseline data for the main outcome measure SCORAD were assessed by two specially trained staff members who were blinded to treatment assignment. Other baseline data (sociodemographic characteristics and outcome measures) were obtained with questionnaires. Patients were asked to respect the blinding of the raters during the ratings. Each patient was assigned to only one rater for the whole study period. After the rating, the homoeopathic case taking and the following

treatment or the conventional treatment could begin. Follow-up data were obtained by ratings and questionnaires at 6 and 12 months. Additionally, diaries included medication intake for atopic eczema about 1 week for weeks 1–12, 23–26 and 49–52, respectively. Treatment was documented by the physicians.

Economic Analyses

The cost comparison analysis was made from a societal perspective and was performed in a diagnosis-specific view. That

means that we only considered direct and indirect costs with a direct relation to atopic eczema.

Data on resource consumption such as physician visits, hospital stays, use of medication and number of sick leave days were obtained from questionnaires and diaries and were valued with German unit prices. Costs for medical aids and adjuvant therapies were obtained directly from the patients' questionnaires. We calculated all costs for 12 months before study onset, for months 0–6 and 7–12 after baseline. In addition to cost analyses, we performed an incremental cost-effectiveness analysis. Therefore we compared cost differences between the treatment groups with respect to effectiveness differences (group differences in SCORAD reduction).

Statistics

For a priori power calculations, we assumed an effect size of 0.4. In this case, after adjustment for group differences, for a two-sided t test ($\alpha = 5\%$), 100 patients per group were needed to achieve a minimum statistical power of 80%. The software n-Query advisor 4.0 was used for calculation. In order to cope with an expected drop-out of 15–20%, we planned to include 120 patients into each group.

The primary analysis was an intention-to-treat analysis and included all patients with baseline values who received treatment. A per-protocol analysis was performed as sensitivity analysis and included all patients who fulfilled the following conditions: complete baseline and 6-month SCORAD, no violation of inclusion and exclusion criteria, no additional use of alternative and complementary therapies, and no change of therapy or physician during the first 6 study months. For primary statistical analysis, we used a multilevel model (ANCOVA) with the physician as random effect and the following fixed effects: baseline value (continuous variable), TIS score (continuous variable), social class (high, average, low), parents' expectation for a good outcome (high, low), children's age (continuous variable) and gender (male/female). For the primary outcome, further sensitivity analyses were performed: using propensity score as fixed effect, replacement of missing data using different methods (last value carried forward and multiple imputation methods), using multiple measurement ANCOVA. Tests were two-sided with a level of significance of 5%.

For cost-effectiveness analyses, we used non-parametric bootstrapping to generate a picture of variability around the arithmetic mean. Therefore, the original sample was bootstrapped 1,000 times in order to obtain 1,000 means for cost and effect differences. Each bootstrap sample was adjusted for confounding variables as it was described before.

All statistical analyses were performed according to a pre-defined statistical analysis plan. For inferential statistics, SPSS version 13.0 (Chicago, Ill., USA) and SAS for Windows, version 9.1 (SAS Institute, Cary, N.C., USA) were used.

Results

Population

In the present study, 52 physicians experienced in the treatment of atopic eczema in children agreed to participate (22 homoeopaths and 30 conventional doctors) of

whom 26 doctors (10 homoeopaths and 16 conventional doctors) recruited patients for the study. Conventional doctors were specialised in dermatology ($n = 9$) or paediatrics ($n = 5$) or had no specialisation ($n = 2$). All homoeopaths were 'classical' homoeopaths either following Kent's (80%) or Hahnemann's (20%) method.

Between January 2005 and June 2006, 135 children were included into the study (mean age 4.01 ± 2.97 years, 48% girls, conventional group $n = 87$, homoeopathic group $n = 48$) (table 1). Six-month follow-up data were available of 46 patients in the homoeopathic group and of 80 patients in the conventional group, respectively. Reasons for missing follow-up data included e.g. refusal of further participation, relocation or inadequate length of study participation (fig. 1).

The groups were comparable with regard to most baseline characteristics (table 1). However, patients in the homoeopathic group showed severer SCORAD values and a trend to a longer symptom duration. However, the TIS score used during recruitment as a screening tool for atopic eczema contradicts the SCORAD values and was higher in the conventional group. Parents in the homoeopathic group were older, had a higher income level and were better educated, i.e. had a higher social status than parents in the conventional group (table 1). Moreover a trend towards higher baseline costs in the homoeopathic group was observable.

Treatment

Treatment and skin care were individualised according to real-life treatment and documented in both groups. The frequency of daily basic skin care was comparable in both groups. The numbers of patients with daily skin care in months 1–6 and 7–12 in the homoeopathic group were 35 (77.8%) and 27 (84.4%) and in the conventional group 64 (85.3%) and 44 (86.3%). During the study period, 41 different homoeopathic remedies were prescribed in the homoeopathic group [e.g. *calcarea carbonica*: 15 patients (31.3%); *sulphur*: 11 (22.9%); *phosphorus*: 10 (20.8%); *Pulsatilla pratensis*: 8 (16.7%); *Belladonna*: 6 (12.5%); *Lycopodium clavatum*: 6 (12.5%); *tuberculinum bovinum*: 6 (12.5%); *natrium muriaticum*: 5 (10.4%); *Thuja occidentalis*: 5 (10.4%)]. The most frequently used potencies were C30 [32 patients (66.7%)] and C200 [31 patients (64.6%)]. Treatment of patients in the conventional group in months 1–6 and 7–12 focused on corticosteroids [29 (38.7%) and 13 (25.5%)], antihistamines [13 (17.3%) and 6 (11.8%)], and pimecrolimus and tacrolimus [22 (29.3%) and 16 (31.4%)]. In the homoeopathic group, some patients also used the following medications: antihistamines [months

Table 1. Baseline characteristics

ITT	Homoeopathy			Conventional treatment			p value
	n	mean ± SD/n (%)	median	n	mean ± SD/n (%)	median	
<i>Patients</i>							
Age, years	48	4.3 ± 2.9	4.0	87	3.9 ± 3.0	3.0	0.300
Female gender	48	26 (54.2)		87	39 (44.8)		0.369
Siblings	47	1.1 ± 1.0	1.0	84	1.0 ± 1.2	1.0	0.530
Symptom duration, years	48	3.5 ± 2.6	3.0	86	2.9 ± 2.7	2.0	0.057
Treatment since, years	46	3.0 ± 2.7	2.0	83	2.7 ± 2.9	1.0	0.364
Additional atopic disease							
Allergic rhinitis	47	4 (8.5)		84	8 (9.5)		1.000
Allergic asthma	47	2 (4.3)		84	8 (9.5)		0.330
Food allergy	47	10 (21.3)		84	10 (11.9)		0.205
Other	47	6 (12.8)		84	8 (9.5)		0.568
Allergy test	48	21 (43.8)		87	36 (41.4)		0.856
Allergen positive	19	11 (57.9)		30	14 (46.7)		0.561
TIS score (0–9) ¹	48	3.8 ± 1.6	3.0	87	4.5 ± 1.5	4.0	0.010
Therapy for AE during previous 12 months							
Basic skin care	47	40 (85.1)		84	73 (86.9)		0.795
Avoidance of certain food	47	25 (53.2)		84	33 (39.3)		0.144
Alternative therapies	47	19 (40.4)		84	3 (3.6)		<0.001
Drug therapy	47	42 (89.4)		84	71 (84.5)		0.598
Number of medications	47	2.2 ± 1.7	2.0	84	2.3 ± 1.9	2.0	0.852
Corticosteroids	47	12 (25.5)		84	40 (47.6)		0.016
Antihistamines	47	9 (19.1)		84	18 (21.4)		0.825
Topical calcineurin inhibitors	47	18 (38.3)		84	26 (31.0)		0.443
SCORAD Total score ²	48	31.3 ± 14.1	30.9	87	22.8 ± 13.4	19.9	0.001
SCORAD Extent	48	18.7 ± 19.4	13.3	87	12.9 ± 16.0	7.0	0.066
SCORAD Intensity	48	6.1 ± 2.7	6.5	87	4.1 ± 2.6	3.0	<0.001
SCORAD Subjective symptoms	48	6.1 ± 4.6	5.0	87	5.9 ± 5.0	5.0	0.856
Children’s QoL CDLQI ³	28	3.8 ± 2.6	3.5	49	4.8 ± 3.6	4.0	0.189
<i>Accompanying parent</i>							
Age, years	47	36.7 ± 6.1	36.0	84	32.7 ± 6.3	32.5	<0.001
Female gender	47	41 (87.2)		84	76 (90.5)		0.568
Single parent	47	7 (14.9)		84	21 (25.0)		0.192
Education	47			84			<0.001
A level		31 (66.0)			22 (26.2)		
University, college		20 (42.6)			13 (15.5)		
Net income per month	38			61			<0.001
<2,000 EUR		16 (42.1)			41 (67.2)		
2,000–4,000 EUR		18 (47.4)			20 (32.8)		
>4,000 EUR		4 (10.5)			0 (0.0)		
Social class	47			84			<0.001
Low		2 (4.3)			29 (34.5)		
Middle		17 (36.2)			34 (40.5)		
High		28 (59.6)			21 (25.0)		
Parents’ QoL ⁴							
Psychosomatic wellbeing	47	65.0 ± 20.9	69.4	84	64.4 ± 21.3	69.4	0.890
Effects on social life	47	87.2 ± 16.7	91.7	84	84.6 ± 15.4	87.5	0.384
Confidence in medical treatment	45	62.8 ± 21.6	60.0	84	67.4 ± 18.1	65.0	0.195
Emotional coping	47	72.9 ± 19.3	75.0	84	71.7 ± 21.5	75.0	0.762
Acceptance of the disease	46	70.4 ± 22.1	75.0	84	68.6 ± 24.4	75.0	0.682
Expected symptom improvement (0–6) ⁵	46	4.4 ± 1.2	4.0	83	3.8 ± 1.2	4.0	0.013

Table 1 (continued)

Costs during 12 months before study, EUR	Homoeopathy			Conventional treatment			P value
	n	mean $\pm$ SD	95% CI	n	mean $\pm$ SD	95% CI	
Medication	48	119.5 $\pm$ 146.5	77.0–162.1	87	109.6 $\pm$ 150.7	77.5–141.7	0.493
Hospital	48	22.6 $\pm$ 156.2	–22.8–67.9	87	12.4 $\pm$ 81.6	–5.0–29.8	0.950
Physician contact	48	86.6 $\pm$ 68.0	66.9–106.4	87	102.3 $\pm$ 95.0	82.1–122.6	0.190
Medical aids and adjuvant therapies	48	254.6 $\pm$ 563.2	91.0–418.1	87	113.5 $\pm$ 264.2	57.1–169.8	0.032
Indirect costs	48	134.0 $\pm$ 460.9	0.2–267.9	87	32.2 $\pm$ 105.1	9.8–54.5	0.527
Total	48	617.3 $\pm$ 841.2	373.0–861.6	87	370.0 $\pm$ 380.8	288.8–451.1	0.164

ITT = Intention to treat; AE = atopic eczema; QoL = quality of life; CDLQI = Children's Dermatology Life Quality Index.

¹ High score = High intensity. ² <25 = Mild disease; 25–50 = moderate disease; >50 = severe disease. ³ High score = Low quality of life (only children aged 3–16 years could be questioned, because the Children's Dermatology Life Quality Index was only validated for that age group). ⁴ High score = High quality of life. ⁵ 0 = Not sure; 6 = very sure.

1–6: 6 (13.3%) and months 7–12: 2 (6.3%)], corticosteroids [1 (2.2%) and 2 (6.3%)], and pimecrolimus and tacrolimus [5 (11.1%) and 5 (15.6%)].

According to the adjusted data, patients in the homoeopathic group showed a tendency to use fewer corticosteroids than patients in the conventional group at 6 and 12 months (table 2). Moreover, differences in average calcineurin inhibitor usage were significant. This class of drugs was used more often in the conventional than in the homoeopathic group at 6 ($p = 0.048$) and 12 months ($p = 0.005$). The average total number of medications was comparable between both groups.

Outcome Parameters

The adjusted primary outcome parameter SCORAD at 6 months showed no significant differences between groups (homoeopathy group: 22.49 ± 3.02 [mean $\pm$ SE], 95% confidence interval, CI = 15.46–29.51, vs. conventional group: 18.20 ± 2.31 , 95% CI = 12.43–23.96; $p = 0.290$) as well as at 12 months (17.41 ± 3.01 , 95% CI = 11.37–23.45, vs. 17.29 ± 2.31 , 95% CI = 12.65–21.92; $p = 0.974$) (fig. 2). SCORAD subscales also showed no significant differences. Moreover per-protocol, unadjusted and sensitivity analyses showed congruent results.

No significant differences could be observed for adjusted response rates which were based on the baseline SCORAD values. At 6 months, 52.6% in the homoeopathic and 59.6% in the conventional group ($p = 0.283$) showed a 33% response (defined as an improvement of at least 33% in the SCORAD). The 33% response rate increased at 12 months to 61.4% in the homoeopathic group and 51.0% in the conventional group ($p = 0.447$). A 50% response could be observed in 22.5% of patients in the

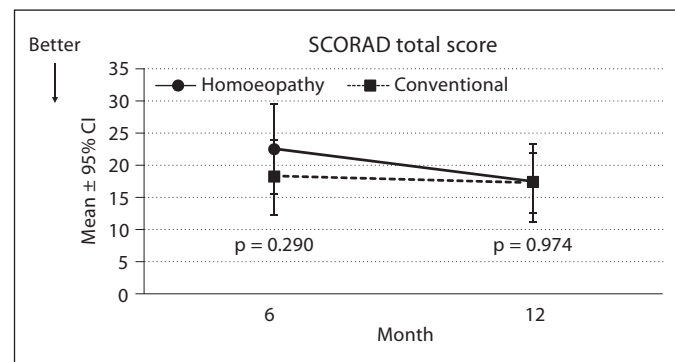


Fig. 2. SCORAD at 6 and 12 months, adjusted mean $\pm$ 95% CI from multilevel models (ANCOVA) with fixed effects age, gender, baseline value, TIS score, social status, parents' expectation and random effect physician; $\alpha = 5\%$.

homoeopathic and 32% of patients in the conventional group at 6 months ($p = 0.247$), and in 24.3 versus 31.2% at 12 months ($p = 0.564$).

The number of patients with adverse events was comparable in both groups at 6 months [homoeopathy 13 (28.9%) patients vs. conventional 22 (29.3%), $p = 1.000$] and at 12 months [3 (9.4%) vs. 8 (15.7%), $p = 0.517$]. Because of worsening of the atopic eczema with additional streptococcus infection, one child in the conventional group needed hospital treatment.

After the study period, parents were asked to judge the therapy's overall effectiveness on a visual analogue scale (0–100 mm; 0 = very effective, 100 = not effective). We found no significant differences between groups (adjusted analysis, homoeopathy: 27.88 ± 4.80 [mean $\pm$ SE],

Table 2. ITT analyses of SCORAD and secondary outcomes: adjusted means and confidence intervals from multilevel models (ANCOVA) with fixed effects age, gender, baseline value, TIS score, social status, parents' expectation and random effect physician ($\alpha = 5\%$)

ITT	6 months				12 months			
	homoeopathy		conventional		homoeopathy		conventional	
	mean	95% CI	mean	95% CI	mean	95% CI	mean	95% CI
<i>Patients</i>								
SCORAD Total score ¹	22.5	15.5–29.5	18.2	12.4–24.0	0.290		17.3	12.7–21.9
SCORAD Extent	14.8	7.9–21.7	8.4	3.0–13.9	0.146		7.4	4.3–10.4
SCORAD Intensity	4.4	3.5–5.3	3.5	2.8–4.1	0.123		3.7	2.9–4.6
SCORAD Subjective symptoms	4.5	2.8–6.2	3.6	2.3–5.0	0.431		3.1	2.0–4.3
Children's QoL CDLQI (0–30) ²	2.1	1.3–3.5	1.9	1.2–3.2	0.825		2.0	1.3–3.1
Number of medications	1.5	1.2–2.0	2.1	1.6–2.9	0.104		1.5	1.1–2.2
Number of corticosteroids	0.04	0.01–0.3	0.3	0.2–0.5	0.064		0.2	0.1–0.4
Number of antihistamines	0.1	0.1–0.3	0.1	0.04–0.4	0.882		0.04	0.01–0.1
Number of topical calcineurin inhibitors	0.1	0.04–0.3	0.3	0.2–0.6	0.048		0.3	0.2–0.6
<i>Accompanying parent</i>								
Parents' QoL ³								
Psychosomatic wellbeing	70.8	65.8–75.8	69.4	65.8–73.0	0.650		69.7	65.6–73.8
Effects on social life	88.8	85.2–92.5	87.2	84.4–89.9	0.469		88.0	84.8–91.2
Confidence in medical treatment	78.0	71.3–84.7	72.7	67.7–77.7	0.215		75.1	69.2–80.9
Emotional coping	78.2	71.7–84.7	77.9	72.8–83.0	0.940		82.7	78.7–86.7
Acceptance of the disease	79.0	71.5–86.6	76.1	70.3–91.9	0.536		82.4	77.6–87.2
<i>Costs</i>								
Medication	67.4	11.4–123.4	89.4	42.4–136.4	0.552		173.8	89.9–257.7
Hospital	0.0	0.0–0.0	1.4	0.0–89.5	0.935		0.0	0.0–124.9
Physician contact	308.8	264.6–353.0	106.2	69.2–143.2	<0.001		156.8	90.3–223.2
Study doctor	259.2	228.1–290.3	51.7	25.7–77.7	<0.001		80.3	32.8–127.7
Other physicians	50.1	20.6–79.5	55.3	30.7–80.0	0.786		77.3	40.1–114.5
Medical aids and adjuvant therapies	403.5	218.9–588.2	103.9	0.0–258.8	0.015		211.0	7.3–414.6
Indirect costs	170.1	2.8–337.4	178.8	38.3–319.3	0.937		148.8	0.0–299.1
Total	935.0	653.9–1,216.1	514.4	276.5–752.4	0.026		721.2	424.8–1,017.7

ITT = Intention to treat; QoL = quality of life; CDLQI = Children's Dermatology Life Quality Index.

¹ <25 = Mild disease; 25–50 = moderate disease; >50 = severe disease. ² High score = Low quality of life. ³ High score = High quality of life.

95% CI = 18.34–37.42; conventional: 26.79 ± 3.60 , 95% CI = 19.62–33.96; $p = 0.858$).

To control for blinding, the raters were asked to assign each of their patients to a treatment group; 50.8% of patients were assigned correctly and 3.2% incorrectly. For 46%, the ‘I don’t know’ option was used.

Economic Analyses

Economic data were available for 135 patients at baseline and during the first 6 months after study onset, and for 95 patients for the study period from 6 to 12 months.

During the 12 months before baseline, costs were EUR 551.52 (95% CI = 248.88–818.16) in the homoeopathic group and EUR 260.64 (95% CI = 37.86–483.43) in the conventional group, but the difference did not reach statistical significance ($p = 0.099$) (table 1).

During the first 6 months after the study onset, we observed costs of about EUR 935.02 (95% CI = 653.93–1,216.11) in the homoeopathic group, compared to EUR 514.44 (95% CI = 276.52–752.36) in conventionally treated children (table 2). This difference was statistically significant ($p = 0.026$) and was mainly affected by higher costs for physician visits (homoeopathy: EUR 308.83, 95% CI = 264.63–353.03; conventional: EUR 106.18, 95% CI = 69.17–143.20; $p < 0.001$) and costs for medical aids and adjuvant therapies (homoeopathy: EUR 403.52, 95% CI = 218.89–588.15; conventional: EUR 103.90, 95% CI = 0–258.78; $p = 0.015$).

During the period from 6 to 12 months after baseline, significant cost differences were found in total costs (homoeopathic group: EUR 492.43, 95% CI = 326.32–685.54; conventional group: EUR 247.34, 95% CI = 96.39–398.28; $p = 0.034$). Also in this period, the physician’s contacts were one of the main cost drivers.

With regard to the whole duration of the 12-month study, we observed total costs of about EUR 1,524.23 (95% CI = 1,198.02–1,850.45) in the homoeopathic group, in contrast to EUR 721.21 (95% CI = 424.78–1,017.65) in conventionally treated children ($p = 0.001$) (table 2).

Adjusted cost differences in relation to adjusted effectiveness differences (in terms of group differences in SCORAD reduction) as well as the adjusted single bootstrap samples are shown in figure 3. During the first 6 months, the probability that the homoeopathic group reached a superior effectiveness level as compared to the conventional group was about 8.1% (81 of 1,000 bootstrap samples). During the period between 6 and 12 months, this probability increased to 35.8%, and with regard to the whole study duration of 12 months, the probability was 35.3%. Moreover, the fact that homoeo-

pathic treatment was associated with additional costs achieved a probability between approximately 94 and 98%.

Discussion

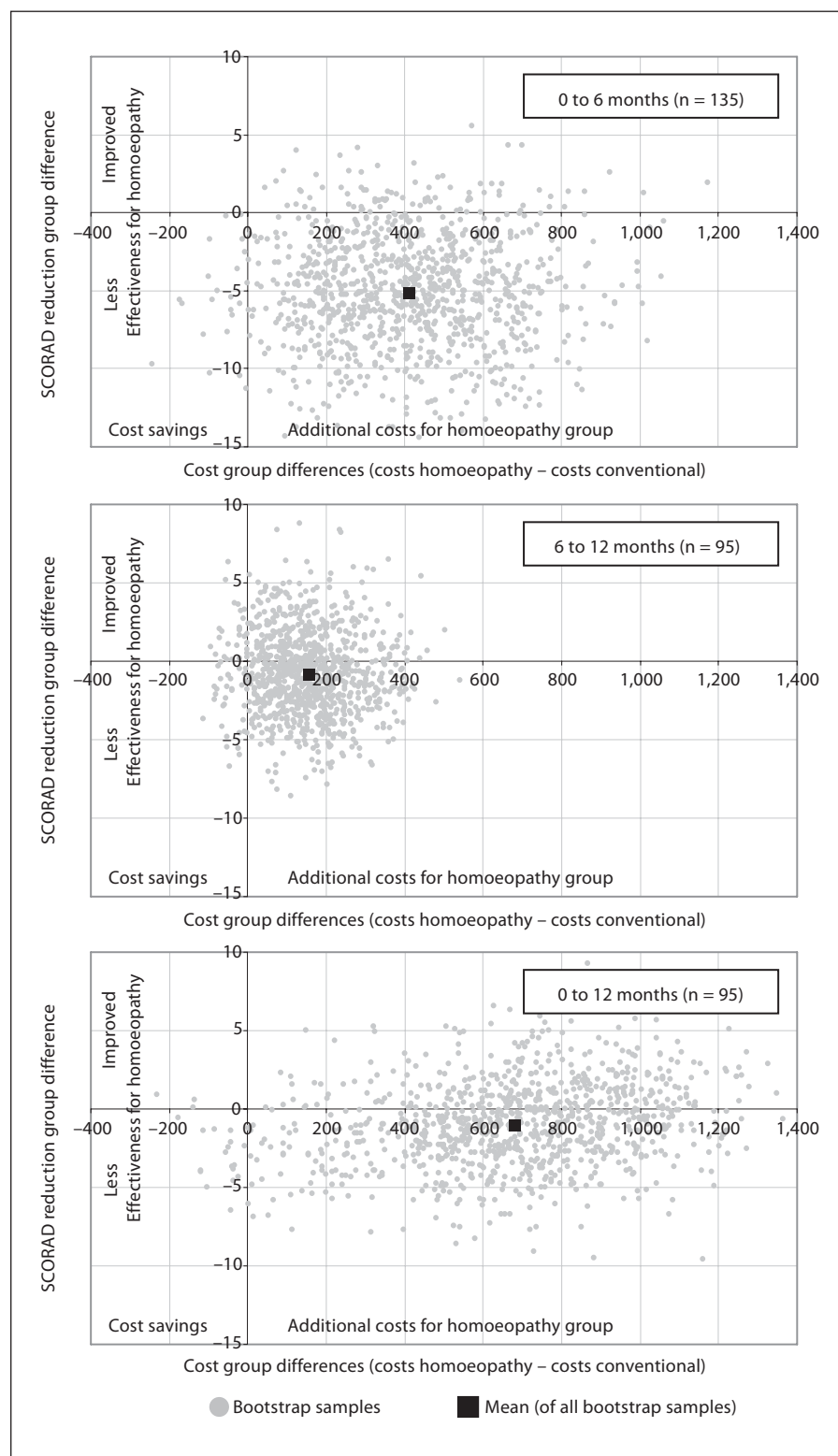
At 6 and 12 months, the skin conditions measured with the SCORAD were comparable in both groups. Moreover, secondary outcome parameters like the children’s and parents’ quality of life showed no significant differences between both groups. However, costs were higher in the homoeopathic than in the conventional group, primarily due to the low fee for conventional doctors, and because parents of children in the homoeopathic group spent more money on medical aids and adjuvant therapies. Both groups substantially improved during the observation period.

In contrast to a randomised controlled trial, which is best suitable to assess a therapy’s effectiveness on a higher level of evidence, the usual-care and multicentre setting of our prospective observational study allows evaluation of a therapy’s effectiveness while taking patients’ preferences into account. We tried to avoid a selective cohort with the aim to produce study results with good external validity. Moreover, outcome measures were collected from a variety of sources including the affected child, the parents, and external blinded raters to improve objectivity and validity of study outcomes.

Since we wanted to consider patients’ or parents’ preferences to reflect real-world situations, randomisation was not possible. This resulted in relevant baseline differences between both groups. Skin conditions according to the SCORAD were less favourable in the homoeopathic group, especially the intensity and extent of atopic eczema, and disease duration was 0.6 years longer than in the conventional group. Moreover, parents in the homoeopathic group were older, had a higher social class background and a higher treatment expectation. We adjusted for the known baseline differences; however, we are aware that other unknown factors may have confounded the results. Therefore, for the internal validity of our results, the non-randomised design is a clear limitation of our study. In our study the treatment was individualised. There is data that both treatment according to an evidence-based algorithm and individualised treatment can effectively control atopic eczema [32].

Interestingly, at baseline the TIS score used as inclusion criterion and the SCORAD showed opposite trends in both groups. Whereas at baseline in the conventional

Fig. 3. Incremental cost-effectiveness planes; the original sample was bootstrapped 1,000 times in order to obtain 1,000 means for cost and effect differences (adjusted means and CI from multilevel models, ANCOVA, with fixed effects age, gender, baseline value, TIS score, social status, parents' expectation and random effect physician); each data point represents the result of one bootstrap sample. Incremental cost-effectiveness points that fall in the lower right quadrant are considered to be more costly and less effective than conventional care. In contrast, data points in the upper left quadrant represent cost savings and higher effectiveness in comparison to conventional care.



group the TIS score was less favourable than in the homoeopathic group, the SCORAD showed reverse results. The reasons for the different assessments are not clear. The SCORAD is more complex and includes information on extent and intensity of eczema, pruritus and sleep disturbance. Moreover the SCORAD is well validated and recommended as an assessment tool for atopic eczema in study settings [28]. The SCORAD was rated by a blinded rater with special training, while the TIS score was rated by the physician without extra training. Possibly conventional physicians tend to a severer rating than homoeopaths. The TIS score was no outcome parameter and only used as inclusion criterion.

Recruitment of homoeopathic patients was more difficult than in previous studies [22, 33], possibly because of the introduction of new drugs against atopic eczema like pimecrolimus (Elidel®) or the economical uncertainty and the lower job safety during the study period. However, 135 subjects could be included into the study, which was 56% of the calculated sample size of 240 patients we had anticipated. Moreover, because of the longer recruitment period, not all subjects could be assessed at 12 months. It seems likely that our study was underpowered. But all outcome parameters were very consistent and one might not expect a substantial difference in a larger sample.

At 6 and more so at 12 months, SCORAD severity was comparable in both groups, although patients in the conventional groups took very potent medication, e.g. corticosteroids, antihistamines or pimecrolimus and tacrolimus. At baseline pimecrolimus and tacrolimus use was comparable in both groups in contrast to less use of corticosteroids in the homoeopathic group than in the conventional group. At 6 months, the use of both potent anti-inflammatory drugs was significantly lower in the homoeopathic group. In both groups the frequency of basic skin care was comparable. However, for interpretation of these results one should also take into account that atopic eczema can improve spontaneously in young children.

At every time point, costs were higher in the homoeopathic than in the conventional group. This may be explained by the relatively high additional costs of homoeopathy at the beginning of treatment because of the extensive case taking at the first visit and the expenditures for medical aids and adjuvant therapies.

The cost analysis was societal, i.e. included both direct and indirect costs, but included only diagnosis-specific costs and not overall costs, which may have been more appropriate. Another limitation may be the cost mea-

surement. Costs were indentified on the basis of the patients' reports complemented by physicians' data. But these data can be biased by recall difficulties. Because patients had different health insurance status, we could not use data of health insurance companies. However, our approach considers private expenditures.

In our study we observed diagnosis-specific costs of about 700 EUR in the conventional group and 1,500 EUR in the homoeopathic group for 1 year of treatment. For Germany, Ehlken et al. [34] identified annual diagnosis-specific costs of 950 EUR for patients with mild atopic eczema. International studies show similar results. Two Australian studies from 1997 and 1999 reported mean total costs per patient between 340 [35] and 870 EUR [36] for mild, and 1,800 [35] to 4,650 EUR [36] for severe disease. In a US study of 2002, Ellis et al. [37] identified annual direct costs for atopic eczema treatment of 450–750 EUR. However, costs were lower in two studies from the UK reporting annual costs independent of disease severity of about 200 EUR [38] and 130 EUR for preschool children [39]. According to a Canadian study, annual per patient expenditure was estimated to be about 200 for patients with mild and about 900 EUR for patients with severe atopic eczema [40]. A study from the Netherlands reported total mean health care costs per patient of about 70 EUR [41].

Our study was planned on the basis of two previous observational studies concerning homoeopathic treatment for chronic diseases. In both studies patients showed significant improvement of atopic eczema already within 3 and 6 months of homoeopathic treatment with an effect until 24 months later [22, 33]. The presented study has a clear disease- and children-specific approach. The diagnosis-specific assessment instrument SCORAD was used, whereas the two other studies used global assessments like numerical rating scales. Moreover the ratings in the previous studies were performed by physicians and patients with potential bias due to expectations or patient-doctor relationship. In contrast, in the present study patients were rated by two blinded independent raters. A later subgroup analysis of one of these studies only for patients with atopic eczema showed similar improvement for both the homoeopathic and conventional groups [8]. Future studies should use a pragmatic randomised design comparing conventional standard treatment versus homoeopathic treatment, and a non-inferiority hypothesis.

To date only one randomised placebo-controlled trial for homoeopathic treatment of children with atopic eczema has been conducted [42]. The study by Siebenwirth

[42] was terminated early because of problems with recruitment. An interim analysis with 24 patients (14 placebo, 10 active agent) was performed. Both groups showed clinical improvement without significant group differences for the outcome parameters.

Conclusion

Taking patient preferences into account, homoeopathic treatment was not superior to conventional treatment for children with mild to moderate atopic eczema. At baseline, patients in the homoeopathic group had a longer disease duration and were more affected by the dis-

ease. Costs were higher in the homoeopathic than in the conventional group, primarily due to the low fee for conventional doctors, and because parents of children in the homoeopathic group spent more money on medical aids and adjuvant therapies.

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