Eur J Med Res (2004) 9: 351-360

ANTHROPOSOPHIC THERAPIES IN CHRONIC DISEASE: THE ANTHROPOSOPHIC MEDICINE OUTCOMES STUDY (AMOS)

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Abstract:
Context: Anthroposophic medicine (AM) is used worldwide for chronic diseases.
Objective: To study clinical outcomes and costs in patients treated with AM therapies for chronic conditions.
Design: Prospective cohort study.
Setting: 141 medical practices in Germany providing AM treatment.
Participants and interventions: 898 outpatients aged 1-75 years referred to AM therapies (art, eurythmy or rhythmical massage, n = 665) or starting AM medical treatment (counselling, medicines, n = 233).
Main outcome measures: Disease severity assessed independently by physician (Disease Score) and patient (Symptom Score), and health-related quality of life (SF-36, KINDL, KITA) after 3, 6, 12, 18, and 24 months; health costs in pre-study year and first study year.
Results: Most common indications were mental disorders (32.0%), and musculoskeletal disorders (18.9%). Disease duration at baseline was median 3.0 years (interquartile range = i.q.r. 1.0-8.5, mean 6.5 ± 8.4 years). Median number of AM therapy sessions was 12 (i.q.r. 10-20), median therapy duration was 120 days (i.q.r. 81-195).

From baseline to 6-month follow-up, Disease Score (0-10) improved from 6.40 ± 1.76 to 3.43 ± 2.23 ($p < 0.001$), Symptom Score (0-10) improved from 5.89 ± 1.75 to 3.35 ± 2.09 ($p < 0.001$). In adults, SF-36 Physical Component Summary improved from mean 43.34 ± 10.58 at baseline to 47.44 ± 10.32 after 6 months ($p < 0.001$), SF-36 Mental Component Summary improved from 38.83 ± 12.45 to 44.93 ± 10.92 ($p < 0.001$). Similar HRQoL improvements were observed in children (KINDL, KITA). All improvements remained stable until 24-month follow-up.

Adverse effects from AM therapies occurred in 2.7% (19/712) of patients. Three (0.5%) patients stopped therapy due to adverse effects. Health costs were 3,637 € per patient in the pre-study year and 3,484 € in the first study year, a decrease of 152 € (4.2%) per patient.
Conclusion: Anthroposophic therapies were associated with long-term reduction of chronic disease symptoms, improvement of health-related quality of life, and health cost reduction.

Key words: anthroposophy, anxiety disorders, art therapy, asthma, attention-deficit disorder with hyperactivity, chronic disease, clinical trials, costs and cost analysis, depressive disorder, eurythmy therapy, low back pain, massage, migraine, neck pain, outcome assessment (health care), sinusitis, tension headache.
Abbreviations: ADHCD: Attention Deficit / Hyperkinetic / Conduct Disorder, AM: anthroposophic medicine, AMOS: Anthroposophic Medicine Outcomes Study, ART: AM art therapy, EY: eurythmy therapy, MED: AM counselling/medication provided by medical doctor, RM: rhythmical massage therapy.

INTRODUCTION

Anthroposophic medicine (AM) was founded in the 1920s by Rudolf Steiner and Ita Wegman [46]. AM aims to stimulate patients' salutogenetic, self-healing capacities [44]. Specific AM treatments include counselling, medication, art and movement therapies, and massage. AM is provided by medical doctors and therapists in hospital and outpatient settings as an extension of conventional medicine. AM is practised in most European countries, the Americas, some African and Asian countries, Australia and New Zealand.

In AM *art therapy* (ART) patients engage in painting, drawing, clay modelling, music or speech under instruction from art therapists [16;24;35]. In eurythmy therapy (EY) patients perform specific movements and gestures selected to treat their condition [31]. Qualification as ART or EY therapist requires 6-7 years training. *Rhythmical massage therapy* (RM) was developed from Swedish massage [23] and is practiced by physiotherapists with 1½-3 years postgraduate training. ART/EY/RM is used for somatic, psycho-somatic and psychiatric conditions.

Clinical documentation of ART/EY/RM has been limited to case reports and small cohort studies. 1998 we started a long-term study of AM in Germany in collaboration with a health insurance company – the Anthroposophic Medicine Outcomes Study (AMOS). This paper reports major findings from AMOS-1, conducted 1998-2003.

AMOS is a prospective real-world observational study of patients starting AM therapies for chronic disease. We did not restrict eligibility criteria to specific diagnoses, as the range and frequency of indications

for AM therapies was not known. Since AM therapy of chronic disease is usually multi-modal – integrating counselling, medicines, ART, EY or RM – we evaluated all AM therapies as a single package, with supplementary analysis of main therapy groups.

Study Topics

This study addressed the following topics:
- Characteristics of AM users: indications for AM, socio-demographics, patient-physician issues
- AM therapy administration
- Disease symptoms and health-related quality of life (HRQoL)
- AM therapy effectiveness and satisfaction ratings
- Adjunctive therapies and health services: use and costs
- Adverse effects

Material, Methods and Statistics

Design
Prospective cohort study

Patient recruitment
Medical doctors certified by the Gesellschaft Anthroposophischer Ärzte in Deutschland recruited patients.

Inclusion criteria: Outpatients aged 1-75 years, starting AM therapy for any indication (primary disease):
- referred to ART, EY or RM,
- or starting AM medical therapy provided by study doctor (MED) after an initial AM consultation ≥ 30 min.

Exclusion criteria: previous ART/EY/RM treatment, or previous AM consultation ≥ 30 min for primary disease.

Primary outcome measures
- Disease severity on numerical scales from 0 (not present) to 10 (worst possible): Disease Score (doctor's global assessment) after 6 and 12 months; Symptom Score (patients' assessment of one to six most relevant symptoms present at baseline) after 3, 6, 12, 18, and 24 months
- HRQoL after 3, 6, 12, 18, and 24 months: SF-36® Health Survey [13] for adults ≥ 17 years; KINDL®-questionnaire [41] for children 8-16; KITA Quality of Life Questionnaire [53] for children 1-7 years

Secondary outcome measures
- Patients' attitudes to AM and conventional medicine
- Therapy and health service utilization in pre-study year and first study year: ART/EY/RM (therapist documentation), AM and non-AM medication, doctor and dentist consultations, paraclinical investigations, hospital and spa treatment, surgery, physical therapy, ergotherapy, psychotherapy, Heilpraktiker (non-medical practitioner) visits, sick leave
- Use of standard therapy for primary disease, according to guidelines of the Association of the Scientific Medical Societies in Germany / Drug Commission of the German Medical Association
- Patient ratings of AM therapy outcome, patient satisfaction with therapy, therapy effectiveness ratings by patient and doctor
- Health costs in pre-study year and in first study year: direct costs (AM therapy, doctor and dentist consultations, psychotherapy, medicines, physical therapy, ergotherapy, hospital treatment, spa), indirect costs (sick leave compensation)
- Adverse effects, Serious Adverse Events (doctor and patient documentation)

Data collection
Except otherwise stated, items were documented by patients. Patient responses were not made available to doctors. Therapy and health service utilization in the pre-study year was documented at study entry, utilization in the first study year was documented after 3 (medicines only), 6 and 12 months.

Data were entered twice by two different persons into MS Access 97®. The two datasets were compared and discrepancies resolved by checking with the original data.

Quality Assurance, adherence to regulations
The study was approved by the Ethics Committee of the Faculty of Medicine Charité, Humboldt University Berlin, and was conducted according to the Helsinki Declaration and GCP guidelines. Written informed consent was obtained from all patients before enrolment.

Data Analysis
Data were analysed on an intention-to-treat basis, using SPSS 11.0® and StatXact 5.0.3®. For continuous data Wilcoxon Signed-Rank test was used for paired samples, Mann-Whitney U-test for independent samples; median differences with 95% confidence intervals were estimated according to Hodges and Lehmann [26]. For binominal data McNemar test and Fisher's exact test were used. All tests were two-tailed. Significance criteria were $p < 0.05$ and 95%-CI not including 0. Pre-post effect sizes were calculated as Standardized Response Mean [34].

Health costs were calculated from average costs per item in Germany, year 2000 (doctors' and dentists' fees, medicines, hospital, spa [3;14]) or from health care benefit catalogues (AM therapies, paraclinical investigations, psychotherapy, physiotherapy, ergotherapy [29;47;48]). Hospital costs were calculated from regional (Bundesländer) averages. Doctors' fees were calculated from average fees of general practitioners + 12 specialist categories in the Accounting Data Record Panel of the Central Research Institute of Ambulatory Health Care in Germany. AM medication costs were calculated using a simplified model of daily doses, dosage forms, and prices, based on AMOS doctors' prescription data, AMOS patients' consumption data, and price lists. Costs of other medications were calculated from average costs in each Anatomical Therapeutic Chemical subgroup [2].

Results

Patient recruitment and follow-up
From 1 July 1998 to 31 March 2001, 141 doctors screened 1095 patients, 898 patients fulfilled all eligi-

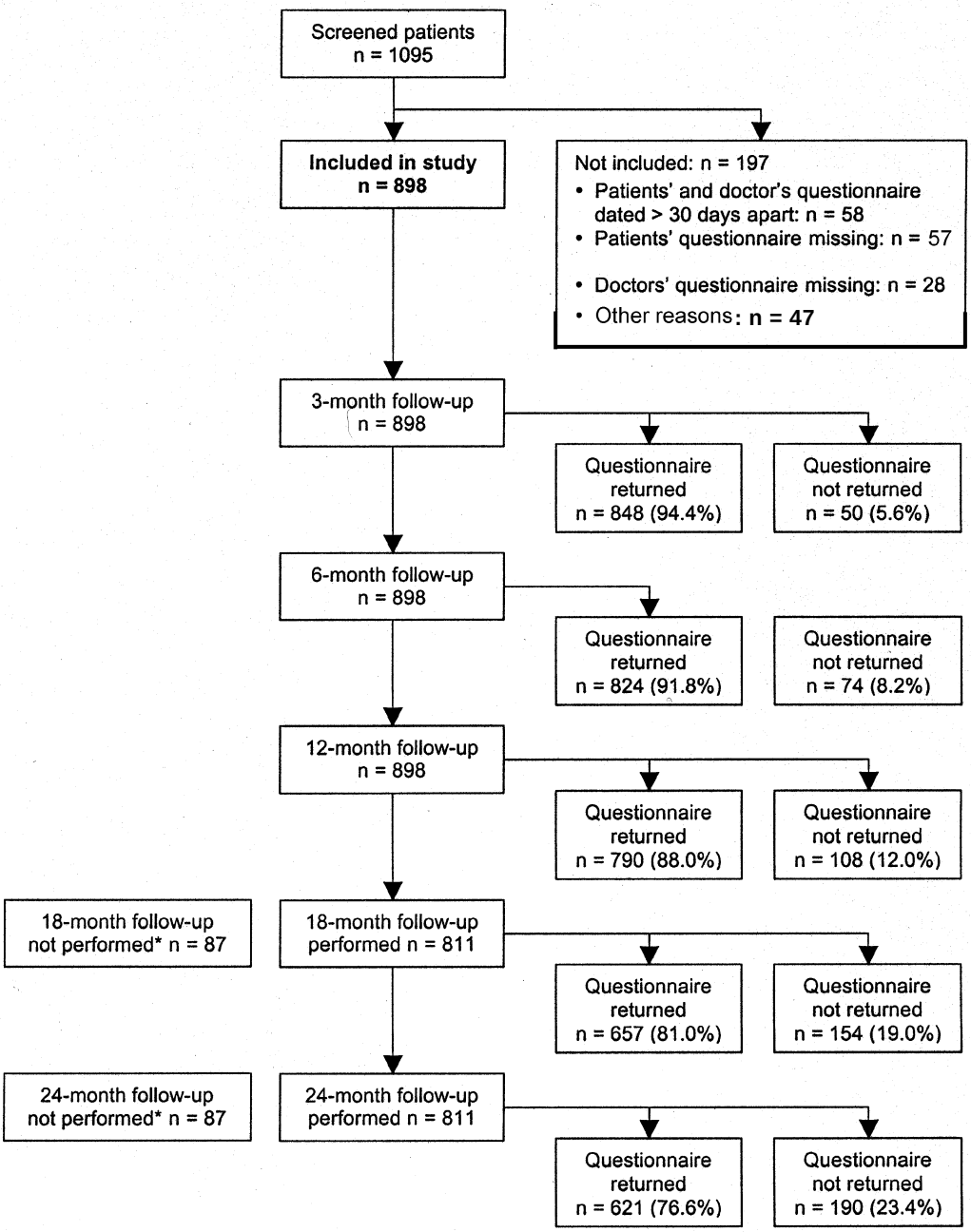

Fig. 1. Patient recruitment and follow-up. *18- and 24-month follow-up was not performed for patients enrolled before 1 Jan 1999.

bility criteria and were included in the study (Fig. 1). Included and not included patients did not differ significantly regarding age and gender.

77% (689/898) of patients were enrolled by general practitioners, 10% by paediatricians, 5% by internists and 9% by other specialist doctors. Each doctor enrolled median 4 patients (interquartile range = i.q.r 2-7). Eight (6%) of the 141 doctors enrolled ≥ 20 patients each, altogether 270 (30%) of 898 study patients. These 270 patients did not differ significantly from the other 628 (70%) study patients regarding Symptom Score at baseline and after 6 and 12 months.

Non-respondents of 6-month follow-up (8%) did not differ significantly from respondents (92%) regarding age, gender, diagnosis, severity or duration of primary disease or baseline Symptom Score. Corresponding dropout analyses for combined 6- and 12-month follow-up (including adjunctive therapy and health service utilization in pre-study year) were also negative, with the exception of dropouts (15%) being 4 years younger and having less primary diseases of the genito-urinary system than respondents (0.9% vs. 5.0%).

Indication for AM therapies

Most primary diseases, classified by ICD-10, were: F00-F99 mental disorders: 32% (n = 287/898 patients); M00-M99 musculoskeletal: 19% (n = 170); J00-J99 respiratory: 9% (n = 79); and G00-G99 CNS: 7% (n = 63). Diagnosis Groups are displayed in Table 1.

Table 1. 10 most common Diagnosis Groups

Diagnosis Group	ICD-10	Most common diagnoses	N	Percent
1. Mood Disorders	F30-F39	Depression (n = 87)	93	10.4%
2. Fatigue	F480, R53	Fatigue (n = 48)	57	6.3%
3. Low Back Pain	M512, M541, M544, M545	Low back pain (n = 27), Lumbar disc prolapse or sciatica (n = 13)	49	5.4%
4. Headache Disorders	G43, G44, R51	Migraine n = 25), Headache (n = 12), Tension headache (n = 3)	41	4.6%
5. Cervical Spinal Disease	M472-M509, M531, M542	Neck pain (n = 22), Cervical disc prolapse (n = 4), Cervical degenerative disease (n = 5)	35	3.9%
6. Asthma	J44-J45	Asthma (n = 30)	33	3.7%
7. Malignancies	C00-C97	Breast (n = 11), Gastrointestinal (n = 4), Thyroid (n = 3), Melanoma (n = 3)	28	3.1%
8. Attention Deficit / Hyperkinetic / Conduct Disorder (ADHCD)	F909, F91-F92, F988	Hyperkinetic syndrome (n = 10), Attention deficit disorder (n = 10)	27	3.0%
9. Anxiety Disorders	F41	Anxiety disorder (n = 16), Panic disorder (n = 4)	25	2.8%
10. Sinusitis	J32, J40-J42	Chronic sinusitis (n = 10), Chronic sinubronchitis (n = 6)	22	2.3%
Other diagnoses			488	54.3%
All patients			898	100.0%

Median duration of primary disease was 3.0 years (i.q.r.: 1.0-8.5, mean: 6.5 ± 8.4 years). In 96% (861/897) of patients disease duration was ≥ 1 month. Patients had median 1 (i.q.r.: 1-2) comorbid diseases, one-third of comorbid disorders were musculoskeletal or mental.

Socio-demographics of AM users

Patients were recruited from 15 out of 16 German states (Bundesländer). Median age was 38.5 years (i.q.r.: 23.0-48.0). 48% of patients were aged 30-49 years; in 60 German primary care practices [30] this age group comprised 30%. Female/male ratio was 2.7/1.0 in the total AMOS cohort, 4.0/1.0 in AMOS Diagnosis Groups, and 1.4/1.0 in corresponding published population or primary care samples, weighted for sample size as in AMOS.

Compared to the German population, AMOS adult patients had higher educational levels, had fewer wage earners, regular smokers, and alcohol consumers, and were less overweight (Table 2).

Table 2. Socio-demographic data of AMOS adult patients and German population samples

Items	AMOS			Germany	
	Subgroup	Proportion of respondents	%	%	Source
"Fachhochschule" or university entrance qualification		382/693	55%	19%	[3]
University degree		151/616	25%	6%	[3]
Wage earners		22/693	3%	34%	[3]
Unemployed during last 12 months	Persons involved in economic activity	27/380	7%	10%	[3]
Living alone		132/687	19%	21%	[3]
Net family income < 900 € per month		75/515	15%	16%	[3]
Alcohol use daily (AMOS) vs. almost daily (Germany)	Male	5/118	4%	28%	[27]
	Female	12/498	2%	11%	
Regular smoking	Male	32/118	27%	37%	[28]
	Female	81/496	16%	28%	
Sports activity ≥ 1 hour weekly	Age 25-69	263/566	46%	39%	[12]
Body mass index < 18.5 (low)	Male	5/117	4%	1%	[45]
	Female	34/494	7%	4%	
Body mass index ≥ 25 (overweight)		159/609	26%	47%	[45]
Permanent work disability pension		49/615	8%	3%	[6]
Severe disability status		57/615	9%	12%	[9]
Sick leave days in the last 12 months (mean ± SD)		29.5 ± 62.4 days		17.0 days	[5]

Patients' attitudes to AM and conventional medicine
Patients enrolled 1998 were asked why they had consulted an AM doctor (n = 76). Positive statements about AM (*„enables a better understanding of my disease"*: 78%; "*enables me to contribute actively to remain in good health*": 71%) were more frequent than negative statements about conventional medicine (*"not effective for my condition"*: 43%; *"too many side effects"*: 40%).

Administration of AM therapies
At enrolment, patients were referred to EY (47%, n = 419/898), ART (18%, n = 161), RM (10%, n = 85), or started MED therapy (26%, n = 233). ART/EY/RM started median 13 days (i.q.r. 2-39) after enrolment, median therapy duration was 120 days (i.q.r. 81-195). Median number of therapy sessions was 12 (i.q.r. 10-20). Patients were treated by 202 different ART/EY/RM therapists. MED patients had median 1 (i.q.r. 0-1) AM consultation ≥60 min, 1 (i.q.r. 0-3) consultation 30-60 min, and 1 (i.q.r. 0-3) consultation 7-30 min with study doctor in the first study year.

Disease symptoms
Disease Score (Fig. 2) improved from 6.40 ± 1.76 at baseline to 3.43 ± 2.23 at 6-month follow-up (median difference: 3.50, 95%-CI: 3.00-3.50, p < 0.001, pre-post effect size: 1.23). An additional improvement was observed between 6 and 12 months after baseline (median difference: 1.00, 95%-CI: 0.50-1.00, p < 0.001). *Symptom Score* (Fig. 3) improved from 5.89 ± 1.75 at baseline to 3.35 ± 2.09 after 6 months (median difference: 2.67, 95%-CI: 2.50–2.83, p < 0.001, effect size 1.09), with a slight further improvement at each subsequent follow-up.

After 6 months, both scores were improved in ca. 85% of patients, respectively. Two-thirds of patients were improved by ≥ 30% of baseline scores.

Improvements in Disease and Symptom Scores were similar in ART, EY, RM, and MED groups, and in children and adults alike. In all 10 Diagnosis Groups (Table 1) both scores improved significantly from baseline to 6-month follow-up; all pre-post effect sizes were large, i. e. ≥ 0.80 (Disease Score: range 1.12-1.76, Symptom Score: range 0.90-1.51) except Disease Score in Malignancies group (0.59).

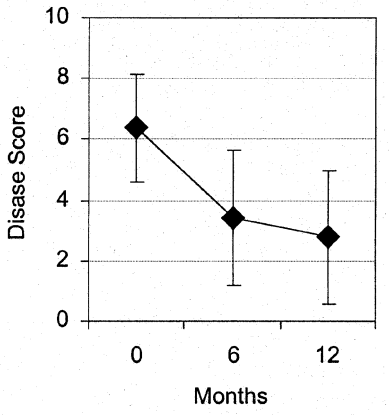

Fig. 2. Disease Score (doctors' assessment), follow-ups after 6 and 12 months, means + SD.

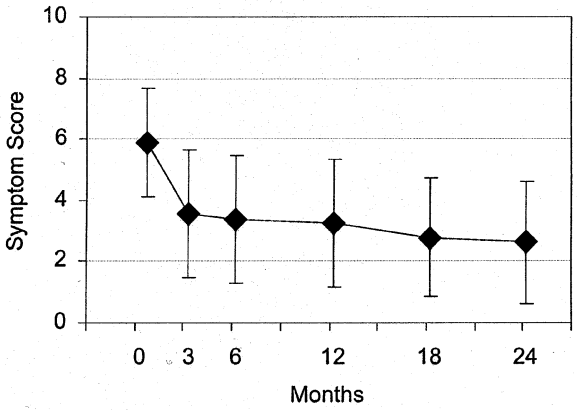

Fig. 3. Symptom Score (patients' assessment, 0 = not present, 10 = worst possible), means + SD.

Health-related quality of life
At baseline, SF-36 Physical Component (PCS, mean 43.21 ± 10.55) and Mental Component Summary scores (MCS, 38.81 ± 12.50) (Fig. 4), as well as all eight SF-36 Subscales and the SF-36 Health Change item were significantly lower (i. e. worse) than in the German population. All SF-36 scores improved significantly between baseline and 6-month follow-up. Median 0-6 month differences were 4.02 (95%-CI: 3.38-4.68, p < 0.001) for PCS, and 5.86 (95%-CI: 4.92-6.84, p < 0.001) for MCS. For both PCS and MCS, improvements were similar in ART, EY, RM and MED groups, and similar in men (n = 134) and women (n = 559). All SF-36 improvements remained stable until the last 24-month follow-up.

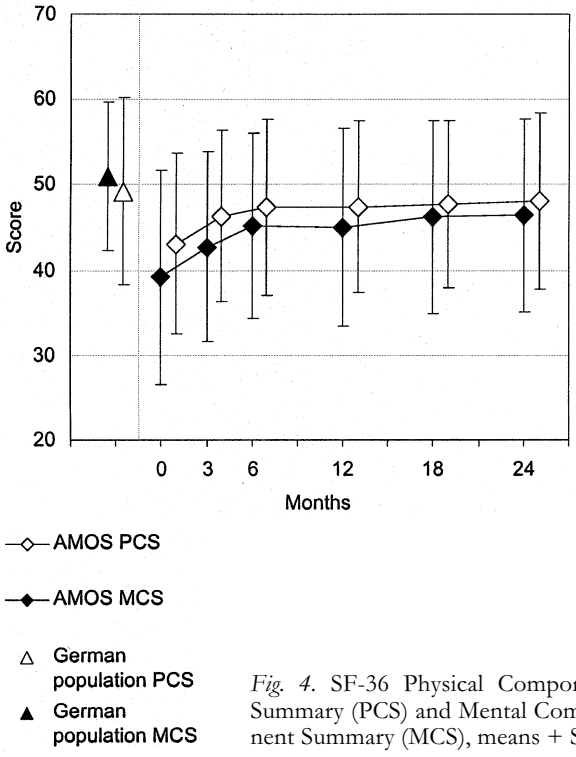

Fig. 4. SF-36 Physical Component Summary (PCS) and Mental Component Summary (MCS), means + SD.

In children aged 8-16, KINDL Summary Score and KINDL Psychic, Somatic and Function Subscales (0-100) improved significantly between baseline and 6-month follow-up. For KINDL Summary Score, median 0-6 month difference was 4.59 (95%-CI: 2.19-7.19, $p < 0.001$). KINDL Social Subscale did not change significantly during the study, all other KINDL scales were significantly improved from baseline at the last 24-month follow-up.

In children aged 1-7, KITA Psychosoma and Daily Life Subscales (0-100) improved progressively until 24-month follow-up. Median 0-6 month difference was 9.38 (95%-CI: 6.25-12.50, $p < 0.001$) for Psychosoma and 8.33 (95%-CI: 4.17-10.42, $p < 0.001$) for Daily Life.

Ratings of therapy outcome, satisfaction and effectiveness

At 6-month follow-up, patients' ratings of therapy outcome (numeric scale: 0 = no help at all, 10 = helped very well) were mean 7.39 ± 2.33; patient satisfaction with therapy (0 = very dissatisfied, 10 = very satisfied) was 8.05 ± 2.18. Patients' ART/EY/RM effectiveness rating (Fig. 5) was "very effective" or "effective" in 86% (487/568) of the responding patients whose ART/EY/RM had started (73% = 487/665 patients referred to ART/EY/RM). Doctors' effectiveness ratings were similar.

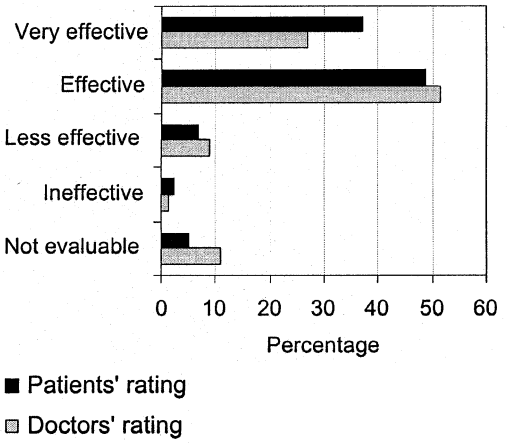

Fig. 5. Effectiveness ratings of art / eurythmy / rhythmical massage therapy at 6-month follow-up: percentage distribution of response categories among respondents where therapy had started. Patients: n = 568, doctors' ratings: n = 527.

Patients' ratings of therapy outcome, satisfaction and effectiveness did not differ significantly between adults (patient rating) and children (proxy rating by caregivers), nor between 6- and 12-month follow-ups. Differences between ART, EY, RM and MED groups and between Diagnosis Groups were small and not consistent at subsequent follow-ups.

Adjunctive therapies, health service utilization, sick leave

Adjunctive therapies, health services and sick leave are listed in Table 3. Comparing pre-study year and first study year, hospital days and paraclinical investigations decreased, psychotherapy and AM medicine use increased, and remaining items did not change significantly. The reduction of hospital days was observed in all age groups except > 70 years (n = 13). Eleven out of twelve listed types of paraclinical investigations decreased, the number of allergy tests increased.

Use of standard therapy

Use of standard therapy for primary disease was analysed in 9 Diagnosis Groups (not in malignancies, since radiotherapy and tumour staging was not documented): Within the first 6 study months, 63% (214/342) of patients had no guideline-supported therapy. This proportion ranged from 40% (19/47, Low Back Pain) to 96% (24/25, ADHCD). The following therapies were not used by any patient in the first 12 study months: prophylactic drugs for migraine or other headaches; antidepressives, anxiolytics or buspirone for anxiety disorders; corticosteroids or surgery for sinusitis; CNS stimulants in ADHCD group.

Table 3. Adjunctive therapies, health service use and sick leave days in pre-study year and first study year. n. s.: not significant. *Heilpraktiker visit: proportion of patients.

Item	-12 to 0 months Mean	± SD*	0 to 12 months* Mean	± SD	p-value	Estimated median difference (95%-CI)
Doctor and dentist consultations	17.96	±20.87	16.73	±17.48	n. s.	n. s.
Paraclinical investigations	6.13	±8.80	5.08	±6.01	p < 0.001	-1.00 (-0.50 to -1.50)
Inpatient hospital days	4.64	±17.44	2.62	±15.41	p = 0.001	-4.50 (-2.00 to -7.50)
Spa days	1.73	±7.70	1.93	±7.51	n. s.	n. s.
Surgeries	0.19	±0.49	0.13	±0.43	n. s.	n. s.
Physical therapy and ergotherapy sessions	9.17	±20.72	9.48	±26.88	n. s.	n. s.
Psychotherapy sessions	3.19	±13.31	4.26	±13.66	p = 0.016	+4.00 (0.50 to 7.50)
AM medicines per day	0.29	±0.65	0.62	±0.85	p < 0.001	+0.33 (0.26 to 0.29)
Non-AM medicines per day	0.69	±1.05	0.78	±1.08	n. s.	n. s.
Sick leave days	30.51	±61.53	32.30	±78.31	n. s.	n. s.
Patients with Heilpraktiker visit*	82/556	(14.8%)	69/556	(12.4%)	n. s.	

Health costs

Direct and indirect health costs were 3,637 € in the pre-study year and 3,484 € per patient in the first study year, a decrease of 152 € (4.2%) per patient (Table 4). Major differences between the two years were an increase in AM costs by 378 €, and a decrease in hospital costs by 623 € per patient. Other costs differed little.

Adverse effects

Adverse effects from ART/EY/RM occurred in 2.7% of patients receiving ART/EY/RM (Table 5). Six (0.8%) patients had adverse effects of severe intensity (categories: mild-moderate-severe), three (0.4%) patients stopped ART/EY/RM due to adverse effects. Adverse drug reactions occurred more than twice as frequent from non-AM medicines (10.4% of users) than from AM medicines (4.5%).

12 patients had Serious Adverse Events (SAE): Five patients died, seven were acutely hospitalized. None of these SAE were related to AM therapies or any medication.

Discussion

Overall study findings

In this prospective real-world outcomes study, 898 outpatients aged 1-75 years were enrolled before starting anthroposophic (AM) art, eurythmy, massage, or medical/counselling therapy for chronic mental, musculoskeletal and other disorders. Mean disease duration before study entry was 6 1/2 years.

Substantial, consistent and stable improvements of disease symptoms and HRQoL were observed during the 2-year follow-up. In the first study year, additional

Table 4. Health costs per patient in pre-study year and first study year.

Item	-12 months to 0 Costs per patient	0 to 12 months Costs per patient	0 to 12 months Percentage of costs	Difference Costs per patient
AM therapies				
Art, eurythmy, rhythmical massage	43 €	417 €	12.0%	+374 €
Doctor's fees for AM consultations	109 €	73 €	2.1%	-36 €
AM medication	45 €	86 €	2.5%	+40 €
Total AM costs	**198 €**	**576 €**	**16.5%**	**+378 €**
Other therapies				
Doctors' non-AM fees, paraclinical investigations	199 €	187 €	5.3%	-12 €
Psychotherapy	179 €	239 €	6.9%	+60 €
Dentists' fees	147 €	151 €	4.3%	+4 €
Non-AM medication	238 €	240 €	6.9%	+2 €
Physical therapy, ergotherapy	103 €	111 €	3.2%	+8 €
Inpatient hospital treatment	1,431 €	808 €	23.2%	-623 €
Spa	112 €	125 €	3.6%	+13 €
Total other therapies	**2,409 €**	**1,861 €**	**53.4%**	**-548 €**
Total direct costs	**2,607 €**	**2,438 €**	**70.0%**	**-169 €**
Indirect costs (sick leave compensation)	1,030 €	1,047 €	30.0%	+17 €
Total direct and indirect costs	**3 637 €**	**3,484 €**	**100.0%**	**-152 €**

Table 5. Frequency of adverse effects. *Number includes patients who had more than one AM therapy

Therapy	Patients with therapy	Patients with adverse effects from therapy		Patients who stopped therapy due to adverse effects	
	N	N	Percentage	N	Percentage
AM therapies	712*	19	2.7%	3	0.4%
-Eurythmy	495*	12	2.4%	0	0.0%
-Art therapy	198*	2	1.0%	0	0.0%
-Rhythmical massage	85	5	5.9%	3	3.5%
Non-AM therapies	?	10	?	3	?
AM medicines	710	32	4.5%	19	2.7%
Non-AM medicines	766	80	10.4%	30	3.9%

costs of AM therapies were outweighed by the cost reduction from a reduced number of hospital days. Use of other health services changed minimally.

Internal validity of study findings

For this study, patient blinding was neither wanted nor possible, since proper conduct of all AM therapies requires non-blind feedback from patients. Randomisation was precluded by strong therapy preferences in AM settings. Since there was no untreated control group, an important question is to which extent the favourable *disease outcomes* were caused by AM therapies or by other factors. Extensive analyses of the potential impact of bias on Symptom Score will be presented and discussed elsewhere (Hamre HJ, Kiene H, manuscript in preparation).

Patient self-reporting of *adjunctive therapies* and *health service utilization* can be affected by recall bias. In this study, however, any systematic recall bias would probably have been conservative, making results appearing less favourable. The reason is: While at study entry patients were asked about therapies and health services during the preceding 12 months, these items were thereafter asked every 6 months (medicine use also after 3 months). Since patients' recall may be less accurate for the 12-month pre-study period than for the shorter periods after study entry, some patients may have underestimated their use in the pre-study-year.

For the combined 6- and 12-month follow-up, the dropout rate was 15%. Dropout analyses were essentially negative, and there is no a priori reason to assume that dropouts use more therapies and health services than respondents, thus dropout is unlikely to have biased therapy and health service analysis.

A notable finding was the reduction of inpatient hospital treatment from average 4.6 days per patient in the pre-study year to 2.6 days in the first study year. This finding was statistically robust (median difference: 4.5 days, 95%-CI: 2.0-7.5, $p = 0.001$), and plausible, as it represents a normalization towards the German average of two days per person. Since the German average decreased only minimally during the study (1998-2001: 2.08 →1.97 days), this decrease cannot explain the observed reduction in AMOS. It also cannot be explained by fluctuating rates of emergencies or accidents, nor by frequent diagnostic hospital stays early in the course of disease (analysis data not shown).

Costs of AM therapies, adjunctive therapies, health services and sick leave compensation were 3,637 € per patient in the pre-study year and 3,484 € in the first study year, a reduction of 152 € per patient. The cost calculation could be affected by errors of

a) the amount of cost-relevant items (e. g. recall bias, see above) and

b) the costs per item applied in the cost calculation (e. g. hospital cost differences depending on hospital ownership and medical specialty).

For each item we estimated the maximum impact of potential errors and calculated its effect on the cost balance. Most errors had modest effects (< ±20 € per patient). Large effects (> ±100 €) were related to hospital costs and sick leave compensation. Combining all "favourable" effects led to a cost reduction of 563 € per patient, combining all "unfavourable" effects diminished cost reduction to 12 € per patient. Thus a significant cost increase is very unlikely.

Representativity of participants

The participation of 343 doctors and therapists from nearly all German Bundesländer suggests a high representativity.

The AMOS sample had a higher proportion of females and of middle-aged persons than German primary care samples; education level and occupational status was higher than in the German population. These findings are in accordance with other studies of patients receiving AM for chronic disease [38;44]. Also the predominance of mental and musculoskeletal disorders in AMOS is in accordance with other findings [44].

Generalisability of the study results

Since patients of different age groups with any clinical condition were included in this study, an important question is whether the positive results are restricted to patient subgroups. Subgroup analyses, however, showed only minor outcome differences between different age and gender groups, between the AM therapies and between Diagnosis Groups. The only exception were SF-36 outcomes differing between Diagnosis Groups. These differences are well-known; they reflect differences in the responsiveness of SF-36 scales between different diseases. In conclusion, generalisability of study results does not appear to be limited to specific subgroups.

Study implications

Considering the almost total lack of previous clinical studies on AM art, eurythmy and rhythmical massage therapy, this large prospective outcomes study represents a step forward in the evaluation of AM therapies.

Most common indications for AM therapy were chronic mental disorders (depression, anxiety, hyperactivity), spinal disorders, asthma, headache syndromes, and chronic sinusitis. These conditions occur frequently in the population (12-month prevalences range from 1.5% for generalized anxiety disorder [51] to 75% for any back pain [32]) and have substantial negative impact on health, HRQoL and work capacity [25;33;40;52]. Based on German [10;21;49] and corresponding Dutch [11] and US [37;42;43] cost calculations, the direct and indirect costs from depressive and anxiety disorders, low back and neck pain, migraine, asthma, and sinusitis amount to 51 billion € per year in Germany.

Standard therapies for these disorders are defined in national guidelines: frequently drugs, physiotherapy and psychotherapy, less frequently multimodal inpatient therapies, for some patients surgery [4;7;8;17;20]. Many patients will not profit from these standard therapies: Non-responder rates in clinical trials range from one in three patients (triptanes in acute migraine, antidepressives in major depression [1;19]) to seven out of eight patients (antibiotics in chronic sinusitis [36]). Standard therapies are usually not curative, and most drugs only work if administered continuously. Furthermore, the generalisability of efficacy data is often strik-

ingly low because of narrow study inclusion criteria: In the case of nonpsychotic unipolar major depression, evidence from randomized trials of antidepressives does not apply to the 86% of patients with clinical features routinely leading to study exclusion [54]. Adverse effects or non-response lead to drug therapy discontinuation or rejection by many patients. For example, it has been found that only 5% of migraineurs and 2% of tension headache sufferers use standard prophylactic drugs [18]. Thus it is not surprising that two-thirds of AMOS patients did not use a guideline-supported therapy for primary disease during the first six study months.

Besides shortcomings of standard treatments, a more frequently stated reason for consulting AM doctors was the patients' positive desire to contribute actively to therapy. This desire is met by exercise therapies like AM art and eurythmy. Anthroposophic counselling and therapy for chronic disease aims to affect underlying causes of the patient's condition, which may not be addressed adequately through passive therapies [44].

AM therapies had favourable risk profiles: Adverse effects occurred in 2.7% of patients and only 0.5% stopped therapy because of adverse effects. Adverse drug reactions occurred less frequently from AM medicines (4.5% of patients) than from other medicines (10.4%). The cost profile was also favourable: Due to a reduction in hospital days, health costs decreased in spite of the new AM therapies. The reduction of hospitalization is in accordance with the policy of AM general practitioners to extend patent care and avoid unnecessary referrals to secondary care [22;44]. In two Dutch studies [15;50] and in a British NHS audit [39], patients of AM doctors had 10%-35% less hospital days than local or national averages.

Conclusion

In this study anthroposophic therapies were associated with substantial long-term reduction of disease severity and improvement of health-related quality of life in patients with musculoskeletal and mental disorders, headache syndromes, asthma and other chronic diseases. Considering the long disease duration before enrolment (average $6\,^1/_2$ years), these results are encouraging. The favourable outcomes were associated with a low frequency of adverse effects and were not accompanied by an increase in health costs.

Acknowledgements: This study was funded by Innungskrankenkasse Hamburg with supplementary grants from Deutsche BKK and Betriebskrankenkasse des Bundesverkehrsministeriums. We thank G. S. Kienle and W. Tröger for valuable help and advice, and M. Kilthau, L. Bak Schröder and P. Siemers for technical assistance.

References

1. Practice guideline for the treatment of patients with major depression. Washington: American Psychiatric Association; 2000
2. Arzneiverordnungs-Report 2001. Berlin, Heidelberg, New York: Springer-Verlag; 2001, 982 p.
3. Statistisches Jahrbuch 2001 für die Bundesrepublik Deutschland. Wiesbaden: Statistisches Bundesamt; 2001, 764 p.
4. Leitlinien der Deutschen Gesellschaft für Psychotherapeutische Medizin (DGPM), Deutsche Gesellschaft für Psychoanalyse, Psychotherapie, Psychosomatik und Tiefenpsychologie (DGPT), Deutsches Kollegium Psychosomatische Medizin (DKPM), Allgemeine Ärztliche Gesellschaft für Psychotherapie (AÄGP). Psychotherapie der Depression. AWMF-Leitlinien-Register Nr 051/023 2002.
5. Statistisches Taschenbuch Gesundheit 2001. Bonn: Bundesministerium für Gesundheit; 2002
6. VDR Statistik Rentenbestand am 31. Dezember 2000. Frankfurt am Main: Verband Deutscher Rentenversicherungsträger; 2003
7. Arzneimittelkommission der deutschen Ärzteschaft. Empfehlungen zur Therapie der Depression. AVP-Sonderheft Therapieempfehlungen 1997;1-17.
8. Arzneimittelkommission der deutschen Ärzteschaft. Evidenzbasierte Therapie-Leitlinien. Köln: Deutscher Ärzte-Verlag; 2002, 295 p.
9. Bergmann E, Ellert U. Sehhilfen, Hörhilfen und Schwerbehinderung. Bundesgesundheitsblatt 2000;(6):432.
10. Bolten W, Kempel-Waibel A, Pförringer W. Analyse der Krankheitskosten bei Rückenschmerzen. Med Klin (Munich) 1998; 93(6):388-393.
11. Borghouts JA, Koes BW, Vondeling H, Bouter LM. Cost-of-illness of neck pain in The Netherlands in 1996. Pain 1999; 80(3):629-636.
12. Breckenkamp J, Laaser U, Danell T. Freizeitinteressen und subjektive Gesundheit. Wiesbaden: Bundesinstitut für Bevölkerungsforschung; 2001, 143 p.
13. Bullinger M, Kirchberger I. SF-36 Fragebogen zum Gesundheitszustand. Handanweisung. Göttingen: Hogrefe-Verlag; 1998, 155 p.
14. Bundesministerium für Gesundheit und Soziale Sicherung. Gesetzliche Krankenversicherung - Kennzahlen und Faustformeln. Statistiken zur GKV. Last update: 11-7-2003. Accessibility verified: 8-12-2003.
15. Coerver MMH, Otten E. Een erste stap in de bewijsvoering. Onderzoek naar de kosteneffecten van de antroposofische huisartsenzorg. Utrecht: Moret Ernst & Young Management Consultants; 1995, 27 p.
16. Collot d'Herbois L. Light, darkness and color in painting therapy. Dornach: Goetheanum Press; 1993, 258 p.
17. Dt.Ges.f.Kinder- und Jugendpsychiatrie und Psychotherapie u.a. Leitlinien zur Diagnostik und Therapie von psychischen Störungen im Säuglings-, Kindes- und Jugendalter. 2. überarbeitete Auflage. Köln: Deutscher Ärzte Verlag; 2003.
18. Edmeads J, Findlay H, Tugwell P, Pryse-Phillips W, Nelson RF, Murray TJ. Impact of migraine and tension-type headache on life-style, consulting behaviour, and medication use: a Canadian population survey. Can J Neurol Sci 1993; 20(2):131-137.
19. Ferrari MD, Roon KI, Lipton RB, Goadsby PJ. Oral triptans (serotonin 5-HT(1B/1D) agonists) in acute migraine treatment: a meta-analysis of 53 trials. Lancet 2001; 358(9294):1668-1675.
20. Ganzer U, Arnold W. Leitlinien der Dt. Ges. f. Hals-Nasen-Ohren-Heilkunde, Kopf- und Hals-Chirurgie: Sinusitis maxillaris / ethmoidalis. AWMF-Leitlinien-Register 017/019. AWMF online. Last update: 2001. Accessibility verified: 1-4-2004.
21. Göbel H. Die Kopfschmerzen: Ursachen, Mechanismen, Diagnostik und Therapie in der Praxis. Berlin, Heidelberg, New York: Springer-Verlag; 1997, 901 p.
22. Hauff MV, Prätorius R. Leistungsstruktur alternativer Arztpraxen. Eine gesundheitspolitische Analyse. Bad Liebenzell: Verein für ein erweitertes Heilwesen e. V.; 1991.

23. Hauschka-Stavenhagen M. Rhythmical massage as indicated by Dr. Ita Wegman. Spring Valley, NY: Mercury Press; 1990, 138 p.
24. Hauschka-Stavenhagen M. Fundamentals of artistic therapy, based on spiritual science. Spring Valley, NY: Mercury Press; 1997, 94 p.
25. Hays RD, Wells KB, Sherbourne CD, Rogers W, Spritzer K. Functioning and well-being outcomes of patients with depression compared with chronic general medical illnesses. Arch Gen Psychiatry 1995; 52(1):11-19.
26. Hodges JL, Lehmann EL. Estimates of location based on rank tests. Ann Math Stat 1963; 34:598-611.
27. Hoffmeister H, Schelp FP, Mensink GB, Dietz E, Bohning D. The relationship between alcohol consumption, health indicators and mortality in the German population. Int J Epidemiol 1999; 28(6):1066-1072.
28. Junge B, Nagel M. Das Rauchverhalten in Deutschland. Gesundheitswesen 1999; 61(Sonderheft 2):S121-S125.
29. Kassenärztliche Bundesvereinigung. Einheitlicher Bewertungsmaßstab (EBM). Inkrafttreten: 1. Juli 2000. Köln: Deutscher Ärzte-Verlag; 2000, 251 p.
30. Kerek-Bodden H, Koch H, Brenner G, Flatten G. Diagnosespektrum und Behandlungsaufwand des allgemeinärztlichen Patientenklientels. Ergebnisse des ADT-Panels des Zentralinstituts für die kassenärztliche Versorgung. Z Ärztl Fortbild Qualitätssich 2000; 94(1):21-30.
31. Kirchner-Bockholt M. Fundamental principles of curative eurythmy. London: Temple Lodge Press; 1977, 192 p.
32. Kohlmann T, Deck R, Raspe H. Prävalenz und Schweregrad von Rückenschmerzen in der Lübecker Bevölkerung. Akt Rheumatol 1995; 20:99-103.
33. Kohlmann T, Raspe HH. Zur Graduierung von Rückenschmerzen. Ther Umsch 1994; 51(6):375-380.
34. Liang MH, Fossel AH, Larson MG. Comparisons of five health status instruments for orthopedic evaluation. Med Care 1990; 28(7):632-642.
35. Lorenz-Poschmann A. Breath, Speech, and Therapy. Spring Valley, NY: Mercury Press; 1982, 16 p.
36. Morris P, Leach A. Antibiotics for persistent nasal discharge (rhinosinusitis) in children. Cochrane Database Syst Rev 2002;(4):CD001094.
37. Nuijten MJ, Hardens M, Souetre E. A Markov process analysis comparing the cost effectiveness of maintenance therapy with citalopram versus standard therapy in major depression. Pharmacoeconomics 1995; 8(2):159-168.
38. Pampallona S, von Rohr E, van Wegberg B, Bernhard J, Helwig S, Heusser P et al. Socio-demographic and medical characteristics of advanced cancer patients using conventional or complementary medicine. Onkologie 2002; 25(2):165-170.
39. Prescription Pricing Authority. PACT Standard Report. Gloucestershire Royal NHS Trust; 1999.
40. Pryse-Phillips W, Findlay H, Tugwell P, Edmeads J, Murray TJ, Nelson RF. A Canadian population survey on the clinical, epidemiologic and societal impact of migraine and tension-type headache. Can J Neurol Sci 1992; 19(3):333-339.
41. Ravens-Sieberer U, Bullinger M. Assessing health-related quality of life in chronically ill children with the German KINDL: first psychometric and content analytical results. Qual Life Res 1998; 7(5):399-407.
42. Ray NF, Baraniuk JN, Thamer M, Rinehart CS, Gergen PJ, Kaliner M et al. Healthcare expenditures for sinusitis in 1996: contributions of asthma, rhinitis, and other airway disorders. J Allergy Clin Immunol 1999; 103(3 Pt 1):408-414.
43. Rice DP, Miller LS. Health economics and cost implications of anxiety and other mental disorders in the United States. Br J Psychiatry Suppl 1998;(34):4-9.
44. Ritchie J, Wilkinson J, Gantley M, Feder G, Carter Y, Formby J. A model of integrated primary care: anthroposophic medicine. London: National Centre for Social Research, Department of General Practice and Primary Care, St Bartholomew's and the Royal London School of Medicine and Dentistry, Queen Mary University of London; 2001, 158 p.
45. Statistisches Bundesamt. Körpermaße der Bevölkerung nach Altersgruppen. Ergebnisse der Mikrozensus-Befragung im April 1999. Gesundheitswesen. Last update: 2002. Accessibility verified: 1-4-2004.
46. Steiner R, Wegman I. Extending practical medicine. Fundamental principles based on the science of the spirit. GA 27. Bristol: Rudolf Steiner Press; 2000, 144 p.
47. Verband der Angestellten-Krankenkassen e.V., Arbeiter-Ersatzkassen-Verband e.V. Vergütungsliste für ergotherapeutische Leistungen - Leistungsverzeichnis - (Preisliste gem. § 125 SGB V). 2000.
48. Verband der Angestellten-Krankenkassen e.V., Arbeiter-Ersatzkassen-Verband e.V. Vergütungsliste für Krankengymnastische/physiotherapeutische Leistungen, Massagen und medizinischen Bäder (Preisliste gem. § 125 SGB V). 2000.
49. Weissflog D, Matthys H, Virchow JC, Jr. Epidemiologie und Kosten von Asthma bronchiale und chronischer Bronchitis in Deutschland. Dtsch Med Wochenschr 2001; 126(28-29):803-808.
50. Witsenburg BC. Anthroposophical medicine: economical care overboard? J Anthroposophic Med 1993; 10(2):46-50.
51. Wittchen HU, Carter RM, Pfister H, Montgomery SA, Kessler RC. Disabilities and quality of life in pure and comorbid generalized anxiety disorder and major depression in a national survey. Int Clin Psychopharmacol 2000; 15(6):319-328.
52. Wittchen HU, Hofler M, Meister W. Prevalence and recognition of depressive syndromes in German primary care settings: poorly recognized and treated? Int Clin Psychopharmacol 2001; 16(3):121-135.
53. Wittorf M. KITA - Fragebogen zur Erfassung der gesundheitsbezogenen Lebensqualität von Kleinkindern zwischen 1 und 6 Jahren. Dissertation. Berlin: Institut für Arbeits-, Sozialmedizin und Epidemiologie der Medizinischen Fakultät Charité der Humboldt-Universität zu Berlin; 2001, 46 p.
54. Zimmerman M, Mattia JI, Posternak MA. Are subjects in pharmacological treatment trials of depression representative of patients in routine clinical practice? Am J Psychiatry 2002; 159(3):469-473.

Received: April 7, 2004 / Accepted: June 7, 2004

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