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Article focus

1. Efficiency of community occupational therapy in Dementia
2. Pragmatic multi-centre RCT in routine care context

Key message

An efficient Dutch community occupational therapy programme did not work better than a comprehensive occupational therapy consultation in German routine health care.

Strengths and limitations

The main strength of this trial was an elaborated multi-centre RCT design using an active control group, a 26 weeks follow-up and a strategy of video rating with fully masked assessors.

The main limitation was that the training time for the interventionists was less than for the therapists of the Dutch original programme.

Abstract

Objective

To determine the benefits and harms of a Dutch Community Occupational Therapy (COTiD) programme for patients with Alzheimer's disease in the German health care system.

Design

A seven-centre, single-blind, active-controlled RCT.

Setting

Patients' homes and outpatient memory centres of five university hospitals, one geriatric clinic and one neurological private practice unit.

Participants

141 patients with mild to moderate Alzheimer's disease living in the community and their primary carers.

Interventions

Experimental 10 home visits by an occupational therapist, educating patients in the performance of simplified daily activities and in the use of aids to compensate for cognitive decline; and carers in coping with behaviours and giving supervision.

Control one home visit including individual counselling of patient and carer and explanation of a leaflet on coping with dementia in daily life.

Outcome measures

The Interview of Deterioration in Daily activities in Dementia (IDDD) and the Perceive, Recall, Plan and Perform System of Task Analysis (PRPP). Participants were evaluated at baseline, 6, 16, 26 and at 52 weeks.

Results

Patients' daily functioning remained stable over 26 weeks in both groups. There was no significant group time interaction effect in the measurements of patients' daily functioning. No adverse events were associated with the interventions.

Conclusions

In the German health care context, intensive community occupational therapy was not superior to a one-session consultation for the daily functioning of people with Alzheimer's disease. Careful cross-national comparisons are needed before complex interventions based on other health care systems can be considered as evidence.

Trial registration

International Clinical Trials Registry Platform, DRKS00000053

INTRODUCTION

Alzheimer's disease causes high health care costs and burdens patients and carers with severe problems in activities of daily living (ADL).[1-2] Consequently, the improvement or the preservation of ADL is evaluated as a patient-related outcome in clinical trials related to dementia.[3] ADL, burden of care, ability to stay in the community, and quality of life issues are probably much more relevant to patients and carers than the deceleration of cognitive decline, another patient-related outcome.[4] A synopsis of four systematic reviews analysing 73 RCTs on the efficacy of pharmacological and psychosocial interventions regarding everyday functioning in dementia concluded that positive effects of drugs on ADL are small (pooled effect sizes < 0.28) and heterogeneous regarding safety. In contrast to the well documented results for pharmacological interventions evidence for psychosocial interventions on ADL is lacking.[5] However, a recent Dutch mono-centre RCT demonstrated large positive effects of occupational therapy on ADL (effect sizes of 2.4, $p < .0001$).[6] Therefore, the purpose of our multi-centre RCT was to replicate the results of the Dutch community occupational therapy programme in a broader health care context and to evaluate its effectiveness and safety.

Occupational therapy specialises in supporting independence in ADL and is recommended in several guidelines for dementia management.[7-9] Occupational therapy uses a combined approach including activity simplification, environmental modification, adaptive aids, problem-solving strategies, skill training and carer training.[7, 10-11] According to the bio-psycho-social health model of the World Health Organization (WHO), the negative impact of cognitive deficits on activities can be diminished by

improving the patient's physical and social environment and by tailoring the intervention to patient's capability.[12-15]

Until October 2010, there was no systematic review on community occupational therapy for people with Alzheimer's disease but two research groups had conducted RCTs in this subject. In the USA study, occupational therapy demonstrated beneficial effects on patients' challenging behaviour but not on ADL. No information on adverse events were given.[14, 16-18] In the Netherlands, occupational therapy tailored to the needs of patients and carers showed benefits on the patient's ADL, mood, health status and quality of life and on the carer's sense of competence, mood, quality of life and costs of informal care. No adverse events were reported in either intervention or control group.[6, 19-20]

In the current randomised trial we tested the hypothesis that the Dutch ten-session Community Occupational Therapy in Dementia Programme (COTiD) would significantly better improve or stabilise the functioning in everyday life of people with mild or moderate dementia than a one-session Community Occupational Therapy Consultation (COTC). Secondary research questions were whether these interventions show a difference in their effect on patient's and primary carer's quality of life and mood; on the carer's sense of competence in the interaction with the patient; and on long-term nursing home placements.

METHODS

Design

In order to evaluate the superiority of COTiD, we used a seven-centre single-blind, active-controlled design with a 1:1 randomisation for two parallel groups.

There was no modification in design or eligibility criteria from the study protocol available at http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2761388/. The study was registered at the German register of clinical trials, which is connected to the International Clinical Trials Registry Platform (http://apps.who.int/trialsearch/ => DRKS00000053).

Participants and Setting

Patients were eligible to participate in the study if they had mild to moderate dementia (MMSE 14-24) and were diagnosed as having Alzheimer's disease or mixed type dementia, according to ICD-10 criteria, by physicians with more than five years of experience in dementia diagnosis. Participants had to dwell in the community either together with their primary carer or with involvement of a carer providing care at least twice a week. Patients with a major need of physical nursing care and a score above 12 on the 30-items Geriatric Depression Scale were excluded. Unstable medical conditions or severe behavioural disturbances, which did not allow participation in the study as judged by the study physicians were criteria for exclusion as well as for discontinuation. Stop criteria were death of patient or primary carer or a long-term nursing home placement of the patient during the treatment phase. The patient gave written informed consent and the carer assented in written form to join and support the treatment procedures.

Patients were recruited from five outpatient memory centres at university hospitals (in Bonn, Freiburg, Mainz, Marburg and Tübingen); one municipal hospital in Karlsruhe specialising in geriatric medicine and one neurological private practice in Berlin specialising in neuropsychiatry and collaborating with an occupational therapy private practice. The seven participating centres are

located throughout Germany in urban regions with catchment areas from about 70,000 to 700,000 inhabitants. They had all provided outpatient dementia care for three to fifteen years. Their standard service comprised diagnostic work-up for dementia and related diagnoses as well as recommendation of risk reduction, dementia medication and non-pharmacological treatments. Principal investigators of the centres were psychiatrists, neurologists or geriatricians with six to thirteen years of experience in dementia care.

Interventions

The experimental intervention (COTiD) was designed to improve the patient's and the primary carer's daily functioning, and was based on an evidence-based treatment manual.[6, 19-23] COTiD consisted of ten occupational therapy sessions of one hour duration held over five weeks at each patient's home. In the diagnostic phase, comprising of 3 to 4 sessions, the occupational therapist explored (1) the patient's preferences and history of daily activities, (2) her or his ability to perform activities and to use compensatory strategies within the familiar environment, (3) the possibilities of modifying the patient's home, (4) the carer's activity preferences, problems in care giving, coping strategies and abilities to supervise and (5) the interaction between carer and patient. In a shared decision-making process during the goal setting session, the patient and the carer selected one or two most meaningful activities out of a list of their preferences for daily activities to work on in occupational therapy. During the treatment phase of 5 to 6 sessions, the occupational therapist defined together with the patient and the carer more effective compensatory and environmental strategies to adapt both the environment and the selected activities to the patient's habits and cognitive abilities. Patient and carer were taught how to use

these suggested adaptations within strategies, activities and the environment, in order to improve their performance of daily activities. In addition, the carer received practical and emotional support and was coached in effective supervision, problem solving and coping strategies by means of cognitive-behavioural interventions. Detailed description of the experimental intervention has been published elsewhere.[23]

For the trial in Germany, MG taught the content of the translated treatment manual to 14 study participant occupational therapists in 16 hours of seminars using presentation, videos and role play with feedback and group discussion. After the seminar and before the study started, they needed to complete a full treatment series for at least one pilot dyad of patient and carer. In the study phase, the interventionists spent about 20 hours per patient for a full treatment series including ten treatment sessions, travel, reports and multidisciplinary briefing. In Germany, a series of ten to thirty sessions is within the normal range of time that occupational therapists use for the treatment of older outpatients diagnosed with other diseases, such as stroke or rheumatoid arthritis.

The control group received one hour occupational therapy consultation (COTC) at the patient's home conducted by the same study interventionists. Based on material of the German Alzheimer Society, two occupational therapists with more than five years of experience in dementia care had prepared a leaflet of ten pages.[24-25] The semi-structured consultation was half a talk on individual problems that arose from patient's and carer's needs and half an hour explanation of this leaflet. This included encouragement to stay active in everyday life, to maintain social contacts and to use dementia services in the region for which local addresses were listed in the leaflet. Occupational therapists were taught the control intervention within a 4-hours seminar.

Consultations of 30 minutes up to one hour duration about such issues are common in German dementia care. Detailed description of the control intervention as well as means of quality assurance in experimental and control intervention has been published elsewhere.[26]

Outcome measures

The primary endpoint was the patients' change of daily functioning from baseline to follow-up time points at week 6, 16 and 26 measured with the performance scale of the Interview for Deterioration in Daily Living Activities in Dementia (IDDD).[27] This scale records carer rating of the patient's need of assistance in the performance of (1) washing oneself, (2) making tea or coffee, (3) dressing, (4) combing one's hair and brushing one's teeth, (5) eating, (6) using the toilet, (7) shopping, (8) using the telephone, (9) preparing a meal, (10) cleaning the house or doing minor repair work and (11) handling finances. Each item is rated never=0, seldom=1, sometimes=2, often=3 or always=4. The sum of scores ranged from 0 to 44. Higher scores indicated higher need for assistance. Since carer rating could not be masked, daily functioning was additionally evaluated by external assessors fully masked to the group assignment. They rated video tapes of a challenging daily living task and used the Perceive, Recall, Plan and Perform System of Task Analysis (PRPP).[28] For the PRPP, assessors had to define single steps of the performed activity, and they identified any activity step in which errors of accuracy, omission, repetition or timing occurred. The number of activity steps rated as incorrectly performed was divided by the total number of activity steps, resulting in an independence-score indicated in a percentage (100% = all steps are error-free).

Table 1: Measurements of secondary endpoints[26]

Endpoint	Measurement
Patient's initiative in daily activities	Interview for Deterioration in Daily Living Activities in Dementia (IDDD), initiative scale
Patient's mood	Cornell Scale for Depression in Dementia (CSDD)
Carer's mood	Center for Epidemiologic Depression Scale (CES-D)
Patient's and carer's quality of life	Dementia Quality of Life Instrument (DQoL), overall item
	SF-12 physical
	SF-12 mental
Carer's interaction with patient	Sense of Competence Questionnaire (SCQ)
Care by primary carer	Resource Utilization in Dementia (RUD), hours per day
Nursing home placement	RUD, nights in nursing home (except respite care)
Harms	Number of adverse events
	RUD, nights in hospital

Secondary endpoints included mood, quality of life, resource utilisation and possible harms. Measurements (Table 1) were completed at baseline, week 6, 16, 26 and 52. All measurement instruments are validated and used in dementia research.[29-30] Data were collected independently from the intervention by study staff members who had a minimum of one year's professional experience with older or cognitively impaired people. Data collectors attended an introductory seminar of 8 hours. They applied the complete assessment during a 2-hour visit at each patient's home including (1) handing out and explaining the questionnaires to the carer, (2) interviewing the patient (DQoL and SF-12) in a separate room, (3) videotaping the patient and (4) receiving back the carer questionnaires, checking it and clarifying answers if necessary. Seminar description and means of quality management for assessment as well as detailed scheme and psychometric properties of all measurement instruments have been reported recently.[26] There was one protocol amendment before recruitment started: the Assessment of Motor and Process Skills (AMPS) was replaced by the PRPP, because the AMPS was not available in the German language within the planned schedule.

Indicators of harm were defined as patient or carer death, number of patients with admission to hospital and number of nights in hospital. These indicators were recorded in interviews with the carer in intervals of 5 to 7 weeks over 52 weeks. Study sites had to report severe adverse events to the study centre immediately when each occurred.

Sample size calculation

A sample size of 42 participants per group was calculated to be necessary to detect an effect size of f = 0.10 on the IDDD performance scale in an analysis of variance of two groups and four time points, using a two-sided 5% significance level, a power of 80%, and a correlation of 0.7 between the measurement time points. According to the Dutch original RCT, we expected a dropout rate of 10% at week 16, which was extrapolated to 40% at week 52. In sum, we anticipated a 9-month inclusion period to recruit the necessary number of 140 patients. Although the Dutch original RCT found effect sizes of d-value=2.4 in the IDDD performance scale at week 12, we calculated the power much more conservatively. This was because we (1) introduced an active control group, (2) investigated the programme effects under varying care conditions in seven centres with interventionists who were introduced in this new treatment and were far not as experienced as the Dutch study therapists and (3) we prolonged the follow up period. Interim analyses were not planned.

Randomisation and masking

The random allocation sequence was computer-generated with blocking by centre and groups of two persons, without stratification and in a ratio of 1:1 by a statistician from a distant site. After enrolment, study site physicians requested

randomisation via e-mail. The statistician e-mailed the individual allocation to COTiD or COTC exclusively to the site interventionist and stored the allocation list at his distant site not available to any study site staff. The interventionist scheduled treatment sessions, faxed records to the distant coordinating study centre and kept all documents strictly separated from any other site staff, in order to avoid contamination. Since the numbers of home visits differed in the experimental and control groups, masking of patients and carers was not possible. However, study information did not include any preference for a special treatment arm. Patients and carers were asked to avoid any talks about the treatment with any study staff, except the interventionist. The procedure of external video rating ensured the full 'blinding' of the assessors. Independent research assistants cleaned the videotapes from any hint of group assignment, before they were rated by Dutch assessors not involved in the trial treatment. Agreement between the actual and the assessor estimation of group assignment was 61%, and thus slightly over the expected 50% agreement by chance. Data analysts were not blinded to the group assignment. However, measurement time points and outcomes had been published before data were available for analysis [26] and any decision to remove patients from the analyses is reported here.

Statistical methods

Data were entered via special MS Access entry masks automatically controlling for data plausibility. In addition, sections of entered data were checked for typing errors by hand, in order to ensure an error rate lower than 0.2%.

The primary intention-to-treat analysis included all allocated participants with valid data whether they did or did not receive the complete intervention. For the

primary outcomes, we performed a multivariate analysis of variance (MANOVA) with repeated measures with two groups and four measurement time points at baseline, week 6, 16 and 26. In this primary analysis, we did not adjust for baseline values or any other co-variate. A univariate ANOVA with five measurement time points (+ week 52) was carried out for the secondary outcomes.

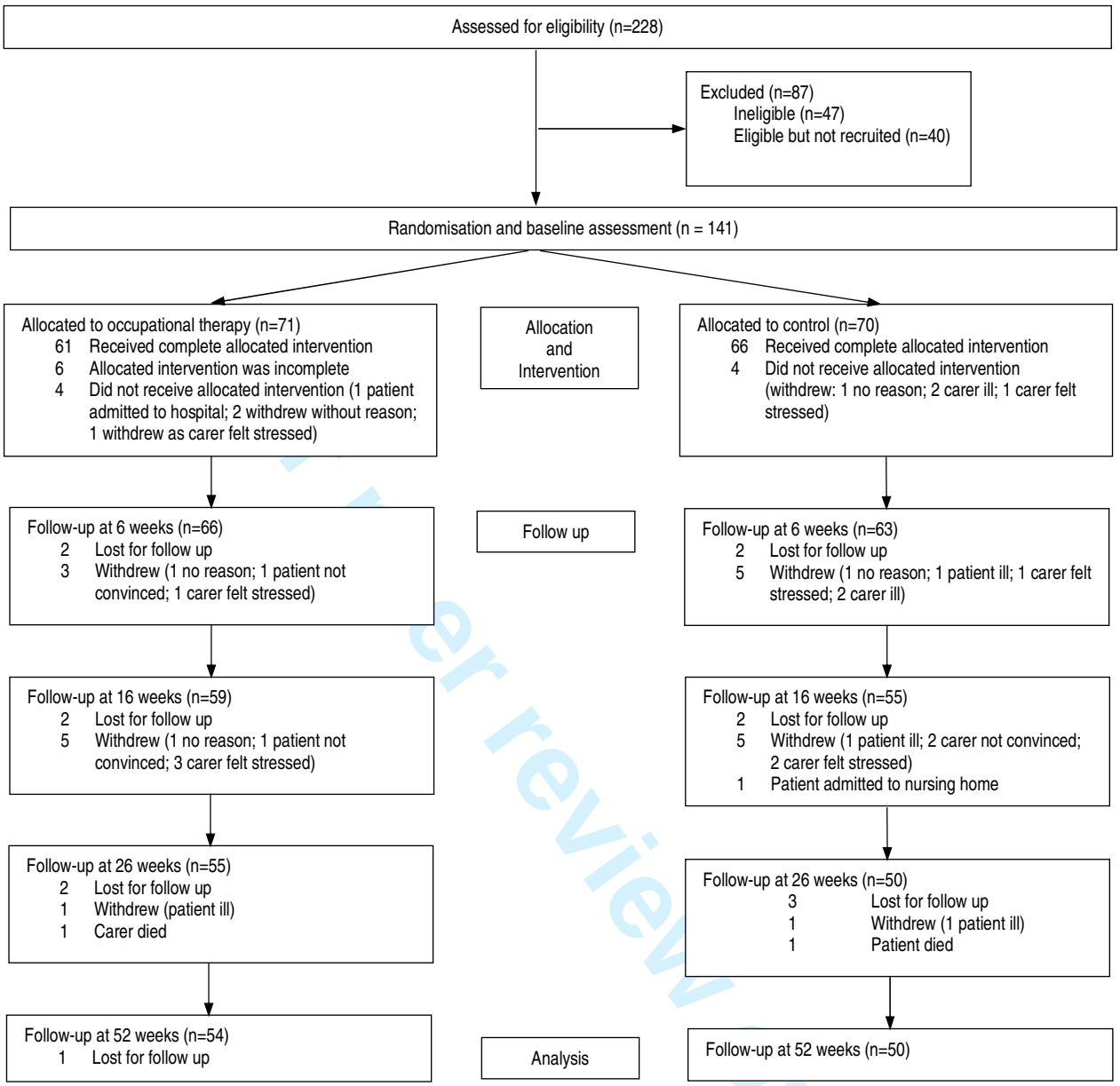
In order to deal with missing data, we performed secondary intention-to-treat analyses with multiple data imputation using the Full Information Maximum Likelihood (FIML) method.[31] All statistical tests were two-sided on an alpha level of 0.05. Subgroup analyses were not planned.

RESULTS

Recruitment and participant flow

We prolonged the planned recruitment period from August 2008 to April 2009 for one additional month up to May 2009. This was in order to recruit the intended sample size. The 52-week follow up was closed in May 2010. 141 participants were recruited. The flow chart (Figure 1) shows that attrition following randomisation did not lead to significant group differences.

Figure 1: Flow of participants through the trial



Baseline Characteristics

Randomisation did avoid imbalances in baseline characteristics (Table 2) and pre-treatment assessment data (Table 3) except in one item. Participants in the control group had more moderate to severe limitations in their financial situation (14% v 2%; p=0.027). Because the financial situation is not known as predictive factor for functional decline, we did not adjust for this imbalance.[32]

Table 2: Demographic and clinical characteristics

	COTiD		Control	
	analysed (n=54)	dropouts (n=17)	analysed (n=50)	dropouts (n=20)
Age, years (SD)	78.0 (7.1)	77.2 (8.5)	78.7 (6.0)	78.3 (7.1)
Sex, female	29 (54 %)	12 (71 %)	30 (60 %)	10 (50 %)
MMSE (SD)	20.4 (3.1)	19.0 (3.3)	20.7 (2.7)	20.3 (2.9)
GDS (SD)	6.9 (3.0)	5.6 (2.9)	5.2 (2.8)	6.1 (2.6)
Education				
low	2 (4 %)	1 (6 %)	1 (2 %)	0 (0 %)
middle	41 (76 %)	13 (76 %)	37 (74 %)	15 (75 %)
high	11 (20 %)	3 (18 %)	12 (24 %)	5 (25 %)
Financial situation				
no limitation	40 (74 %)	14 (82 %)	38 (76 %)	13 (65 %)
minor limitation	12 (22 %)	1 (6 %)	3 (6 %)	3 (15 %)
moderate or severe limitation	1 (2 %)	2 (12 %)	7 (14 %)	4 (20 %)
no data	1 (2 %)	0 (0.0 %)	2 (4 %)	0 (0 %)
Primary carer				
Age, years (SD)	65.4 (16.3)	63.1 (14.0)	65.9 (13.0)	61.4 (17.4)
Sex, female	38 (70 %)	9 (53 %)	35 (70 %)	18 (90 %)
Spouse	32 (59 %)	8 (47 %)	31 (62 %)	9 (45 %)
Daughter or son (in law)	20 (37 %)	7 (41 %)	16 (32 %)	9 (45 %)
Others	2 (4 %)	2 (12 %)	3 (6 %)	2 (10 %)
Living together (%)	41 (76 %)	11 (65 %)	33 (66 %)	14 (70 %)

Intervention delivery

61 of 71 (86%) allocated patient-carer-dyads received complete sessions in the COTiD arm, 66 of 70 (94%) in the control arm. In each group, 4 pairs were lost before intervention. 6 patient-carer dyads in the COTiD had less than 10 sessions. Interventionists rated the delivery of 20 pre-defined treatment sub-processes, ranging from interviewing patient and carer to training of simplified activities or supporting the carer in supervision. They scored treatment delivery

as 78% in the COTiD arm and 80% in the control group. Interventionists rated the patient's adherence in 67 cases of the COTiD group, from 15 as hindering the delivery of treatment; 26 as neutral and 26 as facilitating. Ratings of carers' adherence were 5 hindering; 15 neutral; and 47 facilitating. The adherence of the participants in the control group could not be rated, because interventionists had no further contact after the consultation. Carers and patients were asked to rate their satisfaction with treatment on a 5-point Likert-scale with 1=very content and 5=very discontent. Mean (SD) satisfaction scores of 63 carers in the COTiD group were 1.4 (0.5) and scores of 44 patients were 1.7 (0.6). 62 carers in the control group scored similarly: 1.7 (0.5), 34 patients scored 2.0 (0.7), respectively.

Outcomes

The MANOVA in 104 completers (COTiD: n=54; control: n=50) revealed no significant group time interaction effect in any of the outcome data, neither in primary outcome measurements of patients' daily functioning (Figures 2 and 3) nor in secondary outcomes of patients or carers (results not shown). Tables 3 and 4 show mean, standard deviation and group difference including 95%-confidence intervals for all outcomes. Patients' daily functioning did not significantly change over 26 weeks in either the experimental and control group. In the 52 weeks follow up, the patients' need for assistance increased in both groups, and accordingly the carer's hours of care for basic ADL were higher. Two patients of the COTiD group were placed to nursing homes 33 and 44 weeks after baseline and one patient of the control group after 33 weeks.

To address the problem of missing data in single measurement instruments, we performed a multiple data imputation. We calculated a MANOVA over four

measurement time points for all primary and secondary outcomes for all 104 completers. Ten different data imputations did not reveal any significant time group interaction effects.

Figure 2: ADL task performance of Alzheimer patients following intense occupational therapy compared with a single session control intervention (PRPP independence, Range: 100=erroless to 0=errorful)

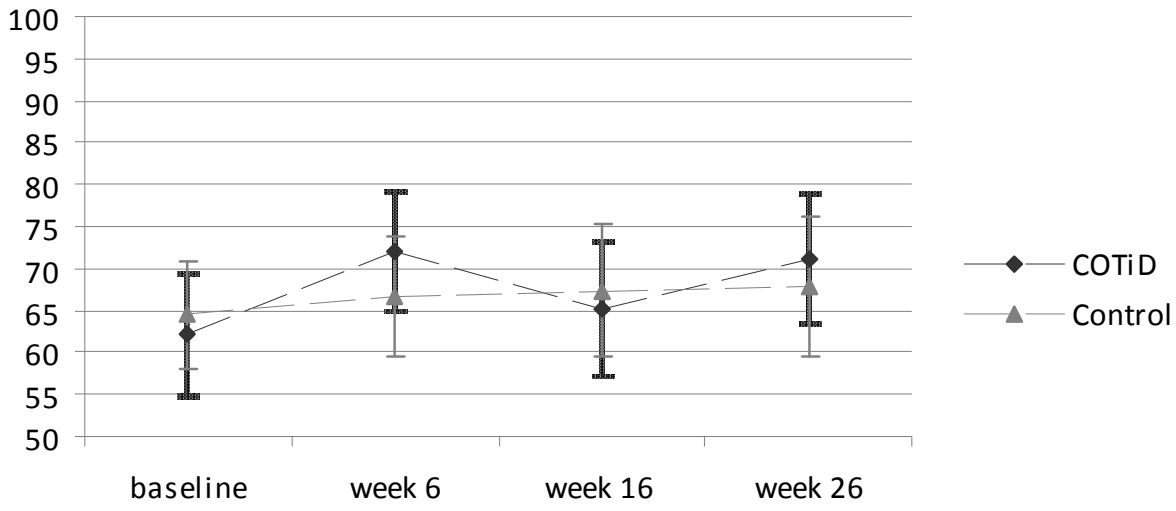
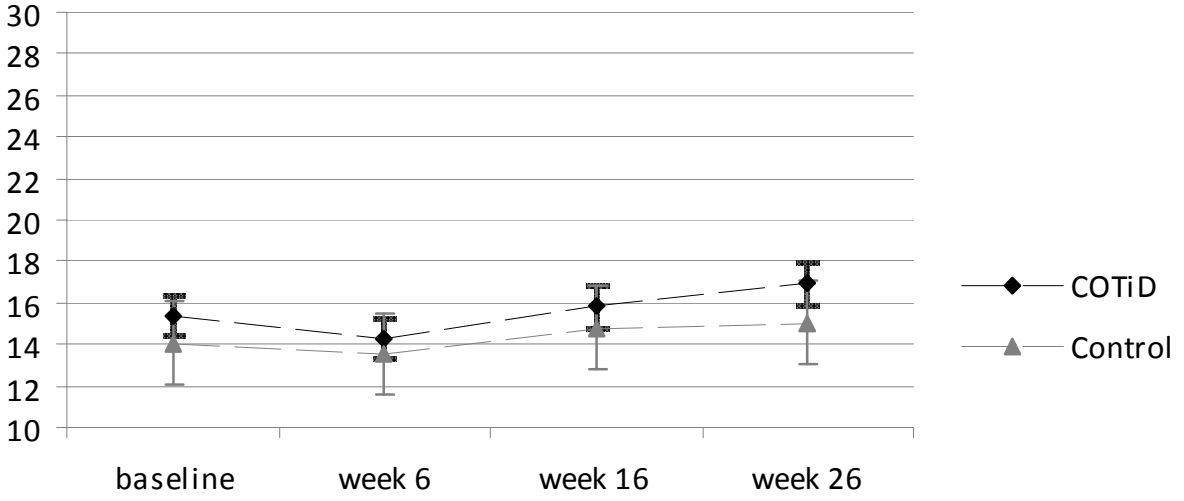


Figure 3: Need for assistance in ADL of Alzheimer patients following intense occupational therapy compared with a single session control intervention (IDDD performance, Range: 0=never assistance to 44=always assistance)



Harms

There were no differences between intervention and control group, neither in the number of adverse events nor in their severity. The study site physicians judged all adverse events as unrelated to trial treatment or assessment contacts. In the total sample of all randomised participants (n=141), two deaths of patients (both in the control arm) and one death of carer (COTiD) were reported. In the COTiD group 14 patients were admitted to hospital for an average of 15 nights, and 10 patients in the control group, for an average of 18 nights. All events were unrelated to the occupational therapy sessions.

Table 3: Patients' outcomes following intense occupational therapy compared with a single session control intervention in Alzheimer patients and their cares

	Sample size		Baseline		6 weeks			16 weeks			26 weeks			52 weeks		
	COTiD	Control	COTiD	Control	COTiD	Control	Group Diff.	COTiD	Control	Group Diff.	COTiD	Control	Group Diff.	COTiD	Control	Group Diff.
	N	N	mean (SD)	mean (SD)	mean (SD)	mean (SD)	mean [95%CI]	mean (SD)	mean (SD)	mean [95%CI]	mean (SD)	mean (SD)	mean [95%CI]	mean (SD)	mean (SD)	mean [95%CI]
PRPP independence 100 to 0*	54	50	62.1 (26.8)	64.6 (23.1)	72.0 (27.1)	66.7 (26.1)	-5.3 [-15.7 to 5.1]	65.2 (30.3)	67.4 (28.2)	2.2 [-9.2 to 13.6]	67.8 (30.1)	71.1 (29.4)	3.3 [-8.3 to 14.9]	-	-	-
IDDD performance 44 to 0*	54	50	15.4 (9.9)	14.1 (10.1)	14.3 (9.5)	13.5 (10.3)	-0.8 [-4.6 to 3.1]	15.8 (10.1)	14.8 (10.1)	-1.0 [-5.0 to 2.9]	16.9 (10.1)	15.0 (10.3)	-1.9 [-5.8 to 2.1]	21.1 (11.9)	18.7 (11.6)	-2.4 [-7.1 to 2.3]
IDDD initiative 0 to 36*	54	50	16.0 (8.7)	15.9 (8.4)	15.0 (8.1)	14.4 (8.7)	-0.6 [-3.9 to 2.7]	15.5 (8.2)	16.4 (9.1)	0.9 [-2.5 to 4.3]	16.1 (8.6)	16.7 (9.3)	0.6 [-2.9 to 4.1]	20.1 (9.9)	19.1 (10.1)	-1.0 [-5.0 to 3.0]
CSDD 0 to 38*	41	37	13.2 (7.6)	10.4 (6.3)	12.7 (7.8)	10.3 (6.1)	-2.4 [-5.5 to 0.8]	11.4 (7.2)	11.3 (6.6)	-0.1 [-3.2 to 3.0]	12.3 (6.8)	10.9 (6.3)	-1.3 [-4.3 to 1.6]	13.8 (6.7)	11.7 (6.7)	-2.0 [-5.1 to 1.0]
DQoL overall 5 to 1*	49	45	2.8 (0.8)	3.1 (0.8)	2.9 (0.9)	3.1 (0.6)	0.3 [-0.04 to 0.6]	2.8 (0.8)	3.1 (0.9)	0.3 [-0.02 to 0.6]	2.9 (0.8)	3.0 (0.8)	0.2 [-0.1 to 0.5]	-	-	-
SF-12 physical 100 to 0*	47	45	42.7 (10.0)	45.0 (9.4)	42.4 (11.4)	45.4 (11.0)	3.0 [-1.7 to 7.6]	41.8 (9.2)	45.1 (11.6)	3.3 [-1.0 to 7.6]	41.8 (11.3)	44.8 (11.1)	3.0 [-1.6 to 7.6]	-	-	-
SF-12 mental 100 to 0*	47	45	49.3 (11.0)	52.2 (9.3)	50.3 (12.3)	51.2 (9.9)	0.9 [-3.7 to 5.6]	51.8 (10.1)	52.8 (9.5)	1.1 [-3.0 to 5.1]	53.1 (9.0)	52.3 (10.6)	-0.8 [-4.9 to 3.3]	-	-	-

*Range: positive to negative, COTiD: Community Occupational Therapy in Dementia Programme, PRPP: Perceive, Recall, Plan and Perform System of Task Analysis, IDDD: Interview for Deterioration in Daily Living Activities in Dementia, CSDD: Cornell Scale for Depression in Dementia, DQoL: Dementia Quality of Life Instrument

Table 4: Carers' outcomes following intense occupational therapy compared with a single session control intervention in Alzheimer patients and their cares

	Sample size		Baseline		6 weeks			16 weeks			26 weeks			52 weeks		
	COTiD	Control	COTiD	Control	COTiD	Control	Group Diff.	COTiD	Control	Group Diff.	COTiD	Control	Group Diff.	COTiD	Control	Group Diff.
	N	N	mean (SD)	mean (SD)	mean (SD)	mean (SD)	mean [95%CI]	mean (SD)	mean (SD)	mean [95%CI]	mean (SD)	mean (SD)	mean [95%CI]	mean (SD)	mean (SD)	mean [95%CI]
SCQ 135 to 27*	50	47	100,8 (17,4)	107,0 (16,4)	103,0 (18,7)	108,6 (17,2)	5,7 [-1,6 to 12,9]	102,7 (18,2)	107,3 (17,8)	4,6 [-2,6 to 11,9]	104,7 (17,0)	107,9 (17,4)	3,2 [-3,7 to 10,1]	99,8 (17,8)	103,6 (18,6)	3,8 [-3,5 to 11,2]
CES-D 0 to 60*	52	46	12,1 (7,7)	11,3 (5,9)	10,6 (7,1)	10,9 (6,9)	0,3 [-2,6 to 3,1]	10,6 (7,7)	10,8 (7,3)	0,3 [-2,8 to 3,3]	10,0 (7,9)	10,0 (6,9)	0,0 [-3,0 to 3,0]	14,3 (10,3)	12,9 (7,7)	-1,4 [-5,1 to 2,3]
DQoL overall 5 to 1*	51	48	3,1 (0,8)	3,1 (0,7)	3,0 (0,6)	3,1 (0,7)	0,0 [-0,2 to 0,3]	3,1 (0,7)	3,0 (0,8)	0,0 [-0,3 to 0,3]	3,0 (0,7)	3,2 (0,8)	0,2 [-0,1 to 0,5]	2,8 (0,8)	3,0 (0,8)	0,2 [-0,1 to 0,5]
SF-12 physical 100 to 0*	40	38	42,4 (11,5)	43,5 (11,3)	45,8 (10,0)	44,0 (10,0)	-1,8 [-6,3 to 2,7]	44,1 (10,8)	46,2 (9,2)	2,1 [-2,5 to 6,6]	45,4 (10,7)	45,0 (10,5)	-0,4 [-5,2 to 4,4]	42,7 (10,7)	41,6 (11,7)	-1,0 [-6,1 to 4,0]
SF-12 mental 100 to 0*	40	38	50,9 (9,1)	49,8 (10,7)	50,6 (11,0)	50,0 (8,7)	-0,6 [-5,1 to 3,9]	52,3 (8,6)	48,5 (11,8)	-3,9 [-8,5 to 0,8]	50,2 (9,1)	50,1 (10,7)	0,0 [-4,5 to 4,4]	49,5 (11,9)	47,7 (10,7)	-1,7 [-6,9 to 3,4]
Basic ADL-care by primary carer (hours per day)	52	43	0.5 (0.8)	0.8 (1.3)	0.8 (1.8)	0.9 (1.4)	0.1 [-0.5 to 0.8]	0.7 (1.2)	1.0 (1.4)	0.2 [-0.3 to 0.7]	0.8 (1.2)	1.0 (1.5)	0.2 [-0.3 to 0.8]	1.6 (2.2)	1.8 (2.2)	0.1 [-0.8 to 1.0]
IADL-care by primary carer (hours per day)	52	45	2.1 (2.7)	2.5 (2.6)	1.9 (2.5)	2.9 (3.0)	1.1 [-0.04 to 2.2]	2.3 (2.6)	2.9 (2.8)	0.6 [-0.5 to 1.7]	2.2 (2.2)	3.2 (2.8)	1.0 [0.0 to 2.0]	2.7 (2.2)	3.2 (2.8)	0.5 [-0.6 to 1.6]

*Range: positive to negative, COTiD: Community Occupational Therapy in Dementia Programme, SCQ: Sense of Competence Questionnaire, CES-D: Center for Epidemiologic Depression Scale, DQoL: Dementia Quality of Life Instrument, ADL: Activities of Daily Living, IADL: Instrumental Activities of Daily Living

DISCUSSION

In the results of this study, a ten-session community occupational therapy in dementia programme (COTiD) was found not to be superior to a one-session consultation concerning short- and middle-term effects on patients' daily functioning. In both groups, the need for assistance in basic and instrumental activities of daily living and the performance of a self-chosen daily living task remained stable up to six months after baseline. No significant group differences could be found on secondary outcomes, which were quality of life and mood of patient and primary carer, patient's initiative in daily activities, carer's sense of competence in interaction with the patient, carer's hours of daily care and the patient's nursing home placement. There were no adverse events associated with experimental or control intervention.

Limitations

Despite an elaborated study design, there are some limitations in our study. We analysed only 104 completer dyads from 141 recruited pairs (74 %). However, (1) baseline data of completers and non-completers did not show imbalance, (2) imputation of data completely missing at a particular measurement time point would have introduced more bias and (3) we kept dyads, whose data were valid, and for whom treatment was intended but not received, in the complete ITT-analysis.

A second shortcoming was that - after the common introductory seminar - the start of the study differed among the sites due to different time lines in administrative matters and approval of the local ethic commissions. For this reason we could not arrange a common repetition seminar for the interventionists after the pilot training on the job. This may have led to some heterogeneity in the intervention, especially because in Germany 11 newly introduced interventionists performed the treatment compared to two experienced experts in the original Dutch trial. We addressed this problem with

feedback on videos of treatment sessions the interventionists sent in. Further, we arranged telephone supervision on demand. However, it is difficult to judge whether these measures could compensate for the potential influence of different educational backgrounds of Dutch and German occupational therapists. In the Netherlands, occupational therapy education takes four years and is more psychosocial oriented than the three years curriculum in Germany.

Comparison

The Dutch RCT on the COTiD with waiting-control-group design showed large effect sizes in the IDDD performance scale at six and twelve weeks after baseline (d=2.3 and 2.4, respectively).[6] The Dutch and the German sample did not differ remarkably in cognition at baseline (MMSE: 19 v 20), but did differ in the need of assistance (IDDD performance: 24 v 15). The German patients showed a low need of assistance already at study start comparable to the IDDD values of the Dutch patients at the end of the treatment. This may have caused a floor effect on the IDDD. Another USA mono-centre RCT compared community occupational therapy and a less intensive telephone consultation in patients with probable dementia (MMSE: 13).[33] The authors found a small effect size in daily functioning (d=0.21). The initial need of assistance in both studies was higher than in the German sample. A systematic review of community programmes in dementia [34] reported one study on exercise and behavioural management with beneficial effects on daily functioning of patients with moderate dementia (MMSE: 17),[35] one trial on occupational therapy with heterogeneous effects [16] and two studies on occupational therapy [36] and music therapy [37] with no significant effects. A current German health technology assessment on non-drug therapies in Alzheimer's disease did not identify further community occupational therapy trials.[38] The comparison of community intervention trials reveals that study samples with a lower MMSE and a higher need

of assistance benefit more than those with initial higher cognitive and daily functioning. Similarly, a standardized synopsis of ADL outcomes in pharmacological dementia trials pointed out that samples with an MMSE between 17 and 10 benefit most in ADL while samples with higher MMSE scores showed less effects.[39] However, different baseline scores of cognitive and daily functioning alone cannot explain the major difference between our findings and the positive results of the Dutch RCT. Detailed process evaluation and exploratory analyses of our study data might show whether variations in study site context and treatment performance has influenced the intervention's effectiveness.

Clinical and research implications

Published evidence for the effectiveness of community occupational therapy in dementia is heterogeneous as indicated by a Dutch trial with large positive effects on daily functioning; a few USA trials with no or small positive effects on ADL and this German study showing that ten sessions were not superior to one consultation. Given the high burden of Alzheimer's disease for patients and carers, a comprehensive one-session consultation may be recommended as standard occupational therapy intervention in the German health care system. This may have a stabilizing effect on functional performance and carer burden over time, as was found in both intervention and control groups. This study has shown that careful cross-national comparisons are highly needed before complex interventions may be considered evidence based in other health care systems. Therefore, further analyses must investigate the role of interventionists' expertise and treatment performance and the role of participants' needs and utilisation of health care resources before conclusions on international implementation of this intense occupational therapy intervention can be drawn.

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CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	3
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	5+6
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	7+8
	2b	Specific objectives or hypotheses	8
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	8
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	9
Participants	4a	Eligibility criteria for participants	9
	4b	Settings and locations where the data were collected	9+10
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	10+11+12
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	12+13+14
	6b	Any changes to trial outcomes after the trial commenced, with reasons	13
Sample size	7a	How sample size was determined	14
	7b	When applicable, explanation of any interim analyses and stopping guidelines	14
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	14
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	14
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	15
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	15
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those	15

		assessing outcomes) and how	
	11b	If relevant, description of the similarity of interventions	10+11
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	15+16
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	16
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	17
	13b	For each group, losses and exclusions after randomisation, together with reasons	17
Recruitment	14a	Dates defining the periods of recruitment and follow-up	16
	14b	Why the trial ended or was stopped	16
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	18
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	19+22
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	22
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	19+20
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	21
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	23+24
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	24+25
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	24+25
Other information			
Registration	23	Registration number and name of trial registry	9
Protocol	24	Where the full trial protocol can be accessed, if available	9
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	26

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.

A multi-centre RCT on community occupational therapy in Alzheimer's disease: Ten sessions are not superior to one consultation.

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A multi-centre RCT on community occupational therapy in Alzheimer's disease: Ten sessions are not superior to one consultation.

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Article focus

1. Efficiency of community occupational therapy in dementia
2. Pragmatic multi-centre RCT in routine care context

Key message

A ten-session community occupational therapy programme did not work more effectively than a comprehensive one-session occupational therapy consultation within German routine health care.

Strengths and limitations

The main strength of this trial was an elaborate multi-centre RCT design within a routine care setting using an active control group, a prolonged follow-up and a strategy of video rating with fully blind assessors.

The main limitation was that the training time for the interventionists was less and interventionists had no treatment experience with the experimental intervention before the start of the trial, in contrast to extensive training time and treatment experience with the experimental intervention of the Dutch therapists. Furthermore, we had to exclude 37 patients (26 %) from the MANOVA of the primary outcome because they withdrew; or the assessment at one or more time points was missing or not within the planned time period. However, the attrition in both groups did not demonstrate a systemic bias, data imputation with the last observation carried forward is inappropriate in dementia research and even the analysis of the reduced patient sample with valid data did not show a tendency to significant group differences. Consequently, the hypothesis of better effects within the experimental group must be rejected.

Abstract

Objective

To compare the benefits and harms of a Dutch ten-session Community Occupational Therapy programme for patients with Alzheimer's disease with the impact of a one session consultation at home in German routine health care.

Design

A seven-centre, parallel group, active controlled RCT. Assessors were blind for treatment allocation.

Setting

Patients' homes.

Participants

141 patients with mild to moderate Alzheimer's disease living in the community and their primary carers were recruited. Follow up data of 104 patient-carer-dyads were analysed.

Interventions

Experimental 10 home visits within 5 weeks by an occupational therapist, educating patients in the performance of simplified daily activities and in the use of aids to compensate for cognitive decline; and educating carers in coping with behaviour of the patient and in giving supervision to the patient.

Control one home visit including individual counselling of patient and carer and explanation of a leaflet on coping with dementia in daily life.

Outcome measures

The Interview of Deterioration in Daily activities in Dementia (IDDD) and the Perceive, Recall, Plan and Perform System of Task Analysis (PRPP) were used. Assessments were at baseline, 6, 16, and 26 weeks, postal assessment at 52 weeks.

Results

Patients' daily functioning did not significantly differ between experimental and control group at week 6, 16, 26 or 52 and remained stable over 26 weeks in both groups. No adverse events were associated with the interventions.

Conclusions

In German health care, a ten-session community occupational therapy was not superior to a one-session consultation for the daily functioning of people with Alzheimer's disease. Careful cross-national research on components for effective translation and evaluation in other health care settings is needed before complex interventions based on other health care systems can be considered as evidence.

International Clinical Trials Registry Platform, DRKS00000053

INTRODUCTION

Alzheimer's disease causes high health care costs and burdens patients and carers with severe problems in activities of daily living (ADL).[1-2] Consequently, the improvement or the preservation of ADL is evaluated as a patient-related outcome in clinical trials related to dementia.[3] ADL, burden of care, ability to stay in the community, and quality of life issues are probably much more relevant to patients and carers than the deceleration of cognitive decline, another patient-related outcome.[4] A synopsis of four systematic reviews analysing 73 RCTs on the efficacy of pharmacological and psychosocial interventions regarding everyday functioning in dementia concluded that positive effects of drugs on ADL are small (pooled effect sizes < 0.28) and heterogeneous regarding safety. In contrast to the well documented results for pharmacological interventions evidence for psychosocial interventions on ADL is lacking.[5] However, a recent Dutch mono-centre RCT demonstrated significant positive effects of occupational therapy on ADL (effect sizes of 2.4, $p < 0.0001$).[6] Therefore, the purpose of our multi-centre RCT was to transfer the Dutch community occupational therapy programme in a broader context of German routine health care and to evaluate its effectiveness and safety in comparison with an active control group intervention.

Occupational therapy specialises in supporting independence in ADL and is recommended in several guidelines for dementia management.[7-9] Occupational therapy uses a combined approach including activity simplification, environmental modification, adaptive aids, problem-solving strategies, skill training and carer training.[7, 10-11] According to the bio-psycho-social health model of the World Health Organization (WHO), the negative impact of cognitive deficits on activities can be diminished by

improving the patient's physical and social environment and by tailoring the intervention to the patient's capability.[12-15]

Until March 2011, there was no systematic review on community occupational therapy for people with Alzheimer's disease but two research groups had conducted RCTs in this subject. In the USA study, occupational therapy demonstrated beneficial effects on patients' challenging behaviours but not on ADL. No information on adverse events were given.[14, 16-18] In the Netherlands, occupational therapy, tailored to the needs of patients and carers showed benefits on the patient's ADL, mood, health status and quality of life and on the carer's sense of competence, mood, quality of life and costs of informal care. No adverse events were reported in either intervention or control group.[6, 19-20]

In the current randomised trial we tested the hypothesis that the Dutch ten-session Community Occupational Therapy in Dementia Programme (COTiD) would significantly improve the daily functioning of people with mild or moderate dementia, more so than a one-session Community Occupational Therapy Consultation (COTC). Secondary research questions were whether these interventions would show a difference in their effect on patient's and primary carer's quality of life and mood; on the carer's sense of competence in the interaction with the patient; and on long-term nursing home placements.

METHODS

Design

In order to evaluate the superiority of COTiD, we used a seven-centre single-blind, active-controlled design with a 1:1 randomisation for two parallel groups. There was no modification in design or eligibility criteria from the study protocol

available at http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2761388/. The study was registered at the German register of clinical trials, which is connected to the International Clinical Trials Registry Platform (http://apps.who.int/trialsearch/ => DRKS00000053). The Medical Ethics Committee of the University Hospital Freiburg gave ethical approval (no. 110/08).

Participants and Setting

Patients were eligible to participate in the study if they had mild to moderate dementia (MMSE 14-24) and were diagnosed as having Alzheimer's disease or mixed type dementia, according to ICD-10 criteria, by physicians with more than five years of experience in dementia diagnosis. Participants had to dwell in the community either together with their primary carer or with involvement of a carer providing care at least twice a week. Patients with a score above 12 on the 30-items Geriatric Depression Scale or a major need of physical nursing care of more than 120 min per day (level 2 or higher according to the German Long-Term Care Insurance Act) were excluded. Unstable medical conditions or severe behavioural disturbances, which did not allow participation in the study as judged by the study physicians were criteria for exclusion as well as for discontinuation. Long-term nursing home placements of the patients during the treatment phase or death of patient or primary carer were criteria for discontinuation. The patient gave written informed consent and the carer consented by written format to join and support the treatment procedures.

Patients were recruited from five outpatient memory centres at university hospitals (in Bonn, Freiburg, Mainz, Marburg and Tübingen); one municipal hospital in Karlsruhe specialising in geriatric medicine; and one neurological private practice in Berlin specialising in neuropsychiatry and collaborating with

an occupational therapy private practice. The seven participating centres are located throughout Germany in urban regions with catchment areas of about 70,000 to 700,000 inhabitants. They had all provided outpatient dementia care for three to fifteen years. Their standard service comprised diagnostic work-up for dementia and related diagnoses as well as recommendation of risk reduction, dementia medication and non-pharmacological treatments. Principal investigators of the centres were psychiatrists, neurologists or geriatricians with six to thirteen years of experience in dementia care.

Interventions

The experimental intervention (COTiD) was designed to improve the patient's and the primary carer's daily functioning, and was based on an evidence-based treatment manual.[6, 19-23] COTiD consisted of ten occupational therapy sessions of one hour duration held over five weeks at each patient's home. In the diagnostic phase, comprising of 3 to 4 sessions, the occupational therapist explored (1) the patient's preferences and history of daily activities, (2) her or his ability to perform activities and to use compensatory strategies within the familiar environment, (3) the possibilities of modifying the patient's home, (4) the carer's activity preferences, problems in care giving, coping strategies and abilities to supervise and (5) the interaction between carer and patient. In a shared decision-making process during the goal setting session, the patient and the carer selected the one or two most meaningful activities out of a list of their preferences for daily activities to work on in occupational therapy. During the treatment phase of 5 to 6 sessions, the occupational therapist defined, together with the patient and the carer, more effective compensatory and environmental strategies to adapt both the environment and the selected activities to the

patient's habits and cognitive abilities. Patient and carer were taught how to use these suggested adaptations within strategies, activities and the environment in order to improve their performance of daily activities. In addition, the carer received practical and emotional support and was coached in effective supervision, problem solving and coping strategies by means of cognitive-behavioural interventions. Detailed description of the experimental intervention has been published elsewhere.[23]

For the German RCT, MG taught the content of the translated treatment manual to 14 study participant occupational therapists in 16 hours of seminars using presentation, videos and role play with feedback and group discussion. After the seminar and before the study started, they needed to complete a full treatment series for at least one pilot dyad of patient and carer. In the study phase, the interventionists spent about 20 hours per patient for a full treatment series including ten treatment sessions, travel, reports and multidisciplinary briefing. In Germany, a series of ten to thirty sessions is within the normal range of time that occupational therapists use for the treatment of older outpatients diagnosed with other diseases, such as stroke or rheumatoid arthritis.

The control group received one hour occupational therapy consultation (COTC) at the patient's home conducted by the same study interventionists. Based on material of the German Alzheimer Society, two occupational therapists with more than five years of experience in dementia care had prepared a leaflet of ten pages.[24-25] The semi-structured consultation was an explanation of 30 min of this leaflet and a talk of 30 min on individual problems that arose from patient's and carer's needs. This included encouragement to stay active in everyday life, to maintain social contacts and to use dementia services in the region for which local addresses were listed in the leaflet. Occupational

therapists were taught the control intervention within a 4-hour seminar. Consultations of 30 minutes up to one hour duration about such issues are common in German dementia care. Detailed description of the control intervention as well as means of quality assurance in experimental and control intervention has been published elsewhere.[26]

Outcome measures

The primary endpoint was the patients' change of daily functioning from baseline to follow-up time points at week 6, 16 and 26 measured with the performance scale of the Interview for Deterioration in Daily Living Activities in Dementia (IDDD).[27] This scale records carer rating of the patient's need of assistance in the performance of (1) washing oneself, (2) making tea or coffee, (3) dressing, (4) combing one's hair and brushing one's teeth, (5) eating, (6) using the toilet, (7) shopping, (8) using the telephone, (9) preparing a meal, (10) cleaning the house or doing minor repair work and (11) handling finances. Each item is rated never=0, seldom=1, sometimes=2, often=3 or always=4. The sum of scores ranged from 0 to 44. Higher scores indicated higher need for assistance. Since carer rating could not be 'masked', daily functioning was additionally evaluated by external raters fully 'blind' to the group assignment. They rated video tapes of a challenging daily living task and used the Perceive, Recall, Plan and Perform System of Task Analysis (PRPP).[28] For the PRPP, raters had to define single steps of the performed activity, and they identified any activity step in which errors of accuracy, omission, repetition or timing occurred. The number of activity steps rated as incorrectly performed was divided by the total number of activity steps, resulting in an independence-score indicated in a percentage (100% = all steps are error-free).

Table 1: Measurements of secondary endpoints[26]

Endpoint	Measurement
Patient's initiative in daily activities	Interview for Deterioration in Daily Living Activities in Dementia (IDDD), initiative scale
Patient's mood	Cornell Scale for Depression in Dementia (CSDD)
Carer's mood	Center for Epidemiologic Depression Scale (CES-D)
Patient and carer's quality of life	Dementia Quality of Life Instrument (DQoL), overall item
	SF-12 physical
	SF-12 mental
Carer's interaction with patient	Sense of Competence Questionnaire (SCQ)
Care by primary carer	Resource Utilization in Dementia (RUD), hours per day
Nursing home placement	RUD, nights in nursing home (except respite care)
Harms	Number of adverse events
	RUD, nights in hospital

Secondary endpoints included mood, quality of life, resource utilisation and possible harms. Assessors 'blind' for the group assignment, completed measurements at the patient's home at baseline, week 6, 16 and 26 and arranged a postal survey of carer questionnaires at week 52. The assessors had a minimum of one year's professional experience with older or cognitively impaired people. They attended an introductory seminar of 8 hours. The complete assessment was applied during a 2-hour visit at each patient's home including (1) handing out and explaining the questionnaires to the carer, (2) interviewing the patient (DQoL and SF-12) in a separate room, (3) videotaping the patient and (4) receiving back the carer questionnaires, checking it and clarifying answers if necessary. Seminar description and means of quality management for assessment as well as detailed scheme and psychometric properties of all measurement instruments have been reported recently.[26]

All measurement instruments are validated and used in dementia research.[29-30] For the present study, we translated the IDDD into German according to high methodological standards with two independent forward and backward translations, analysis of discrepancies and final agreement by discussion with

all translators. There was no need to translate the PRPP because, because it was established in the Netherlands and applied by Dutch raters. There was one protocol amendment before recruitment started. The Assessment of Motor and Process Skills (AMPS) was replaced by the PRPP, because the AMPS was not available in the German language within the planned schedule.

Indicators of harm were defined as patient or carer death, number of patients with admission to hospital and number of nights in hospital. These indicators were recorded in interviews with the carer at intervals of 5 to 7 weeks over 52 weeks. Study sites had to report severe adverse events to the study centre immediately when each occurred. We did not assume a direct association between the defined harms and either the experimental or the control intervention. However, increased daily activities in the interventions group might have resulted in a higher risk of falls or accidents and thus may indirectly have led to more nights in hospital or in the worst case to death.

Sample size calculation

A sample size of 42 participants per group was calculated to be necessary to detect an effect size of f = 0.10 on the IDDD performance scale in an analysis of variance of two groups and four time points; using a two-sided 5% significance level, a power of 80%, and a correlation of 0.7 between the measurement time points [31]. According to the Dutch original RCT, we expected a dropout rate of 10% at week 16, which was extrapolated to 40% at week 52. A nine-month inclusion period was anticipated as necessary in order to recruit the 140 patients. Although the Dutch original RCT found effect sizes of d-value=2.4 in the IDDD performance scale at week 12, for this study the power was calculated much more conservatively. This was because we (1) introduced an

active control group, (2) investigated the programme effects under varying care conditions in seven centres with interventionists who were introduced in this new treatment and were far not as experienced as the Dutch study therapists and (3) we prolonged the follow up period. Interim analyses were not planned.

Randomisation and masking

The random allocation sequence was computer-generated with blocking by centre and groups of two persons, without stratification and in a ratio of 1:1 by a statistician from a distant site. After enrolment, study site physicians requested randomisation via e-mail. The statistician e-mailed the individual allocation to COTiD or COTC exclusively to the site interventionist and stored the allocation list at his distant site which was not available to any study site staff. The interventionist scheduled treatment sessions, faxed records to the distant coordinating study centre and kept all documents strictly separated from any other site staff. This was in order to avoid contamination. Since the numbers of home visits differed in the experimental and control groups, masking of patients and carers was not possible. However, study information did not include any preference for a special treatment 'arm'. Patients and carers were asked to give no information about their treatment package to assessors or study physicians. All study personal was 'blind' for group assignment, except the interventionists. Agreement between the assessors' estimation of group assignment and the actual group assignment was 61%, and thus slightly over the expected 50% of agreement by chance. The procedure of external video rating ensured the full 'blinding' of the external raters for the PRPP primary outcome measure. Independent research assistants cleaned the videotapes of any hint of group assignment before they were rated by two Dutch raters not involved in the trial

treatment. In order to establish the inter-rater reliability, we tested ten double ratings of the same video by the two raters and found an intra-class correlation coefficient of 0.9. Data analysts were not 'blind' for the group assignment. However, measurement time points and outcomes had been published before data were available for analysis [26] and any decision to remove patients from the analyses is reported in the present publication.

Statistical methods

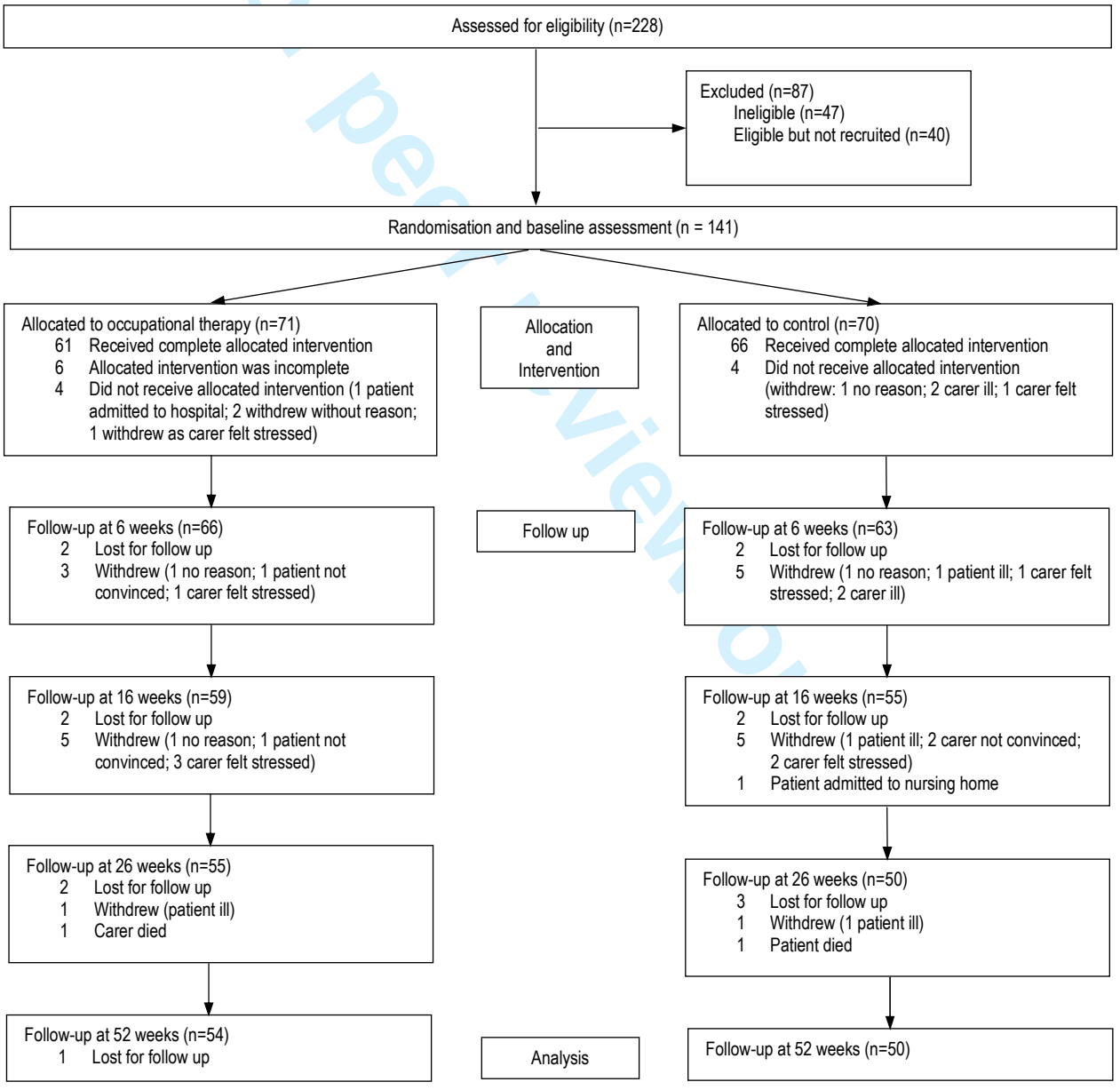
Data were entered via special MS Access entry masks automatically controlling for data plausibility. In addition, sections of entered data were checked for typing errors by hand, in order to ensure an error rate lower than 0.2%. The primary intention-to-treat analysis included all allocated participants with valid data whether they did or did not receive the complete intervention. For the primary outcomes, we performed a multivariate analysis of variance (MANOVA) with repeated measures with two groups and four measurement time points at baseline, week 6, 16 and 26. In this primary analysis, we did not adjust for baseline values or any other co-variate. A univariate ANOVA with five measurement time points (+ week 52) was carried out for the secondary outcomes. In order to deal with missing data, we performed secondary intention-to-treat analyses with multiple data imputation using the Full Information Maximum Likelihood (FIML) method.[32] We imputed data for all secondary outcome measurements and all time points using SPSS (version 19). All statistical tests were two-sided on an alpha level of 0.05. Subgroup analyses were not planned.

RESULTS

Recruitment and participant flow

We prolonged the planned recruitment period from August 2008 to April 2009 by one additional month, up to May 2009. This was in order to recruit the intended sample size. The 52-week follow up was closed in May 2010.

Figure 1: Flow of participants through the trial



141 participants were recruited (Berlin: 19, Bonn: 21, Freiburg: 26, Karlsruhe: 15, Mainz: 24, Marburg: 21, Tübingen: 15). The flow chart (Figure 1) shows that attrition following randomisation did not lead to significant group differences.

Baseline Characteristics

Randomisation did avoid imbalances in baseline characteristics (Table 2) and pre-treatment assessment data (Table 3) except in one item. Participants in the control group had more moderate to severe limitations in their financial situation (14% v 2%; p=0.027). Because the financial situation is not known as predictive factor for functional decline, we did not adjust for this imbalance.[33]

Table 2: Demographic and clinical characteristics

	COTiD			Control		
	analysed (n=54)	dropouts (n=17)	total (n=71)	analysed (n=50)	dropouts (n=20)	total (n=70)
Age, years (SD)	78.0 (7.1)	77.2 (8.5)	77.8 (7.4)	78.7 (6.0)	78.3 (7.1)	78.5 (6.3)
Sex, female	29 (54 %)	12 (71 %)	41 (58 %)	30 (60 %)	10 (50 %)	40 (57 %)
MMSE (SD)	20.4 (3.1)	19.0 (3.3)	20.2 (3.2)	20.7 (2.7)	20.3 (2.9)	20.7 (2.7)
GDS (SD)	6.9 (3.0)	5.6 (2.9)	6.5 (3.0)	5.2 (2.8)	6.1 (2.6)	5.5 (2.8)
Education						
no school graduation	2 (4 %)	1 (6 %)	3 (4 %)	1 (2 %)	0 (0 %)	1 (1 %)
middle school graduation (9 or 10 years)	41 (76 %)	13 (76 %)	54 (76 %)	37 (74 %)	15 (75 %)	52 (74 %)
high school graduation (12 or 13 years)	11 (20 %)	3 (18 %)	14 (20 %)	12 (24 %)	5 (25 %)	17 (24 %)
Financial situation as perceived by the carer						
no limitation	40 (74 %)	14 (82 %)	54 (76%)	38 (76 %)	13 (65 %)	51 (73 %)
minor limitation	12 (22 %)	1 (6 %)	13 (18 %)	3 (6 %)	3 (15 %)	6 (9 %)
moderate or severe limitation	1 (2 %)	2 (12 %)	3 (4 %)	7 (14 %)	4 (20 %)	11 (16 %)
no data	1 (2 %)	0 (0.0 %)	1 (1 %)	2 (4 %)	0 (0 %)	2 (3 %)
Primary carer						
Age, years (SD)	65.4 (16.3)	63.1 (14.0)	64.9 (15.7)	65.9 (13.0)	61.4 (17.4)	64.5 (14.4)
Sex, female	38 (70 %)	9 (53 %)	47 (66 %)	35 (70 %)	18 (90 %)	53 (76 %)
Spouse	32 (59 %)	8 (47 %)	40 (56 %)	31 (62 %)	9 (45 %)	40 (57 %)
Daughter or son (in law)	20 (37 %)	7 (41 %)	27 (38 %)	16 (32 %)	9 (45 %)	25 (36 %)
Others	2 (4 %)	2 (12 %)	4 (6%)	3 (6 %)	2 (10 %)	5 (7 %)
Living together (%)	41 (76 %)	11 (65 %)	52 (73%)	33 (66 %)	14 (70 %)	47 (67 %)

Intervention delivery

61 of 71 (86%) allocated patient-carer dyads received complete sessions in the COTiD group, 66 of 70 (94%) in the control group. In each group, 4 pairs were

lost before intervention. Six patient-carer dyads in the COTiD had less than 10 sessions. Interventionists rated the delivery of 20 pre-defined treatment sub-processes, ranging from interviewing patient and carer to training of simplified activities or supporting the carer in supervision. They scored treatment delivery as 78% in the COTiD group and 80% in the control group. Interventionists rated the patient's adherence in 67 cases of the COTiD group, from 15 as hindering the delivery of treatment; 26 as neutral and 26 as facilitating. Rating criteria were the patient's cooperation during interview, goal setting and training; the daily changing mental capacity; collaboration with the carer; and the acceptance of innovations. Ratings of carers' adherence were 5 hindering; 15 neutral; and 47 facilitating. The carer adherence was assessed with regard to the cooperation during scheduling, interview, goal setting and training to supervise; the encouragement of the patient; the acceptance of support service; and the implementation of innovations. The adherence of the participants in the control group could not be rated, because interventionists had no further contact after the consultation.

Outcomes

The MANOVA in 104 completers (COTiD: n=54; control: n=50) revealed no significant group time interaction effect in the primary outcome measurements of patients' daily functioning (Figures 2 and 3). Tables 3 and 4 show mean, standard deviation and group difference including 95%-confidence intervals of an ANOVA for all outcomes. Patients' daily functioning did not significantly change over 26 weeks in either the experimental and control group. In the postal 52 weeks follow up, the patients' need for assistance increased in both groups, and accordingly the carer's hours of care for basic ADL were higher.

Two patients of the COTiD group were placed to nursing homes 33 and 44 weeks after baseline and one patient of the control group after 33 weeks.

To address the problem of missing data in single measurement instruments, we performed a multiple data imputation. We calculated a MANOVA over four measurement time points for all primary and secondary outcomes for all 104 completers. Ten different data imputations did not reveal any significant time group interaction effects. We also tested for study sites effects. We included the baseline values of all outcome measurements in a MANOVA with the factors *study sites* and *intervention groups* and found no significant differences between the study sites ($F(66, 432)=1.079$, $p=0.323$). Furthermore, no study site effect was found in a MANOVA of the primary outcome considering the measurement time points baseline, week 6, 16 and 26 (IDDD: $F(6, 90)=0.724$, $p=0.631$; PRPP: $F(6, 90)=1.758$, $p=0.117$).

Figure 2: ADL task performance of Alzheimer patients following intense occupational therapy compared with a single session control intervention; means and 95%-confidence intervals of the PRPP independence scale (range: 100=no errors to 0=all errors)

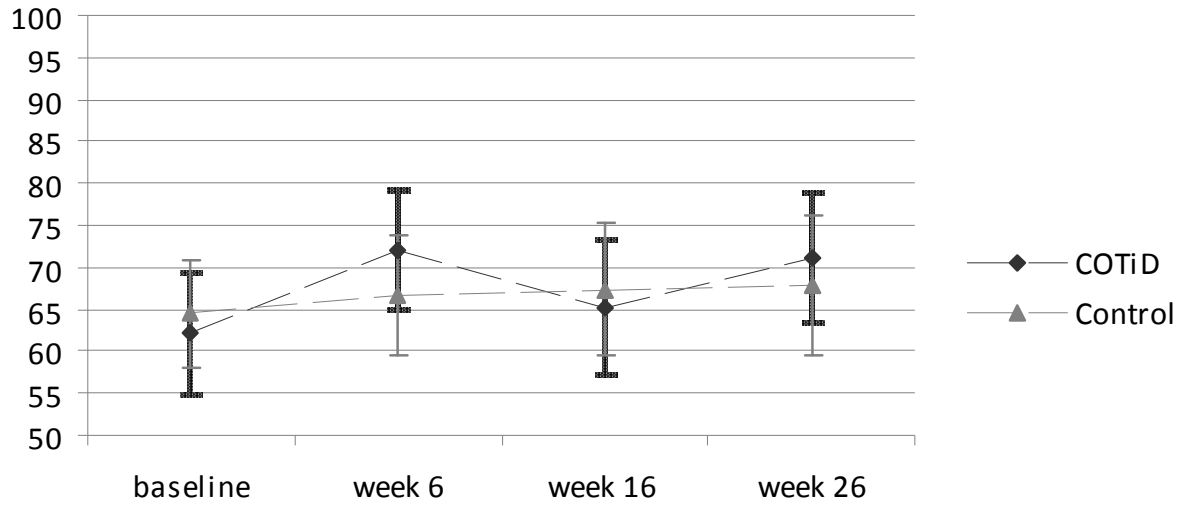
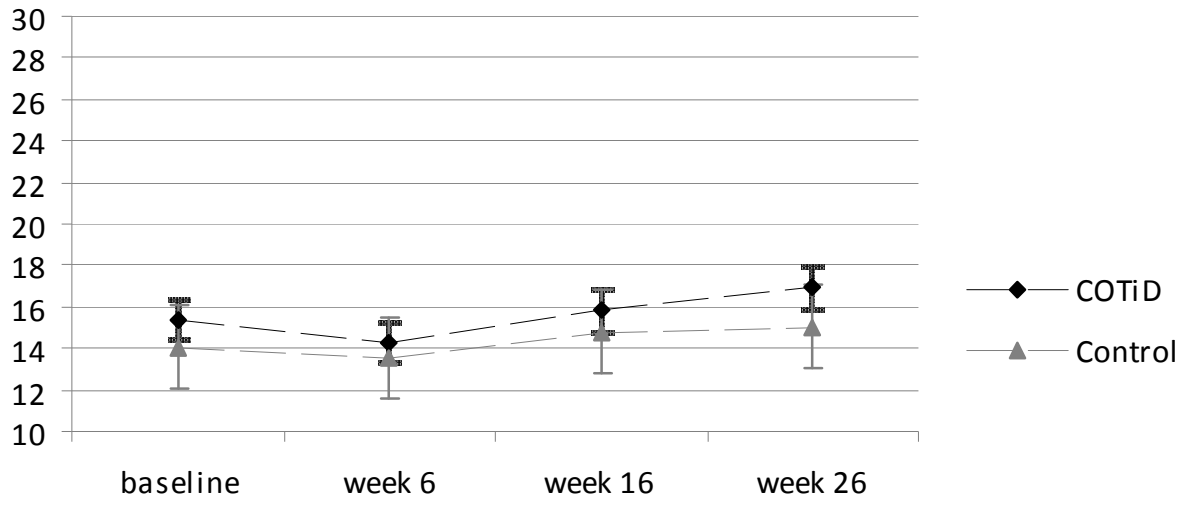


Figure 3: Need for assistance in ADL of Alzheimer patients following intense occupational therapy compared with a single session control intervention; means and 95%-confidence intervals of the IDDD performance scale (range: 0=never needed assistance to 44=always needed assistance)



Harms

There were no differences between intervention and control group, neither in the number of adverse events nor in their severity. The study site physicians judged all adverse events as unrelated to trial treatment or assessment contacts. In the total sample of all randomised participants (n=141), two deaths of patients (both in the control group) and one death of carer (in the COTiD group) were reported. In the COTiD group, 14 patients were admitted to hospital for an average of 15 nights; and 10 patients in the control group, for an average of 18 nights. The group difference was not significant ($F(1, 97)=2.785$, $p=0.1$). All events were unrelated to the occupational therapy sessions.

Table 3: Patients' outcomes following intense occupational therapy compared with a single session control intervention in Alzheimer patients and their carers

	Sample size		Baseline		6 weeks			16 weeks			26 weeks			52 weeks (postal carer rating)		
	COTiD	Control	COTiD	Control	COTiD	Control	Group Diff.	COTiD	Control	Group Diff.	COTiD	Control	Group Diff.	COTiD	Control	Group Diff.
	N	N	mean (SD)	mean (SD)	mean (SD)	mean (SD)	mean [95%CI]	mean (SD)	mean (SD)	mean [95%CI]	mean (SD)	mean (SD)	mean [95%CI]	mean (SD)	mean (SD)	mean [95%CI]
PRPP independence 100 to 0*	54	50	62.1 (26.8)	64.6 (23.1)	72.0 (27.1)	66.7 (26.1)	-5.3 [-15.7 to 5.1]	65.2 (30.3)	67.4 (28.2)	2.2 [-9.2 to 13.6]	67.8 (30.1)	71.1 (29.4)	3.3 [-8.3 to 14.9]	-	-	-
IDDD performance 44 to 0*	54	50	15.4 (9.9)	14.1 (10.1)	14.3 (9.5)	13.5 (10.3)	-0.8 [-4.6 to 3.1]	15.8 (10.1)	14.8 (10.1)	-1.0 [-5.0 to 2.9]	16.9 (10.1)	15.0 (10.3)	-1.9 [-5.8 to 2.1]	21.1 (11.9)	18.7 (11.6)	-2.4 [-7.1 to 2.3]
IDDD initiative 0 to 36*	54	50	16.0 (8.7)	15.9 (8.4)	15.0 (8.1)	14.4 (8.7)	-0.6 [-3.9 to 2.7]	15.5 (8.2)	16.4 (9.1)	0.9 [-2.5 to 4.3]	16.1 (8.6)	16.7 (9.3)	0.6 [-2.9 to 4.1]	20.1 (9.9)	19.1 (10.1)	-1.0 [-5.0 to 3.0]
CSDD 0 to 38*	41	37	13.2 (7.6)	10.4 (6.3)	12.7 (7.8)	10.3 (6.1)	-2.4 [-5.5 to 0.8]	11.4 (7.2)	11.3 (6.6)	-0.1 [-3.2 to 3.0]	12.3 (6.8)	10.9 (6.3)	-1.3 [-4.3 to 1.6]	13.8 (6.7)	11.7 (6.7)	-2.0 [-5.1 to 1.0]
DQoL overall 5 to 1*	49	45	2.8 (0.8)	3.1 (0.8)	2.9 (0.9)	3.1 (0.6)	0.3 [-0.04 to 0.6]	2.8 (0.8)	3.1 (0.9)	0.3 [-0.02 to 0.6]	2.9 (0.8)	3.0 (0.8)	0.2 [-0.1 to 0.5]	-	-	-
SF-12 physical 100 to 0*	47	45	42.7 (10.0)	45.0 (9.4)	42.4 (11.4)	45.4 (11.0)	3.0 [-1.7 to 7.6]	41.8 (9.2)	45.1 (11.6)	3.3 [-1.0 to 7.6]	41.8 (11.3)	44.8 (11.1)	3.0 [-1.6 to 7.6]	-	-	-
SF-12 mental 100 to 0*	47	45	49.3 (11.0)	52.2 (9.3)	50.3 (12.3)	51.2 (9.9)	0.9 [-3.7 to 5.6]	51.8 (10.1)	52.8 (9.5)	1.1 [-3.0 to 5.1]	53.1 (9.0)	52.3 (10.6)	-0.8 [-4.9 to 3.3]	-	-	-

*Range: positive to negative, COTiD: Community Occupational Therapy in Dementia Programme, PRPP: Perceive, Recall, Plan and Perform System of Task Analysis, IDDD: Interview for Deterioration in Daily Living Activities in Dementia, CSDD: Cornell Scale for Depression in Dementia, DQoL: Dementia Quality of Life Instrument

Table 4: Carers' outcomes following intense occupational therapy compared with a single session control intervention in Alzheimer patients and their carers

	Sample size		Baseline		6 weeks			16 weeks			26 weeks			52 weeks (postal carer rating)		
	COTiD	Control	COTiD	Control	COTiD	Control	Group Diff.	COTiD	Control	Group Diff.	COTiD	Control	Group Diff.	COTiD	Control	Group Diff.
	N	N	mean (SD)	mean (SD)	mean (SD)	mean (SD)	mean [95%CI]	mean (SD)	mean (SD)	mean [95%CI]	mean (SD)	mean (SD)	mean [95%CI]	mean (SD)	mean (SD)	mean [95%CI]
SCQ 135 to 27*	50	47	100,8 (17,4)	107,0 (16,4)	103,0 (18,7)	108,6 (17,2)	5,7 [-1,6 to 12,9]	102,7 (18,2)	107,3 (17,8)	4,6 [-2,6 to 11,9]	104,7 (17,0)	107,9 (17,4)	3,2 [-3,7 to 10,1]	99,8 (17,8)	103,6 (18,6)	3,8 [-3,5 to 11,2]
CES-D 0 to 60*	52	46	12,1 (7,7)	11,3 (5,9)	10,6 (7,1)	10,9 (6,9)	0,3 [-2,6 to 3,1]	10,6 (7,7)	10,8 (7,3)	0,3 [-2,8 to 3,3]	10,0 (7,9)	10,0 (6,9)	0,0 [-3,0 to 3,0]	14,3 (10,3)	12,9 (7,7)	-1,4 [-5,1 to 2,3]
DQoL overall 5 to 1*	51	48	3,1 (0,8)	3,1 (0,7)	3,0 (0,6)	3,1 (0,7)	0,0 [-0,2 to 0,3]	3,1 (0,7)	3,0 (0,8)	0,0 [-0,3 to 0,3]	3,0 (0,7)	3,2 (0,8)	0,2 [-0,1 to 0,5]	2,8 (0,8)	3,0 (0,8)	0,2 [-0,1 to 0,5]
SF-12 physical 100 to 0*	40	38	42,4 (11,5)	43,5 (11,3)	45,8 (10,0)	44,0 (10,0)	-1,8 [-6,3 to 2,7]	44,1 (10,8)	46,2 (9,2)	2,1 [-2,5 to 6,6]	45,4 (10,7)	45,0 (10,5)	-0,4 [-5,2 to 4,4]	42,7 (10,7)	41,6 (11,7)	-1,0 [-6,1 to 4,0]
SF-12 mental 100 to 0*	40	38	50,9 (9,1)	49,8 (10,7)	50,6 (11,0)	50,0 (8,7)	-0,6 [-5,1 to 3,9]	52,3 (8,6)	48,5 (11,8)	-3,9 [-8,5 to 0,8]	50,2 (9,1)	50,1 (10,7)	0,0 [-4,5 to 4,4]	49,5 (11,9)	47,7 (10,7)	-1,7 [-6,9 to 3,4]
Basic ADL-care by primary carer (hours per day)	52	43	0.5 (0.8)	0.8 (1.3)	0.8 (1.8)	0.9 (1.4)	0.1 [-0.5 to 0.8]	0.7 (1.2)	1.0 (1.4)	0.2 [-0.3 to 0.7]	0.8 (1.2)	1.0 (1.5)	0.2 [-0.3 to 0.8]	1.6 (2.2)	1.8 (2.2)	0.1 [-0.8 to 1.0]
IADL-care by primary carer (hours per day)	52	45	2.1 (2.7)	2.5 (2.6)	1.9 (2.5)	2.9 (3.0)	1.1 [-0.04 to 2.2]	2.3 (2.6)	2.9 (2.8)	0.6 [-0.5 to 1.7]	2.2 (2.2)	3.2 (2.8)	1.0 [0.0 to 2.0]	2.7 (2.2)	3.2 (2.8)	0.5 [-0.6 to 1.6]

*Range: positive to negative, COTiD: Community Occupational Therapy in Dementia Programme, SCQ: Sense of Competence Questionnaire, CES-D: Center for Epidemiologic Depression Scale, DQoL: Dementia Quality of Life Instrument, ADL: Activities of Daily Living, IADL: Instrumental Activities of Daily Living

DISCUSSION

In the results of this study, a ten-session community occupational therapy in dementia programme (COTiD) was found to be no more beneficial than a one-session consultation concerning short- and middle-term effects on patients' daily functioning. In both groups, the need for assistance in basic and instrumental activities of daily living and the performance of a self-chosen daily living task remained stable up to six months after baseline. No significant group differences could be found on secondary outcomes, which were quality of life and mood of patient and primary carer; patient's initiative in daily activities; carer's sense of competence in interaction with the patient; carer's hours of daily care; and the patient's nursing home placement. There were no adverse events associated with experimental or control intervention.

Limitations

Despite an elaborate study design, there are some limitations in this study. We analysed only 104 completer dyads from 141 recruited pairs (74 %). However, (1) baseline data of completers and non-completers did not show imbalance, (2) data imputation with the last observation carried forward is inappropriate in dementia research, (3) dyads were maintained, whose data were valid, and for whom treatment was intended but not received in the complete ITT-analysis and (4) even the analysis of the reduced patient sample with valid data did not show a tendency towards significant group differences. Thus the hypothesis of group differences must be rejected, because the analysis of completers usually favours results in the direction of group differences.

A second shortcoming was that following the common introductory seminar the start of the study differed amongst the sites due to different time lines in administrative

matters and approval of the local ethic commissions. Therefore, a common repetition seminar for the interventionists could not be arranged after the pilot training. This may have led to some heterogeneity in the intervention, especially because in Germany eleven newly introduced interventionists performed the treatment compared to two experienced experts in the original Dutch trial. We addressed this problem with feedback on videos of treatment sessions the interventionists sent in. Furthermore, we arranged telephone supervision on demand. However, it is difficult to judge whether these measures could compensate for the potential influence of different educational backgrounds of Dutch and German occupational therapists. In the Netherlands, occupational therapy education takes four years and is more psychosocial oriented than the three years curriculum in Germany.

We consider the contamination of the control intervention with knowledge from the experimental intervention to be low, because any specific intervention such as activity selection, simplification or training was precluded by the limited time to carry out the control intervention.

Comparison

The Dutch RCT on the COTiD with waiting-control-group design showed large effect sizes in the IDDD performance scale at six and twelve weeks after baseline (d=2.3 and 2.4, respectively).[6] The Dutch and the German sample did not differ remarkably in cognition at baseline (MMSE: 19 v 20), but did differ in the need of assistance (IDDD performance: 24 v 15). The German patients showed a low need of assistance at the beginning of the study. This was comparable to the IDDD values of the Dutch patients at the end of the treatment. This may have caused a floor effect on the IDDD. Another mono-centre RCT in the USA compared community occupational therapy and a less intensive telephone consultation in patients with probable dementia (MMSE: 13).[34] The authors found a small effect size in daily

functioning (d=0.21). The initial need of assistance in both studies was higher than in the German sample. A systematic review of community programmes in dementia [35] reported one study on exercise and behavioural management with beneficial effects on daily functioning of patients with moderate dementia (MMSE: 17) [36]; one trial on occupational therapy with heterogeneous effects [16]; and two studies on occupational therapy [37] and music therapy [38] with no significant effects. A current German health technology assessment on non-drug therapies in Alzheimer's disease did not identify further community occupational therapy trials.[39] The comparison of community intervention trials reveals that study samples with a lower MMSE and a higher need of assistance benefit more than those with initial higher cognitive and daily functioning. Similarly, a standardized synopsis of ADL outcomes in pharmacological dementia trials indicated that samples with an MMSE between 17 and 10 benefit most in ADL while samples with higher MMSE scores showed less effects.[40] However, different baseline scores of cognitive and daily functioning alone cannot explain the major difference between the findings in this German study and the positive results of the Dutch RCT. Detailed process evaluation and exploratory analyses of the study data might show whether variations in study site context and treatment performance influenced the intervention's effectiveness.

Clinical and research implications

Published evidence for the effectiveness of community occupational therapy in dementia is heterogeneous as indicated by a Dutch trial with large positive effects on daily functioning; a few USA trials with no or small positive effects on ADL and this German study showing that ten sessions were not superior to one consultation. A preventative one-session consultation might be hypothesised as beneficial for people with mild dementia and an improved 10-session programme more specifically adapted to the German health care system as beneficial for dementia patients with

moderate need of assistance in ADL, as was shown in the Dutch study in which most people with dementia had moderate to high need for assistance at baseline.

Although we had expected smaller effect sizes than in the Dutch original trial due to changed study design with (1) the introduction of an active control group, (2) a variance in treatment performance in several centres, (3) a prolonged follow up time and (4) rigorous reduction of the analysed sample to participants with valid data, it remains surprising that significant group difference could not be found in any of the primary or secondary outcomes.

This study has shown that careful cross-national comparisons are greatly needed, especially in complex interventions, before they can be considered evidence based and implemented effectively in other health care systems. Therefore, further analyses must investigate the role of interventionists' expertise and treatment performance, and the role of participants' needs and utilisation of health care resources, before conclusions on international implementation of this intense occupational therapy intervention can be drawn.

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Data sharing statement: Complete data sets can be provided on request for research fellows in scope of collaborative projects and publications.

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CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	3
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	5+6
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	7+8
	2b	Specific objectives or hypotheses	8
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	8
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	9
Participants	4a	Eligibility criteria for participants	9
	4b	Settings and locations where the data were collected	9+10
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	10+11+12
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	12+13+14
	6b	Any changes to trial outcomes after the trial commenced, with reasons	13
Sample size	7a	How sample size was determined	14
	7b	When applicable, explanation of any interim analyses and stopping guidelines	14
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	14
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	14
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	15
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	15
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those	15

		assessing outcomes) and how	
	11b	If relevant, description of the similarity of interventions	10+11
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	15+16
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	16
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	17
	13b	For each group, losses and exclusions after randomisation, together with reasons	17
Recruitment	14a	Dates defining the periods of recruitment and follow-up	16
	14b	Why the trial ended or was stopped	16
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	18
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	19+22
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	22
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	19+20
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	21
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	23+24
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	24+25
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	24+25
Other information			
Registration	23	Registration number and name of trial registry	9
Protocol	24	Where the full trial protocol can be accessed, if available	9
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	26

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.

A multi-centre RCT on community occupational therapy in Alzheimer's disease: Ten sessions are not superior to one consultation.

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A multi-centre RCT on community occupational therapy in Alzheimer's disease: Ten sessions are not superior to one consultation.

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Keywords: Alzheimer Disease – Occupational Therapy – Randomized Controlled Trial

Article focus

1. Efficiency of community occupational therapy in dementia
2. Pragmatic multi-centre RCT in routine care context

Key message

A ten-session community occupational therapy programme did not work more effectively than a comprehensive one-session occupational therapy consultation within German routine health care.

Strengths and limitations

The main strength of this trial was an elaborate multi-centre RCT design within a routine care setting using an active control group, a prolonged follow-up and a strategy of video rating with fully blind assessors. However, patients and carer could not be masked.

The main limitation was that the training time for the interventionists was less and interventionists had no treatment experience with the experimental intervention before the start of the trial, in contrast to extensive training time and treatment experience with the experimental intervention of the Dutch therapists. Furthermore, we had to exclude 37 patients (26 %) from the MANOVA of the primary outcome because they withdrew; or the assessment at one or more time points was missing or not within the planned time period. However, the attrition in both groups did not demonstrate a systematic bias; the analysis of the reduced patient sample with valid data did not show a tendency to significant group differences; and an additional mixed model analysis of all

randomised patients did not reveal significant differences. Consequently, the hypothesis of better effects within the experimental group must be rejected.

Abstract

Objective

To compare the benefits and harms of a Dutch ten-session Community Occupational Therapy programme for patients with Alzheimer's disease with the impact of a one session consultation at home in German routine health care.

Design

A seven-centre, parallel group, active controlled RCT. Assessors were blind for treatment allocation.

Setting

Patients' homes.

Participants

141 patients with mild to moderate Alzheimer's disease living in the community and their primary carers were recruited. Follow up data of 104 patient-carer-dyads were analysed.

Interventions

Experimental 10 home visits within 5 weeks by an occupational therapist, educating patients in the performance of simplified daily activities and in the use of aids to compensate for cognitive decline; and educating carers in coping with behaviour of the patient and in giving supervision to the patient.

Control one home visit including individual counselling of patient and carer and explanation of a leaflet on coping with dementia in daily life.

Outcome measures

The Interview of Deterioration in Daily activities in Dementia (IDDD) and the Perceive, Recall, Plan and Perform System of Task Analysis (PRPP) were used. Assessments were at baseline, 6, 16, and 26 weeks, postal assessment at 52 weeks.

Results

Patients' daily functioning did not significantly differ between experimental and control group at week 6, 16, 26 or 52 and remained stable over 26 weeks in both groups. No adverse events were associated with the interventions.

Conclusions

In German health care, a ten-session community occupational therapy was not superior to a one-session consultation for the daily functioning of people with Alzheimer's disease. Careful cross-national research on components for effective translation and evaluation in other health care settings is needed before complex interventions based on other health care systems can be considered as evidence.

International Clinical Trials Registry Platform, DRKS00000053

INTRODUCTION

Alzheimer's disease causes high health care costs and burdens patients and carers with severe problems in activities of daily living (ADL).[1-2] Consequently, the improvement or the preservation of ADL is evaluated as a patient-related outcome in clinical trials related to dementia.[3] ADL, burden of care, ability to stay in the community, and quality of life issues are probably much more relevant to patients and carers than the deceleration of cognitive decline, another patient-related outcome.[4] A synopsis of four systematic reviews analysing 73 RCTs on the efficacy of pharmacological and psychosocial interventions regarding everyday functioning in dementia concluded that positive effects of drugs on ADL are small (pooled effect sizes < 0.28) and heterogeneous regarding safety. In contrast to the well documented results for pharmacological interventions evidence for psychosocial interventions on ADL is lacking.[5] However, a recent Dutch mono-centre RCT demonstrated significant positive effects of occupational therapy on ADL (effect sizes of 2.4, $p < 0.0001$).[6] Therefore, the purpose of our multi-centre RCT was to transfer the Dutch community occupational therapy programme in a broader context of German routine health care and to evaluate its effectiveness and safety in comparison with an active control group intervention.

Occupational therapy specialises in supporting independence in ADL and is recommended in several guidelines for dementia management.[7-9] Occupational therapy uses a combined approach including activity simplification, environmental modification, adaptive aids, problem-solving strategies, skill training and carer training.[7, 10-11] According to the bio-psycho-social health model of the World Health Organization (WHO), the negative impact of cognitive deficits on activities can be diminished by

improving the patient's physical and social environment and by tailoring the intervention to the patient's capability.[12-15]

Until March 2011, there was no systematic review on community occupational therapy for people with Alzheimer's disease but two research groups had conducted RCTs in this subject. In the USA study, occupational therapy demonstrated beneficial effects on patients' challenging behaviours but not on ADL. No information on adverse events were given.[14, 16-18] In the Netherlands, occupational therapy, tailored to the needs of patients and carers showed benefits on the patient's ADL, mood, health status and quality of life and on the carer's sense of competence, mood, quality of life and costs of informal care. No adverse events were reported in either intervention or control group.[6, 19-20]

In the current randomised trial we tested the hypothesis that the Dutch ten-session Community Occupational Therapy in Dementia Programme (COTiD) would significantly improve the daily functioning of people with mild or moderate dementia, more so than a one-session Community Occupational Therapy Consultation (COTC). Secondary research questions were whether these interventions would show a difference in their effect on patient's and primary carer's quality of life and mood; on the carer's sense of competence in the interaction with the patient; and on long-term nursing home placements.

METHODS

Design

In order to evaluate the superiority of COTiD, we used a seven-centre single-blind, active-controlled design with a 1:1 randomisation for two parallel groups. There was no modification in design or eligibility criteria from the study protocol

available at http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2761388/. The study was registered at the German register of clinical trials, which is connected to the International Clinical Trials Registry Platform (http://apps.who.int/trialsearch/ => DRKS00000053). The Medical Ethics Committee of the University Hospital Freiburg gave ethical approval (no. 110/08).

Participants and Setting

Patients were eligible to participate in the study if they had mild to moderate dementia (MMSE 14-24) and were diagnosed as having Alzheimer's disease or mixed type dementia, according to ICD-10 criteria, by physicians with more than five years of experience in dementia diagnosis. Participants had to dwell in the community either together with their primary carer or with involvement of a carer providing care at least twice a week. Patients with a score above 12 on the 30-items Geriatric Depression Scale or a major need of physical nursing care of more than 120 min per day (level 2 or higher according to the German Long-Term Care Insurance Act) were excluded. Unstable medical conditions or severe behavioural disturbances, which did not allow participation in the study as judged by the study physicians were criteria for exclusion as well as for discontinuation. Long-term nursing home placements of the patients during the treatment phase or death of patient or primary carer were criteria for discontinuation. The patient gave written informed consent and the carer consented by written format to join and support the treatment procedures.

Patients were recruited from five outpatient memory centres at university hospitals (in Bonn, Freiburg, Mainz, Marburg and Tübingen); one municipal hospital in Karlsruhe specialising in geriatric medicine; and one neurological private practice in Berlin specialising in neuropsychiatry and collaborating with

an occupational therapy private practice. The seven participating centres are located throughout Germany in urban regions with catchment areas of about 70,000 to 700,000 inhabitants. They had all provided outpatient dementia care for three to fifteen years. Their standard service comprised diagnostic work-up for dementia and related diagnoses as well as recommendation of risk reduction, dementia medication and non-pharmacological treatments. Principal investigators of the centres were psychiatrists, neurologists or geriatricians with six to thirteen years of experience in dementia care.

Interventions

The experimental intervention (COTiD) was designed to improve the patient's and the primary carer's daily functioning, and was based on an evidence-based treatment manual.[6, 19-23] COTiD consisted of ten occupational therapy sessions of one hour duration held over five weeks at each patient's home. In the diagnostic phase, comprising of 3 to 4 sessions, the occupational therapist explored (1) the patient's preferences and history of daily activities, (2) her or his ability to perform activities and to use compensatory strategies within the familiar environment, (3) the possibilities of modifying the patient's home, (4) the carer's activity preferences, problems in care giving, coping strategies and abilities to supervise and (5) the interaction between carer and patient. In a shared decision-making process during the goal setting session, the patient and the carer selected the one or two most meaningful activities out of a list of their preferences for daily activities to work on in occupational therapy. During the treatment phase of 5 to 6 sessions, the occupational therapist defined, together with the patient and the carer, more effective compensatory and environmental strategies to adapt both the environment and the selected activities to the

patient's habits and cognitive abilities. Patient and carer were taught how to use these suggested adaptations within strategies, activities and the environment in order to improve their performance of daily activities. In addition, the carer received practical and emotional support and was coached in effective supervision, problem solving and coping strategies by means of cognitive-behavioural interventions. Detailed description of the experimental intervention has been published elsewhere.[23]

For the German RCT, MG taught the content of the translated treatment manual to 14 study participant occupational therapists in 16 hours of seminars using presentation, videos and role play with feedback and group discussion. After the seminar and before the study started, they needed to complete a full treatment series for at least one pilot dyad of patient and carer. In the study phase, the interventionists spent about 20 hours per patient for a full treatment series including ten treatment sessions, travel, reports and multidisciplinary briefing. In Germany, a series of ten to thirty sessions is within the normal range of time that occupational therapists use for the treatment of older outpatients diagnosed with other diseases, such as stroke or rheumatoid arthritis.

The control group received one hour occupational therapy consultation (COTC) at the patient's home conducted by the same study interventionists. Based on material of the German Alzheimer Society, two occupational therapists with more than five years of experience in dementia care had prepared a leaflet of ten pages.[24-25] The semi-structured consultation was an explanation of 30 min of this leaflet and a talk of 30 min on individual problems that arose from patient's and carer's needs. This included encouragement to stay active in everyday life, to maintain social contacts and to use dementia services in the region for which local addresses were listed in the leaflet. Occupational

therapists were taught the control intervention within a 4-hour seminar. Consultations of 30 minutes up to one hour duration about such issues are common in German dementia care. Detailed description of the control intervention as well as means of quality assurance in experimental and control intervention has been published elsewhere.[26]

Outcome measures

The primary endpoint was the patients' change of daily functioning from baseline to follow-up time points at week 6, 16 and 26 measured with the performance scale of the Interview for Deterioration in Daily Living Activities in Dementia (IDDD).[27] This scale records carer rating of the patient's need of assistance in the performance of (1) washing oneself, (2) making tea or coffee, (3) dressing, (4) combing one's hair and brushing one's teeth, (5) eating, (6) using the toilet, (7) shopping, (8) using the telephone, (9) preparing a meal, (10) cleaning the house or doing minor repair work and (11) handling finances. Each item is rated never=0, seldom=1, sometimes=2, often=3 or always=4. The sum of scores ranged from 0 to 44. Higher scores indicated higher need for assistance. Since carer rating could not be 'masked', daily functioning was additionally evaluated by external raters fully 'blind' to the group assignment. They rated video tapes of a challenging daily living task and used the Perceive, Recall, Plan and Perform System of Task Analysis (PRPP).[28] For the PRPP, raters had to define single steps of the performed activity, and they identified any activity step in which errors of accuracy, omission, repetition or timing occurred. The number of activity steps rated as incorrectly performed was divided by the total number of activity steps, resulting in an independence-score indicated in a percentage (100% = all steps are error-free).

Table 1: Measurements of secondary endpoints[26]

Endpoint	Measurement
Patient's initiative in daily activities	Interview for Deterioration in Daily Living Activities in Dementia (IDDD), initiative scale
Patient's mood	Cornell Scale for Depression in Dementia (CSDD)
Carer's mood	Center for Epidemiologic Depression Scale (CES-D)
Patient and carer's quality of life	Dementia Quality of Life Instrument (DQoL), overall item
	SF-12 physical
	SF-12 mental
Carer's interaction with patient	Sense of Competence Questionnaire (SCQ)
Care by primary carer	Resource Utilization in Dementia (RUD), hours per day
Nursing home placement	RUD, nights in nursing home (except respite care)
Harms	Number of adverse events
	RUD, nights in hospital

Secondary endpoints included mood, quality of life, resource utilisation and possible harms. Assessors 'blind' for the group assignment, completed measurements at the patient's home at baseline, week 6, 16 and 26 and arranged a postal survey of carer questionnaires at week 52. The assessors had a minimum of one year's professional experience with older or cognitively impaired people. They attended an introductory seminar of 8 hours. The complete assessment was applied during a 2-hour visit at each patient's home including (1) handing out and explaining the questionnaires to the carer, (2) interviewing the patient (DQoL and SF-12) in a separate room, (3) videotaping the patient and (4) receiving back the carer questionnaires, checking it and clarifying answers if necessary. Seminar description and means of quality management for assessment as well as detailed scheme and psychometric properties of all measurement instruments have been reported recently.[26]

All measurement instruments are validated and used in dementia research.[29-30] For the present study, we translated the IDDD into German according to high methodological standards with two independent forward and backward translations, analysis of discrepancies and final agreement by discussion with all translators. There was no need to translate the PRPP because, because it

was established in the Netherlands and applied by Dutch raters. There was one protocol amendment before recruitment started. The Assessment of Motor and Process Skills (AMPS) was replaced by the PRPP, because the AMPS was not available in the German language within the planned schedule.

Indicators of harm were defined as patient or carer death, number of patients with admission to hospital and number of nights in hospital. These indicators were recorded in interviews with the carer at intervals of 5 to 7 weeks over 52 weeks. Study sites had to report severe adverse events to the study centre immediately when each occurred. We did not assume a direct association between the defined harms and either the experimental or the control intervention. However, increased daily activities in the interventions group might have resulted in a higher risk of falls or accidents and thus may indirectly have led to more nights in hospital or in the worst case to death.

Sample size calculation

A sample size of 42 participants per group was calculated to be necessary to detect an effect size of f = 0.10 on the IDDD performance scale in an analysis of variance of two groups and four time points; using a two-sided 5% significance level, a power of 80%, and a correlation of 0.7 between the measurement time points [31]. According to the Dutch original RCT, we expected a dropout rate of 10% at week 16, which was extrapolated to 40% at week 52. A nine-month inclusion period was anticipated as necessary in order to recruit the 140 patients. Our assumed effect size of f = 0.10 is based on a group by time interaction and compatible to Cohen's d = 0.20, which corresponds to a small effect size and any d over 0.8 is large. Although the Dutch original RCT found

effect sizes of d = 2.4 in the IDDD performance scale at week 12, for this study the power was calculated much more conservatively.

This was because we (1) introduced an active control group, (2) investigated the programme effects under varying care conditions in seven centres with interventionists who were introduced in this new treatment and were far not as experienced as the Dutch study therapists and (3) we prolonged the follow up period. Interim analyses were not planned.

Randomisation and masking

The random allocation sequence was computer-generated with blocking by centre and groups of two persons, without stratification and in a ratio of 1:1 by a statistician from a distant site. After enrolment, study site physicians requested randomisation via e-mail. The statistician e-mailed the individual allocation to COTiD or COTC exclusively to the site interventionist and stored the allocation list at his distant site which was not available to any study site staff. The interventionist scheduled treatment sessions, faxed records to the distant coordinating study centre and kept all documents strictly separated from any other site staff. This was in order to avoid contamination. Since the numbers of home visits differed in the experimental and control groups, masking of patients and carers was not possible. However, study information did not include any preference for a special treatment 'arm'. Patients and carers were asked to give no information about their treatment package to assessors or study physicians. All study personal was 'blind' for group assignment, except the interventionists. Agreement between the assessors' estimation of group assignment and the actual group assignment was 61%, and thus slightly over the expected 50% of agreement by chance. The procedure of external video rating ensured the full

'blinding' of the external raters for the PRPP primary outcome measure. Independent research assistants cleaned the videotapes of any hint of group assignment before they were rated by two Dutch raters not involved in the trial treatment. In order to establish the inter-rater reliability, we tested ten double ratings of the same video by the two raters and found an intra-class correlation coefficient of 0.9. Data analysts were not 'blind' for the group assignment. However, measurement time points and outcomes had been published before data were available for analysis [26] and any decision to remove patients from the analyses is reported in the present publication.

Statistical methods

Data were entered via special MS Access entry masks automatically controlling for data plausibility. In addition, sections of entered data were checked for typing errors by hand, in order to ensure an error rate lower than 0.2%. The primary intention-to-treat analysis included all allocated participants with valid data whether they did or did not receive the complete intervention. For the IDDD and the PRPP measurements of the primary outcome, we performed a multivariate analysis of variance (MANOVA) with repeated measures with two groups and four measurement time points at baseline, week 6, 16 and 26. A univariate ANOVA with five measurement time points (+ postal assessment in week 52) was carried out for the secondary outcomes and the IDDD. We did not adjust for baseline values, because we found no marked group differences. In order to deal with missing data occurring not in the primary but in the secondary outcomes, we performed secondary intention-to-treat analyses with multiple data imputation using the Full Information Maximum Likelihood (FIML) method.[32] We imputed data for all secondary outcome measurements and all

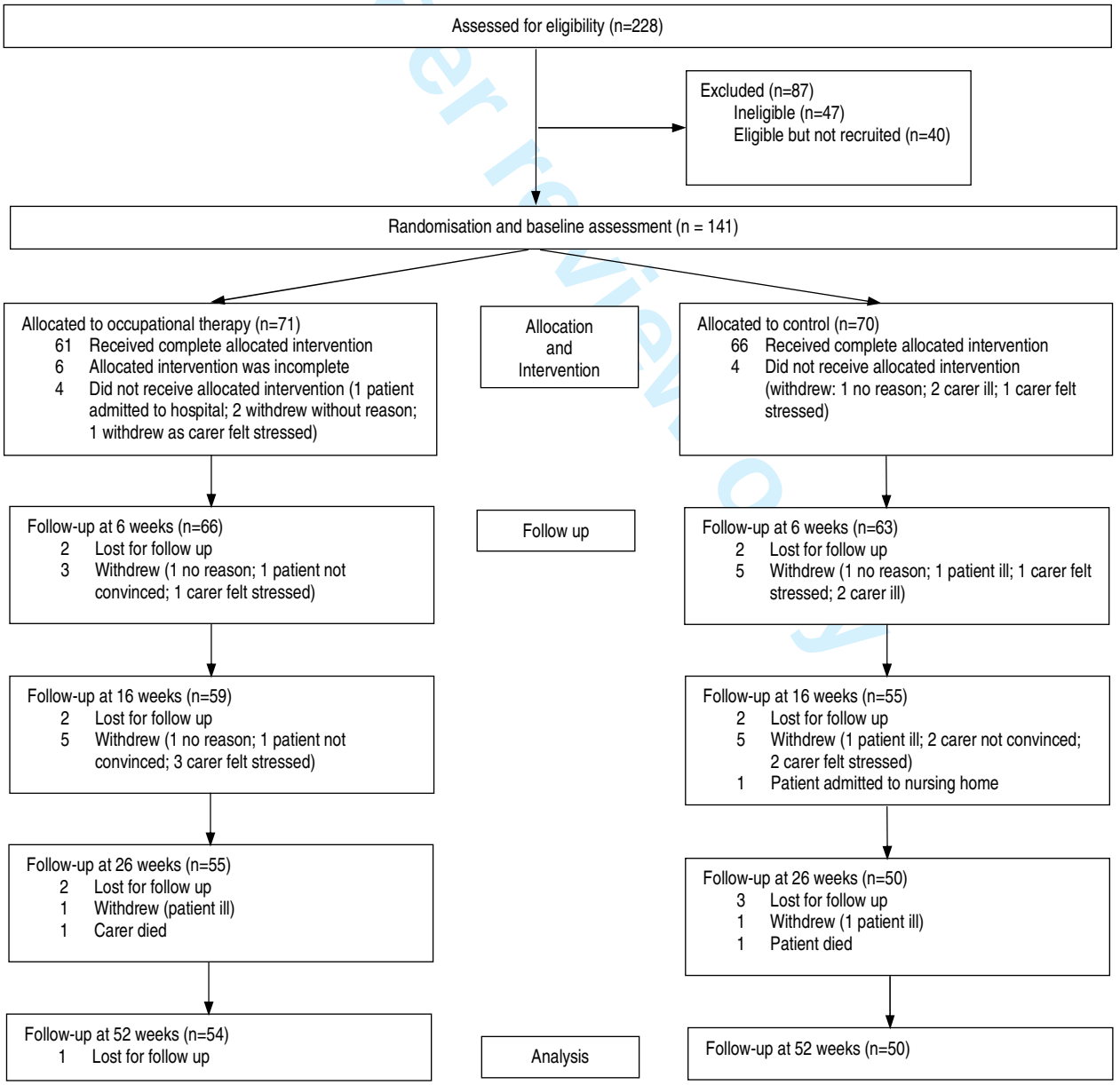
time points using SPSS (version 19). All statistical tests were two-sided on an alpha level of 0.05. Subgroup analyses were not planned.

RESULTS

Recruitment and participant flow

We prolonged the planned recruitment period from August 2008 to April 2009 by one additional month, up to May 2009. This was in order to recruit the intended sample size. The 52-week follow up was closed in May 2010.

Figure 1: Flow of participants through the trial



141 participants were recruited (Berlin: 19, Bonn: 21, Freiburg: 26, Karlsruhe: 15, Mainz: 24, Marburg: 21, Tübingen: 15). The flow chart (Figure 1) shows that attrition following randomisation did not lead to significant group differences.

Baseline Characteristics

Randomisation did avoid imbalances in baseline characteristics (Table 2) and pre-treatment assessment data (Table 3) except in one item. Participants in the control group had more moderate to severe limitations in their financial situation (14% v 2%; p=0.027). Because the financial situation is not known as predictive factor for functional decline, we did not adjust for this imbalance.[33]

Table 2: Demographic and clinical characteristics

	COTiD			Control		
	analysed (n=54)	dropouts (n=17)	total (n=71)	analysed (n=50)	dropouts (n=20)	total (n=70)
Age, years (SD)	78.0 (7.1)	77.2 (8.5)	77.8 (7.4)	78.7 (6.0)	78.3 (7.1)	78.5 (6.3)
Sex, female	29 (54 %)	12 (71 %)	41 (58 %)	30 (60 %)	10 (50 %)	40 (57 %)
MMSE (SD)	20.4 (3.1)	19.0 (3.3)	20.2 (3.2)	20.7 (2.7)	20.3 (2.9)	20.7 (2.7)
GDS (SD)	6.9 (3.0)	5.6 (2.9)	6.5 (3.0)	5.2 (2.8)	6.1 (2.6)	5.5 (2.8)
Education						
no school graduation	2 (4 %)	1 (6 %)	3 (4 %)	1 (2 %)	0 (0 %)	1 (1 %)
middle school graduation (9 or 10 years)	41 (76 %)	13 (76 %)	54 (76 %)	37 (74 %)	15 (75 %)	52 (74 %)
high school graduation (12 or 13 years)	11 (20 %)	3 (18 %)	14 (20 %)	12 (24 %)	5 (25 %)	17 (24 %)
Financial situation as perceived by the carer						
no limitation	40 (74 %)	14 (82 %)	54 (76%)	38 (76 %)	13 (65 %)	51 (73 %)
minor limitation	12 (22 %)	1 (6 %)	13 (18 %)	3 (6 %)	3 (15 %)	6 (9 %)
moderate or severe limitation	1 (2 %)	2 (12 %)	3 (4 %)	7 (14 %)	4 (20 %)	11 (16 %)
no data	1 (2 %)	0 (0.0 %)	1 (1 %)	2 (4 %)	0 (0 %)	2 (3 %)
Primary carer						
Age, years (SD)	65.4 (16.3)	63.1 (14.0)	64.9 (15.7)	65.9 (13.0)	61.4 (17.4)	64.5 (14.4)
Sex, female	38 (70 %)	9 (53 %)	47 (66 %)	35 (70 %)	18 (90 %)	53 (76 %)
Spouse	32 (59 %)	8 (47 %)	40 (56 %)	31 (62 %)	9 (45 %)	40 (57 %)
Daughter or son (in law)	20 (37 %)	7 (41 %)	27 (38 %)	16 (32 %)	9 (45 %)	25 (36 %)
Others	2 (4 %)	2 (12 %)	4 (6%)	3 (6 %)	2 (10 %)	5 (7 %)
Living together (%)	41 (76 %)	11 (65 %)	52 (73%)	33 (66 %)	14 (70 %)	47 (67 %)

Intervention delivery

61 of 71 (86%) allocated patient-carer dyads received complete sessions in the COTiD group, 66 of 70 (94%) in the control group. In each group, 4 pairs were

lost before intervention. Six patient-carer dyads in the COTiD had less than 10 sessions. Interventionists rated the delivery of 20 pre-defined treatment sub-processes, ranging from interviewing patient and carer to training of simplified activities or supporting the carer in supervision. They scored treatment delivery as 78% in the COTiD group and 80% in the control group. Interventionists rated the patient's adherence in 67 cases of the COTiD group, from 15 as hindering the delivery of treatment; 26 as neutral and 26 as facilitating. Rating criteria were the patient's cooperation during interview, goal setting and training; the daily changing mental capacity; collaboration with the carer; and the acceptance of innovations. Ratings of carers' adherence were 5 hindering; 15 neutral; and 47 facilitating. The carer adherence was assessed with regard to the cooperation during scheduling, interview, goal setting and training to supervise; the encouragement of the patient; the acceptance of support service; and the implementation of innovations. The adherence of the participants in the control group could not be rated, because interventionists had no further contact after the consultation.

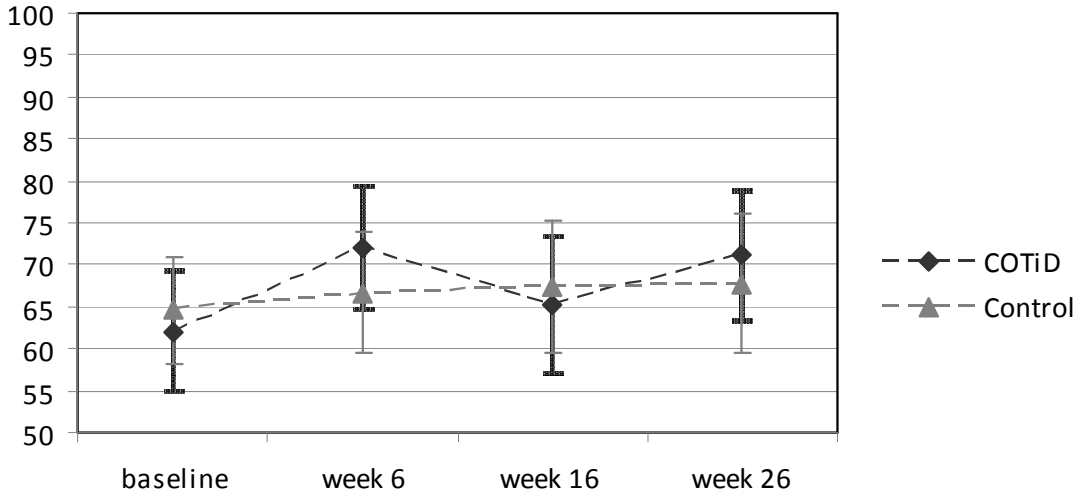
Outcomes

The MANOVA in 104 completers (COTiD: n=54; control: n=50) revealed no significant group time interaction effect in the primary outcome measurements of patients' daily functioning (Figures 2 and 3). Using the arcsine transform [34] for the PRPR percentage did not change results (original: p = 0.243; arcsine-transform: p = 0.216). An additional mixed models analysis of all randomised patients (N=141) as recommended by Coley and colleagues [35] did reveal no significant interactions for the IDDD (p=0.340) and the PRPP (p=0.785). Tables 3 and 4 show mean, standard deviation and group difference including 95%-

confidence intervals of an ANOVA for all outcomes. Patients' daily functioning did not significantly change over 26 weeks in either the experimental and control group. In the postal 52 weeks follow up, the patients' need for assistance increased in both groups, and accordingly the carer's hours of care for basic ADL were higher. Two patients of the COTiD group were placed to nursing homes 33 and 44 weeks after baseline and one patient of the control group after 33 weeks.

To address the problem of missing data in single measurement instruments, we performed a multiple data imputation. We calculated a MANOVA over four measurement time points for all primary and secondary outcomes for all 104 completers. Ten different data imputations did not reveal any significant time group interaction effects.

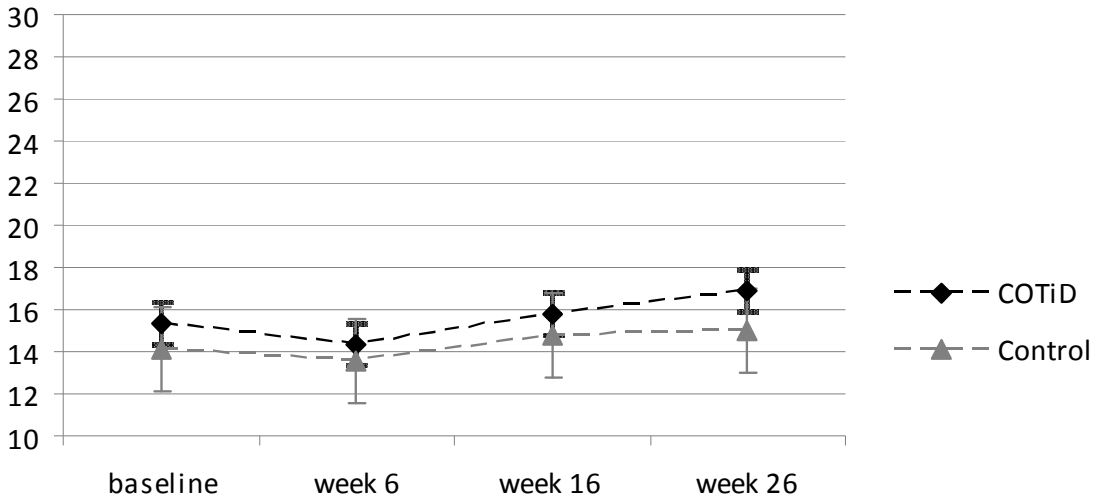
Figure 2: ADL task performance of Alzheimer patients following intense occupational therapy compared with a single session control intervention; means and 95%-confidence intervals of the PRPP independence scale (N=104 completers; range: 100=no errors to 0=all errors)



We also tested for study sites differences at baseline and found no significant differences in a MANOVA with the factors *study sites* and *intervention groups* ($F(66, 432)=1.079$, $p=0.323$). Furthermore, no study site effect was found in the

primary outcome analysing IDDD and PRPP data of baseline, week 6, 16 and 26 (IDDD: F(6, 90)=0.724, p=0.631; PRPP: F(6, 90)=1.758, p=0.117).

Figure 3: Need for assistance in ADL of Alzheimer patients following intense occupational therapy compared with a single session control intervention; means and 95%-confidence intervals of the IDDD performance scale (N=104 completers; range: 0=never needed assistance to 44=always needed assistance)



Harms

There were no differences between intervention and control group, neither in the number of adverse events nor in their severity. The study site physicians judged all adverse events as unrelated to trial treatment or assessment contacts. In the total sample of all randomised participants (n=141), two deaths of patients (both in the control group) and one death of carer (in the COTiD group) were reported. In the COTiD group, 14 patients were admitted to hospital for an average of 15 nights; and 10 patients in the control group, for an average of 18 nights. There was no difference between the two groups in average number of nights admitted to hospital (F(1, 97)=2.785, p=0.1). All events were unrelated to the occupational therapy sessions.

Table 3: Patients' outcomes following intense occupational therapy compared with a single session control intervention in Alzheimer patients and their carers

	Sample size		Baseline		6 weeks			16 weeks			26 weeks			52 weeks (postal carer rating)		
	COTiD	Control	COTiD	Control	COTiD	Control	Group Diff.	COTiD	Control	Group Diff.	COTiD	Control	Group Diff.	COTiD	Control	Group Diff.
	N	N	mean (SD)	mean (SD)	mean (SD)	mean (SD)	mean [95%CI]	mean (SD)	mean (SD)	mean [95%CI]	mean (SD)	mean (SD)	mean [95%CI]	mean (SD)	mean (SD)	mean [95%CI]
PRPP independence 100 to 0*	54	50	62.1 (26.8)	64.6 (23.1)	72.0 (27.1)	66.7 (26.1)	-5.3 [-15.7 to 5.1]	65.2 (30.3)	67.4 (28.2)	2.2 [-9.2 to 13.6]	67.8 (30.1)	71.1 (29.4)	3.3 [-8.3 to 14.9]	-	-	-
IDDD performance 44 to 0*	54	50	15.4 (9.9)	14.1 (10.1)	14.3 (9.5)	13.5 (10.3)	-0.8 [-4.6 to 3.1]	15.8 (10.1)	14.8 (10.1)	-1.0 [-5.0 to 2.9]	16.9 (10.1)	15.0 (10.3)	-1.9 [-5.8 to 2.1]	21.1 (11.9)	18.7 (11.6)	-2.4 [-7.1 to 2.3]
IDDD initiative 0 to 36*	54	50	16.0 (8.7)	15.9 (8.4)	15.0 (8.1)	14.4 (8.7)	-0.6 [-3.9 to 2.7]	15.5 (8.2)	16.4 (9.1)	0.9 [-2.5 to 4.3]	16.1 (8.6)	16.7 (9.3)	0.6 [-2.9 to 4.1]	20.1 (9.9)	19.1 (10.1)	-1.0 [-5.0 to 3.0]
CSDD 0 to 38*	41	37	13.2 (7.6)	10.4 (6.3)	12.7 (7.8)	10.3 (6.1)	-2.4 [-5.5 to 0.8]	11.4 (7.2)	11.3 (6.6)	-0.1 [-3.2 to 3.0]	12.3 (6.8)	10.9 (6.3)	-1.3 [-4.3 to 1.6]	13.8 (6.7)	11.7 (6.7)	-2.0 [-5.1 to 1.0]
DQoL overall 5 to 1*	49	45	2.8 (0.8)	3.1 (0.8)	2.9 (0.9)	3.1 (0.6)	0.3 [-0.04 to 0.6]	2.8 (0.8)	3.1 (0.9)	0.3 [-0.02 to 0.6]	2.9 (0.8)	3.0 (0.8)	0.2 [-0.1 to 0.5]	-	-	-
SF-12 physical 100 to 0*	47	45	42.7 (10.0)	45.0 (9.4)	42.4 (11.4)	45.4 (11.0)	3.0 [-1.7 to 7.6]	41.8 (9.2)	45.1 (11.6)	3.3 [-1.0 to 7.6]	41.8 (11.3)	44.8 (11.1)	3.0 [-1.6 to 7.6]	-	-	-
SF-12 mental 100 to 0*	47	45	49.3 (11.0)	52.2 (9.3)	50.3 (12.3)	51.2 (9.9)	0.9 [-3.7 to 5.6]	51.8 (10.1)	52.8 (9.5)	1.1 [-3.0 to 5.1]	53.1 (9.0)	52.3 (10.6)	-0.8 [-4.9 to 3.3]	-	-	-

*Range: positive to negative, COTiD: Community Occupational Therapy in Dementia Programme, PRPP: Perceive, Recall, Plan and Perform System of Task Analysis, IDDD: Interview for Deterioration in Daily Living Activities in Dementia, CSDD: Cornell Scale for Depression in Dementia, DQoL: Dementia Quality of Life Instrument

Table 4: Carers' outcomes following intense occupational therapy compared with a single session control intervention in Alzheimer patients and their carers

	Sample size		Baseline		6 weeks			16 weeks			26 weeks			52 weeks (postal carer rating)		
	COTiD	Control	COTiD	Control	COTiD	Control	Group Diff.	COTiD	Control	Group Diff.	COTiD	Control	Group Diff.	COTiD	Control	Group Diff.
	N	N	mean (SD)	mean (SD)	mean (SD)	mean (SD)	mean [95%CI]	mean (SD)	mean (SD)	mean [95%CI]	mean (SD)	mean (SD)	mean [95%CI]	mean (SD)	mean (SD)	mean [95%CI]
SCQ 135 to 27*	50	47	100,8 (17,4)	107,0 (16,4)	103,0 (18,7)	108,6 (17,2)	5,7 [-1,6 to 12,9]	102,7 (18,2)	107,3 (17,8)	4,6 [-2,6 to 11,9]	104,7 (17,0)	107,9 (17,4)	3,2 [-3,7 to 10,1]	99,8 (17,8)	103,6 (18,6)	3,8 [-3,5 to 11,2]
CES-D 0 to 60*	52	46	12,1 (7,7)	11,3 (5,9)	10,6 (7,1)	10,9 (6,9)	0,3 [-2,6 to 3,1]	10,6 (7,7)	10,8 (7,3)	0,3 [-2,8 to 3,3]	10,0 (7,9)	10,0 (6,9)	0,0 [-3,0 to 3,0]	14,3 (10,3)	12,9 (7,7)	-1,4 [-5,1 to 2,3]
DQoL overall 5 to 1*	51	48	3,1 (0,8)	3,1 (0,7)	3,0 (0,6)	3,1 (0,7)	0,0 [-0,2 to 0,3]	3,1 (0,7)	3,0 (0,8)	0,0 [-0,3 to 0,3]	3,0 (0,7)	3,2 (0,8)	0,2 [-0,1 to 0,5]	2,8 (0,8)	3,0 (0,8)	0,2 [-0,1 to 0,5]
SF-12 physical 100 to 0*	40	38	42,4 (11,5)	43,5 (11,3)	45,8 (10,0)	44,0 (10,0)	-1,8 [-6,3 to 2,7]	44,1 (10,8)	46,2 (9,2)	2,1 [-2,5 to 6,6]	45,4 (10,7)	45,0 (10,5)	-0,4 [-5,2 to 4,4]	42,7 (10,7)	41,6 (11,7)	-1,0 [-6,1 to 4,0]
SF-12 mental 100 to 0*	40	38	50,9 (9,1)	49,8 (10,7)	50,6 (11,0)	50,0 (8,7)	-0,6 [-5,1 to 3,9]	52,3 (8,6)	48,5 (11,8)	-3,9 [-8,5 to 0,8]	50,2 (9,1)	50,1 (10,7)	0,0 [-4,5 to 4,4]	49,5 (11,9)	47,7 (10,7)	-1,7 [-6,9 to 3,4]
Basic ADL-care by primary carer (hours per day)	52	43	0.5 (0.8)	0.8 (1.3)	0.8 (1.8)	0.9 (1.4)	0.1 [-0.5 to 0.8]	0.7 (1.2)	1.0 (1.4)	0.2 [-0.3 to 0.7]	0.8 (1.2)	1.0 (1.5)	0.2 [-0.3 to 0.8]	1.6 (2.2)	1.8 (2.2)	0.1 [-0.8 to 1.0]
IADL-care by primary carer (hours per day)	52	45	2.1 (2.7)	2.5 (2.6)	1.9 (2.5)	2.9 (3.0)	1.1 [-0.04 to 2.2]	2.3 (2.6)	2.9 (2.8)	0.6 [-0.5 to 1.7]	2.2 (2.2)	3.2 (2.8)	1.0 [0.0 to 2.0]	2.7 (2.2)	3.2 (2.8)	0.5 [-0.6 to 1.6]

*Range: positive to negative, COTiD: Community Occupational Therapy in Dementia Programme, SCQ: Sense of Competence Questionnaire, CES-D: Center for Epidemiologic Depression Scale, DQoL: Dementia Quality of Life Instrument, ADL: Activities of Daily Living, IADL: Instrumental Activities of Daily Living

DISCUSSION

In the results of this study, a ten-session community occupational therapy in dementia programme (COTiD) was found to be no more beneficial than a one-session consultation concerning short- and middle-term effects on patients' daily functioning. In both groups, the need for assistance in basic and instrumental activities of daily living and the performance of a self-chosen daily living task remained stable up to six months after baseline. No significant group differences could be found on secondary outcomes, which were quality of life and mood of patient and primary carer; patient's initiative in daily activities; carer's sense of competence in interaction with the patient; carer's hours of daily care; and the patient's nursing home placement. There were no adverse events associated with experimental or control intervention.

Limitations

Despite an elaborate study design, there are some limitations in this study. We analysed only 104 completer dyads from 141 recruited pairs (74 %). However, (1) baseline data of completers and non-completers did not show imbalance; (2) dyads were maintained, whose data were valid, and for whom treatment was intended but not received in the complete ITT-analysis; (3) an additional mixed model analysis of all randomised patients did also not reveal significant differences; and (4) the analysis of the reduced patient sample with valid data did not show even a tendency towards significant group differences. Thus the hypothesis of group differences must be rejected, because the analysis of completers usually favours results in the direction of group differences.

A second shortcoming was that following the common introductory seminar the start of the study differed amongst the sites due to different time lines in administrative

matters and approval of the local ethic commissions. Therefore, a common repetition seminar for the interventionists could not be arranged after the pilot training. This may have led to some heterogeneity in the intervention, especially because in Germany eleven newly introduced interventionists performed the treatment compared to two experienced experts in the original Dutch trial. We addressed this problem with feedback on videos of treatment sessions the interventionists sent in. Furthermore, we arranged telephone supervision on demand.

We consider the contamination of the control intervention with knowledge from the experimental intervention to be low, because any specific intervention such as activity selection, simplification or training was precluded by the limited time to carry out the control intervention.

Comparison

The Dutch RCT on the COTiD with waiting-control-group design showed large effect sizes in the IDDD performance scale at six and twelve weeks after baseline (d=2.3 and 2.4, respectively).[6] The Dutch and the German sample did not differ remarkably in cognition at baseline (MMSE: 19 v 20), but did differ in the need of assistance (IDDD performance: 24 v 15). The German patients showed a low need of assistance at the beginning of the study. This was comparable to the IDDD values of the Dutch patients at the end of the treatment. This may have caused a floor effect on the IDDD. Another mono-centre RCT in the USA compared community occupational therapy and a less intensive telephone consultation in patients with probable dementia (MMSE: 13).[36] The authors found a small effect size in daily functioning (d=0.21). The initial need of assistance in both studies was higher than in the German sample. A systematic review of community programmes in dementia [37] reported one study on exercise and behavioural management with beneficial effects on daily functioning of patients with moderate dementia (MMSE: 17); one trial on

occupational therapy with heterogeneous effects; and two studies on occupational therapy and music therapy with no significant effects. A current German health technology assessment on non-drug therapies in Alzheimer's disease did not identify further community occupational therapy trials [38]. The comparison of community intervention trials reveals that study samples with a lower MMSE and a higher need of assistance benefit more than those with initial higher cognitive and daily functioning. Similarly, a standardized synopsis of ADL outcomes in pharmacological dementia trials indicated that samples with an MMSE between 17 and 10 benefit most in ADL while samples with higher MMSE scores showed less effects.[39] However, different baseline scores of cognitive and daily functioning alone cannot explain the major difference between the findings in this German study and the positive results of the Dutch RCT. Detailed process evaluation and exploratory analyses of the study data might show whether variations in study site context and treatment performance influenced the intervention's effectiveness.

Clinical and research implications

Published evidence for the effectiveness of community occupational therapy in dementia is heterogeneous as indicated by a Dutch trial with large positive effects on daily functioning; a few USA trials with no or small positive effects on ADL and this German study showing that ten sessions were not superior to one consultation. A preventative one-session consultation might be hypothesised as beneficial for people with mild dementia and an improved 10-session programme more specifically adapted to the German health care system as beneficial for dementia patients with moderate need of assistance in ADL, as was shown in the Dutch study in which most people with dementia had moderate to high need for assistance at baseline.

Although we had expected smaller effect sizes than in the Dutch original trial due to changed study design with (1) the introduction of an active control group, (2) a

variance in treatment performance in several centres, (3) a prolonged follow up time and (4) rigorous reduction of the analysed sample to participants with valid data, it remains surprising that significant group difference could not be found in any of the primary or secondary outcomes.

This study has shown that careful cross-national comparisons are greatly needed, especially in complex interventions, before they can be considered evidence based and implemented effectively in other health care systems. Therefore, further analyses must investigate the role of interventionists' expertise and treatment performance, and the role of participants' needs and utilisation of health care resources, before conclusions on international implementation of this intense occupational therapy intervention can be drawn.

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Data sharing statement: Complete data sets can be provided on request for research fellows in scope of collaborative projects and publications.

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CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	3
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	5+6
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	7+8
	2b	Specific objectives or hypotheses	8
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	8
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	9
Participants	4a	Eligibility criteria for participants	9
	4b	Settings and locations where the data were collected	9+10
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	10+11+12
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	12+13+14
	6b	Any changes to trial outcomes after the trial commenced, with reasons	13
Sample size	7a	How sample size was determined	14
	7b	When applicable, explanation of any interim analyses and stopping guidelines	14
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	14
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	14
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	15
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	15
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those	15

		assessing outcomes) and how	
	11b	If relevant, description of the similarity of interventions	10+11
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	15+16
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	16
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	17
	13b	For each group, losses and exclusions after randomisation, together with reasons	17
Recruitment	14a	Dates defining the periods of recruitment and follow-up	16
	14b	Why the trial ended or was stopped	16
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	18
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	19+22
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	22
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	19+20
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	21
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	23+24
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	24+25
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	24+25
Other information			
Registration	23	Registration number and name of trial registry	9
Protocol	24	Where the full trial protocol can be accessed, if available	9
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	26

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.

A multi-centre RCT on community occupational therapy in Alzheimer's disease: Ten sessions are not superior to one consultation.

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A multi-centre RCT on community occupational therapy in Alzheimer's disease: Ten sessions are not superior to one consultation.

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Article focus

1. Efficiency of community occupational therapy in dementia
2. Pragmatic multi-centre RCT in routine care context

Key message

A ten-session community occupational therapy programme did not work more effectively than a comprehensive one-session occupational therapy consultation within German routine health care.

Strengths and limitations

The main strength of this trial was an elaborate multi-centre RCT design within a routine care setting using an active control group, a prolonged follow-up and a strategy of video rating with fully blind assessors. However, patients and carer could not be masked.

The main limitation was that the training time for the interventionists was less and interventionists had no treatment experience with the experimental intervention before the start of the trial, in contrast to extensive training time and treatment experience with the experimental intervention of the Dutch therapists. Furthermore, we had to exclude 37 patients (26 %) from the MANOVA of the primary outcome because they withdrew; or the assessment at one or more time points was missing or not within the planned time period. However, the attrition in both groups did not demonstrate a systematic bias; the analysis of the reduced patient sample with valid data did not show a tendency to significant group differences; and an additional mixed model analysis of all

randomised patients did not reveal significant differences. Consequently, the hypothesis of better effects within the experimental group must be rejected.

Abstract

Objective
To compare the benefits and harms of a Dutch ten-session Community Occupational Therapy programme for patients with Alzheimer's disease with the impact of a one session consultation at home in German routine health care.

Design
A seven-centre, parallel group, active controlled RCT. Patients and carers were not masked. Assessors were fully blind for treatment allocation for one of two primary outcome measurements.

Setting
Patients' homes.

Participants
Patients with mild to moderate Alzheimer's disease (MMSE 14-24), living in the community with primary carer available and without severe depression or behavioural symptoms were eligible.

Interventions
Experimental 10 home visits within 5 weeks by an occupational therapist, educating patients in the performance of simplified daily activities and in the use of aids to compensate for cognitive decline; and educating carers in coping with behaviour of the patient and in giving supervision to the patient.
Control one home visit including individual counselling of patient and carer and explanation of a leaflet on coping with dementia in daily life.

Outcome measures
The primary outcome was the patient's daily functioning measured with the Interview of Deterioration in Daily activities in Dementia (IDDD) and the Perceive, Recall, Plan and Perform System of Task Analysis (PRPP). Assessments were at baseline, 6, 16, and 26 weeks, postal assessment at 52 weeks.

Results
141 patients were 1:1 randomised to experimental (N=71) and control group (N=70). Data of 54 and 50 participants were analysed. Patients' daily functioning did not significantly differ between experimental and control group at week 6, 16, 26 or 52 and remained stable over 26 weeks in both groups. No adverse events were associated with the interventions.

Conclusions
In German health care, a Dutch ten-session community occupational therapy was not superior to a one-session consultation for the daily functioning of people with Alzheimer's disease. Further research on the transfer of complex psychosocial interventions is needed.

INTRODUCTION

Alzheimer's disease causes high health care costs and burdens patients and carers with severe problems in activities of daily living (ADL).[1-2] Consequently, the improvement or the preservation of ADL is evaluated as a patient-related outcome in clinical trials related to dementia.[3] ADL, burden of care, ability to stay in the community, and quality of life issues are probably much more relevant to patients and carers than the deceleration of cognitive decline, another patient-related outcome.[4] A synopsis of four systematic reviews analysing 73 RCTs on the efficacy of pharmacological and psychosocial interventions regarding everyday functioning in dementia concluded that positive effects of drugs on ADL are small (pooled effect sizes < 0.28) and heterogeneous regarding safety. In contrast to the well documented results for pharmacological interventions evidence for psychosocial interventions on ADL is lacking.[5] However, a recent Dutch mono-centre RCT demonstrated significant positive effects of occupational therapy on ADL (effect sizes of 2.4, $p < 0.0001$).[6] Therefore, the purpose of our multi-centre RCT was to transfer the Dutch community occupational therapy programme in a broader context of German routine health care and to evaluate its effectiveness and safety in comparison with an active control group intervention.

Occupational therapy specialises in supporting independence in ADL and is recommended in several guidelines for dementia management.[7-9] Occupational therapy uses a combined approach including activity simplification, environmental modification, adaptive aids, problem-solving strategies, skill training and carer training.[7, 10-11] According to the bio-psycho-social health model of the World Health Organization (WHO), the

negative impact of cognitive deficits on activities can be diminished by improving the patient's physical and social environment and by tailoring the intervention to the patient's capability.[12-15]

Until March 2011, there was no systematic review on community occupational therapy for people with Alzheimer's disease but two research groups had conducted RCTs in this subject. In the USA study, occupational therapy demonstrated beneficial effects on patients' challenging behaviours but not on ADL. No information on adverse events were given.[14, 16-18] In the Netherlands, occupational therapy, tailored to the needs of patients and carers showed benefits on the patient's ADL, mood, health status and quality of life and on the carer's sense of competence, mood, quality of life and costs of informal care. No adverse events were reported in either intervention or control group.[6, 19-20]

In the current randomised trial we tested the hypothesis that the Dutch ten-session Community Occupational Therapy in Dementia Programme (COTiD) would significantly improve the daily functioning of people with mild or moderate dementia, more so than a one-session Community Occupational Therapy Consultation (COTC). Secondary research questions were whether these interventions would show a difference in their effect on patient's and primary carer's quality of life and mood; on the carer's sense of competence in the interaction with the patient; and on long-term nursing home placements.

METHODS

Design

In order to evaluate the superiority of COTiD, we used a seven-centre single-blind, active-controlled design with a 1:1 randomisation for two parallel groups.

There was no modification in design or eligibility criteria from the study protocol available at http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2761388/. The study was registered at the German register of clinical trials, which is connected to the International Clinical Trials Registry Platform (http://apps.who.int/trialsearch/ => DRKS00000053). The Medical Ethics Committee of the University Hospital Freiburg gave ethical approval (no. 110/08).

Participants and Setting

Patients were eligible to participate in the study if they had mild to moderate dementia (MMSE 14-24) and were diagnosed as having Alzheimer's disease or mixed type dementia, according to ICD-10 criteria, by physicians with more than five years of experience in dementia diagnosis. Participants had to dwell in the community either together with their primary carer or with involvement of a carer providing care at least twice a week. Patients with a score above 12 on the 30-items Geriatric Depression Scale or a major need of physical nursing care of more than 120 min per day (level 2 or higher according to the German Long-Term Care Insurance Act) were excluded. Unstable medical conditions or severe behavioural disturbances, which did not allow participation in the study as judged by the study physicians were criteria for exclusion as well as for discontinuation. Long-term nursing home placements of the patients during the treatment phase or death of patient or primary carer were criteria for discontinuation. The patient gave written informed consent and the carer consented by written format to join and support the treatment procedures.

Patients were recruited from five outpatient memory centres at university hospitals (in Bonn, Freiburg, Mainz, Marburg and Tübingen); one municipal hospital in Karlsruhe specialising in geriatric medicine; and one neurological

private practice in Berlin specialising in neuropsychiatry and collaborating with an occupational therapy private practice. The seven participating centres are located throughout Germany in urban regions with catchment areas of about 70,000 to 700,000 inhabitants. They had all provided outpatient dementia care for three to fifteen years. Their standard service comprised diagnostic work-up for dementia and related diagnoses as well as recommendation of risk reduction, dementia medication and non-pharmacological treatments. Principal investigators of the centres were psychiatrists, neurologists or geriatricians with six to thirteen years of experience in dementia care.

Interventions

The experimental intervention (COTiD) was designed to improve the patient's and the primary carer's daily functioning, and was based on an evidence-based treatment manual.[6, 19-23] COTiD consisted of ten occupational therapy sessions of one hour duration held over five weeks at each patient's home. In the diagnostic phase, comprising of 3 to 4 sessions, the occupational therapist explored (1) the patient's preferences and history of daily activities, (2) her or his ability to perform activities and to use compensatory strategies within the familiar environment, (3) the possibilities of modifying the patient's home, (4) the carer's activity preferences, problems in care giving, coping strategies and abilities to supervise and (5) the interaction between carer and patient. In a shared decision-making process during the goal setting session, the patient and the carer selected the one or two most meaningful activities out of a list of their preferences for daily activities to work on in occupational therapy. During the treatment phase of 5 to 6 sessions, the occupational therapist defined, together with the patient and the carer, more effective compensatory and environmental

strategies to adapt both the environment and the selected activities to the patient's habits and cognitive abilities. Patient and carer were taught how to use these suggested adaptations within strategies, activities and the environment in order to improve their performance of daily activities. In addition, the carer received practical and emotional support and was coached in effective supervision, problem solving and coping strategies by means of cognitive-behavioural interventions. Detailed description of the experimental intervention has been published elsewhere.[23]

For the German RCT, MG taught the content of the translated treatment manual to 14 study participant occupational therapists in 16 hours of seminars using presentation, videos and role play with feedback and group discussion. After the seminar and before the study started, they needed to complete a full treatment series for at least one pilot dyad of patient and carer. In the study phase, the interventionists spent about 20 hours per patient for a full treatment series including ten treatment sessions, travel, reports and multidisciplinary briefing. In Germany, a series of ten to thirty sessions is within the normal range of time that occupational therapists use for the treatment of older outpatients diagnosed with other diseases, such as stroke or rheumatoid arthritis.

The control group received one hour occupational therapy consultation (COTC) at the patient's home conducted by the same study interventionists. Based on material of the German Alzheimer Society, two occupational therapists with more than five years of experience in dementia care had prepared a leaflet of ten pages.[24-25] The semi-structured consultation was an explanation of 30 min of this leaflet and a talk of 30 min on individual problems that arose from patient's and carer's needs. This included encouragement to stay active in everyday life, to maintain social contacts and to use dementia services in the

region for which local addresses were listed in the leaflet. Occupational therapists were taught the control intervention within a 4-hour seminar. Consultations of 30 minutes up to one hour duration about such issues are common in German dementia care. Detailed description of the control intervention as well as means of quality assurance in experimental and control intervention has been published elsewhere.[26]

Outcome measures

The primary endpoint was the patients' change of daily functioning from baseline to follow-up time points at week 6, 16 and 26 measured with the performance scale of the Interview for Deterioration in Daily Living Activities in Dementia (IDDD).[27] This scale records carer rating of the patient's need of assistance in the performance of (1) washing oneself, (2) making tea or coffee, (3) dressing, (4) combing one's hair and brushing one's teeth, (5) eating, (6) using the toilet, (7) shopping, (8) using the telephone, (9) preparing a meal, (10) cleaning the house or doing minor repair work and (11) handling finances. Each item is rated never=0, seldom=1, sometimes=2, often=3 or always=4. The sum of scores ranged from 0 to 44. Higher scores indicated higher need for assistance. Since carer rating could not be 'masked', daily functioning was additionally evaluated by external raters fully 'blind' to the group assignment. They rated video tapes of a challenging daily living task and used the Perceive, Recall, Plan and Perform System of Task Analysis (PRPP).[28] For the PRPP, raters had to define single steps of the performed activity, and they identified any activity step in which errors of accuracy, omission, repetition or timing occurred. The number of activity steps rated as incorrectly performed was

divided by the total number of activity steps, resulting in an independence-score indicated in a percentage (100% = all steps are error-free).

Table 1: Measurements of secondary endpoints[26]

Endpoint	Measurement
Patient's initiative in daily activities	Interview for Deterioration in Daily Living Activities in Dementia (IDDD), initiative scale
Patient's mood	Cornell Scale for Depression in Dementia (CSDD)
Carer's mood	Center for Epidemiologic Depression Scale (CES-D)
Patient and carer's quality of life	Dementia Quality of Life Instrument (DQoL), overall item
	SF-12 physical
	SF-12 mental
Carer's interaction with patient	Sense of Competence Questionnaire (SCQ)
Care by primary carer	Resource Utilization in Dementia (RUD), hours per day
Nursing home placement	RUD, nights in nursing home (except respite care)
Harms	Number of adverse events
	RUD, nights in hospital

Secondary endpoints included mood, quality of life, resource utilisation and possible harms. Assessors 'blind' for the group assignment, completed measurements at the patient's home at baseline, week 6, 16 and 26 and arranged a postal survey of carer questionnaires at week 52. The assessors had a minimum of one year's professional experience with older or cognitively impaired people. They attended an introductory seminar of 8 hours. The complete assessment was applied during a 2-hour visit at each patient's home including (1) handing out and explaining the questionnaires to the carer, (2) interviewing the patient (DQoL and SF-12) in a separate room, (3) videotaping the patient and (4) receiving back the carer questionnaires, checking it and clarifying answers if necessary. Seminar description and means of quality management for assessment as well as detailed scheme and psychometric properties of all measurement instruments have been reported recently.[26]

All measurement instruments are validated and used in dementia research.[29-30] For the present study, we translated the IDDD into German according to high methodological standards with two independent forward and backward

translations, analysis of discrepancies and final agreement by discussion with all translators. There was no need to translate the PRPP because, because it was established in the Netherlands and applied by Dutch raters. There was one protocol amendment before recruitment started. The Assessment of Motor and Process Skills (AMPS) was replaced by the PRPP, because the AMPS was not available in the German language within the planned schedule.

Indicators of harm were defined as patient or carer death, number of patients with admission to hospital and number of nights in hospital. These indicators were recorded in interviews with the carer at intervals of 5 to 7 weeks over 52 weeks. Study sites had to report severe adverse events to the study centre immediately when each occurred. We did not assume a direct association between the defined harms and either the experimental or the control intervention. However, increased daily activities in the interventions group might have resulted in a higher risk of falls or accidents and thus may indirectly have led to more nights in hospital or in the worst case to death.

Sample size calculation

A sample size of 42 participants per group was calculated to be necessary to detect an effect size of f = 0.10 on the IDDD performance scale in an analysis of variance of two groups and four time points; using a two-sided 5% significance level, a power of 80%, and a correlation of 0.7 between the measurement time points [31]. According to the Dutch original RCT, we expected a dropout rate of 10% at week 16, which was extrapolated to 40% at week 52. A nine-month inclusion period was anticipated as necessary in order to recruit the 140 patients. Our assumed effect size of f = 0.10 is based on a group by time interaction and compatible to Cohen's d = 0.20, which corresponds to a small

effect size and any d over 0.8 is large. Although the Dutch original RCT found effect sizes of d = 2.4 in the IDDD performance scale at week 12, for this study the power was calculated much more conservatively.

This was because we (1) introduced an active control group, (2) investigated the programme effects under varying care conditions in seven centres with interventionists who were introduced in this new treatment and were far not as experienced as the Dutch study therapists and (3) we prolonged the follow up period. Interim analyses were not planned.

Randomisation and masking

The random allocation sequence was computer-generated with blocking by centre and groups of two persons, without stratification and in a ratio of 1:1 by a statistician from a distant site. After enrolment, study site physicians requested randomisation via e-mail. The statistician e-mailed the individual allocation to COTiD or COTC exclusively to the site interventionist and stored the allocation list at his distant site which was not available to any study site staff. The interventionist scheduled treatment sessions, faxed records to the distant coordinating study centre and kept all documents strictly separated from any other site staff. This was in order to avoid contamination. Since the numbers of home visits differed in the experimental and control groups, masking of patients and carers was not possible. However, study information did not include any preference for a special treatment 'arm'. Patients and carers were asked to give no information about their treatment package to assessors or study physicians. All study personal was 'blind' for group assignment, except the interventionists. Agreement between the assessors' estimation of group assignment and the actual group assignment was 61%, and thus slightly over the expected 50% of

agreement by chance. The procedure of external video rating ensured the full 'blinding' of the external raters for the PRPP primary outcome measure. Independent research assistants cleaned the videotapes of any hint of group assignment before they were rated by two Dutch raters not involved in the trial treatment. In order to establish the inter-rater reliability, we tested ten double ratings of the same video by the two raters and found an intra-class correlation coefficient of 0.9. Data analysts were not 'blind' for the group assignment. However, measurement time points and outcomes had been published before data were available for analysis [26] and any decision to remove patients from the analyses is reported in the present publication.

Statistical methods

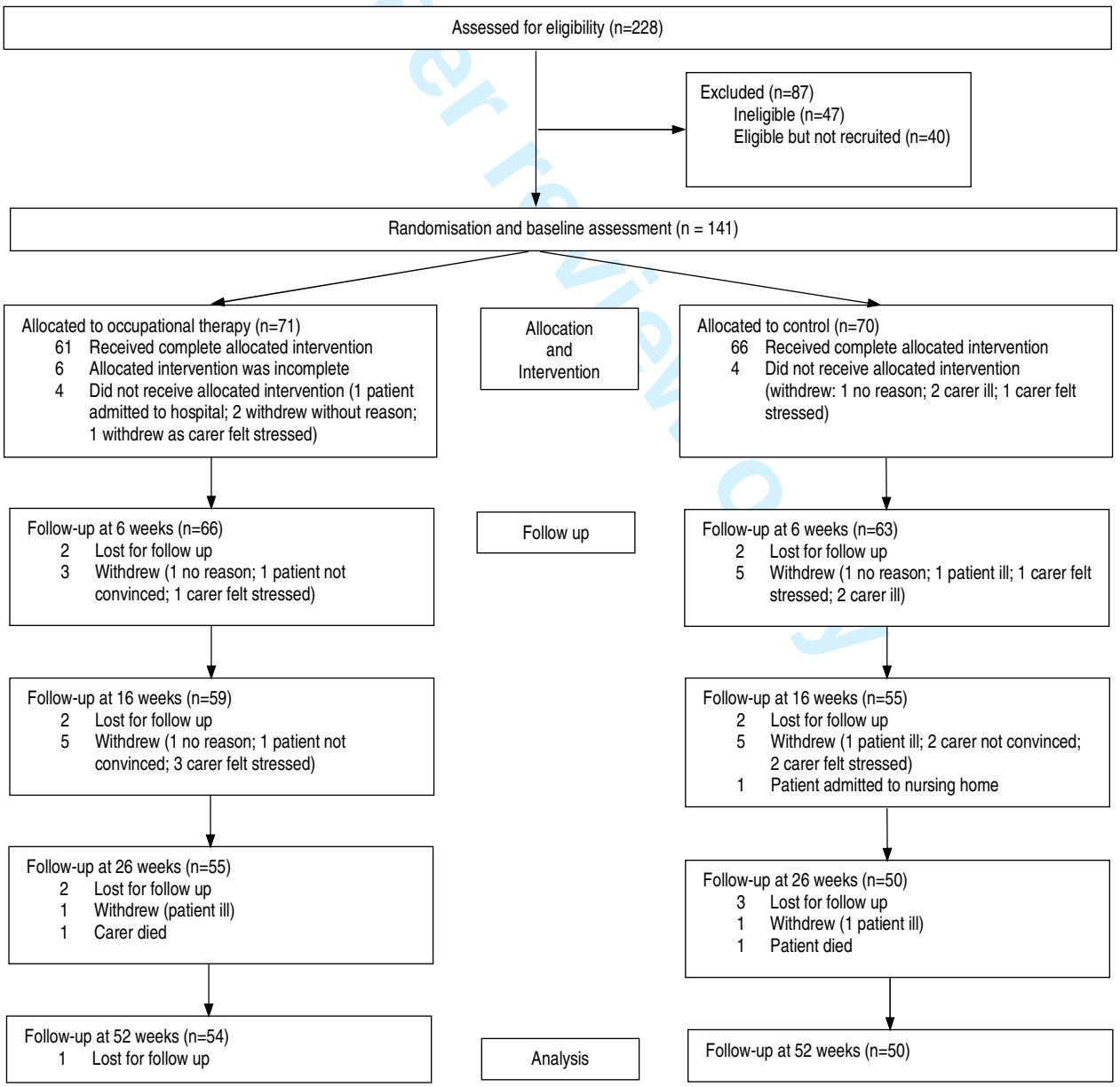
Data were entered via special MS Access entry masks automatically controlling for data plausibility. In addition, sections of entered data were checked for typing errors by hand, in order to ensure an error rate lower than 0.2%. The primary intention-to-treat analysis included all allocated participants with valid data whether they did or did not receive the complete intervention. For the IDDD and the PRPP measurements of the primary outcome, we performed a multivariate analysis of variance (MANOVA) with repeated measures with two groups and four measurement time points at baseline, week 6, 16 and 26. A univariate ANOVA with five measurement time points (+ postal assessment in week 52) was carried out for the secondary outcomes and the IDDD. We did not adjust for baseline values, because we found no marked group differences. In order to deal with missing data occurring not in the primary but in the secondary outcomes, we performed secondary intention-to-treat analyses with multiple data imputation using the Full Information Maximum Likelihood (FIML)

method.[32] We imputed data for all secondary outcome measurements and all time points using SPSS (version 19). In an additional analysis we used the linear mixed-effects models (MIXED) procedure in SPSS, which allows an unequal number of repetitions and a better handling of missing values.

All statistical tests were two-sided on an alpha level of 0.05. Subgroup analyses were not planned.

RESULTS

Figure 1: Flow of participants through the trial



Recruitment and participant flow

We prolonged the planned recruitment period from August 2008 to April 2009 by one additional month, up to May 2009. This was in order to recruit the intended sample size. The 52-week follow up was closed in May 2010. 141 participants were recruited (Berlin: 19, Bonn: 21, Freiburg: 26, Karlsruhe: 15, Mainz: 24, Marburg: 21, Tübingen: 15). The flow chart (Figure 1) shows that attrition following randomisation did not lead to significant group differences.

Baseline Characteristics

Randomisation did avoid imbalances in baseline characteristics (Table 2) and pre-treatment assessment data (Table 3) except in one item. Participants in the control group had more moderate to severe limitations in their financial situation (14% v 2%; p=0.027). Because the financial situation is not known as predictive factor for functional decline, we did not adjust for this imbalance.[33]

Table 2: Demographic and clinical characteristics

	COTiD			Control		
	analysed (n=54)	dropouts (n=17)	total (n=71)	analysed (n=50)	dropouts (n=20)	total (n=70)
Age, years (SD)	78.0 (7.1)	77.2 (8.5)	77.8 (7.4)	78.7 (6.0)	78.3 (7.1)	78.5 (6.3)
Sex, female	29 (54 %)	12 (71 %)	41 (58 %)	30 (60 %)	10 (50 %)	40 (57 %)
MMSE (SD)	20.4 (3.1)	19.0 (3.3)	20.2 (3.2)	20.7 (2.7)	20.3 (2.9)	20.7 (2.7)
GDS (SD)	6.9 (3.0)	5.6 (2.9)	6.5 (3.0)	5.2 (2.8)	6.1 (2.6)	5.5 (2.8)
Education						
no school graduation	2 (4 %)	1 (6 %)	3 (4 %)	1 (2 %)	0 (0 %)	1 (1 %)
middle school graduation (9 or 10 years)	41 (76 %)	13 (76 %)	54 (76 %)	37 (74 %)	15 (75 %)	52 (74 %)
high school graduation (12 or 13 years)	11 (20 %)	3 (18 %)	14 (20 %)	12 (24 %)	5 (25 %)	17 (24 %)
Financial situation as perceived by the carer						
no limitation	40 (74 %)	14 (82 %)	54 (76%)	38 (76 %)	13 (65 %)	51 (73 %)
minor limitation	12 (22 %)	1 (6 %)	13 (18 %)	3 (6 %)	3 (15 %)	6 (9 %)
moderate or severe limitation	1 (2 %)	2 (12 %)	3 (4 %)	7 (14 %)	4 (20 %)	11 (16 %)
no data	1 (2 %)	0 (0.0 %)	1 (1 %)	2 (4 %)	0 (0 %)	2 (3 %)
Primary carer						
Age, years (SD)	65.4 (16.3)	63.1 (14.0)	64.9 (15.7)	65.9 (13.0)	61.4 (17.4)	64.5 (14.4)
Sex, female	38 (70 %)	9 (53 %)	47 (66 %)	35 (70 %)	18 (90 %)	53 (76 %)
Spouse	32 (59 %)	8 (47 %)	40 (56 %)	31 (62 %)	9 (45 %)	40 (57 %)
Daughter or son (in law)	20 (37 %)	7 (41 %)	27 (38 %)	16 (32 %)	9 (45 %)	25 (36 %)
Others	2 (4 %)	2 (12 %)	4 (6%)	3 (6 %)	2 (10 %)	5 (7 %)
Living together (%)	41 (76 %)	11 (65 %)	52 (73%)	33 (66 %)	14 (70 %)	47 (67 %)

Intervention delivery

61 of 71 (86%) allocated patient-carer dyads received complete sessions in the COTiD group, 66 of 70 (94%) in the control group. In each group, 4 pairs were lost before intervention. Six patient-carer dyads in the COTiD had less than 10 sessions. Interventionists rated the delivery of 20 pre-defined treatment sub-processes, ranging from interviewing patient and carer to training of simplified activities or supporting the carer in supervision. They scored treatment delivery as 78% in the COTiD group and 80% in the control group. Interventionists rated the patient's adherence in 67 cases of the COTiD group, from 15 as hindering the delivery of treatment; 26 as neutral and 26 as facilitating. Rating criteria were the patient's cooperation during interview, goal setting and training; the daily changing mental capacity; collaboration with the carer; and the acceptance of innovations. Ratings of carers' adherence were 5 hindering; 15 neutral; and 47 facilitating. The carer adherence was assessed with regard to the cooperation during scheduling, interview, goal setting and training to supervise; the encouragement of the patient; the acceptance of support service; and the implementation of innovations. The adherence of the participants in the control group could not be rated, because interventionists had no further contact after the consultation.

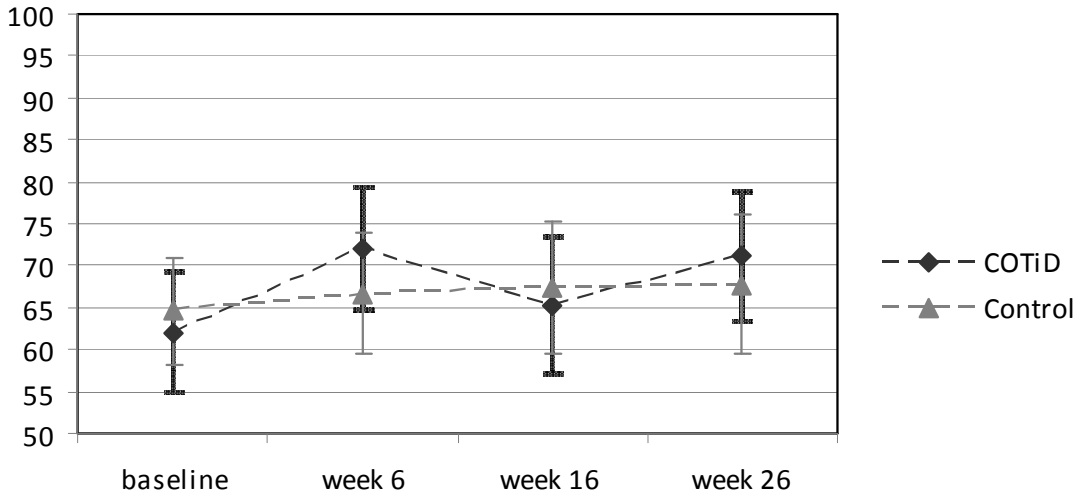
Outcomes

The MANOVA in 104 completers (COTiD: n=54; control: n=50) revealed no significant group time interaction effect in the primary outcome measurements of patients' daily functioning (Figures 2 and 3). Using the arcsine transform [34] for the PRPR percentage did not change results (original: p = 0.243; arcsine-transform: p = 0.216). An additional mixed models analysis of all randomised

patients (N=141) as recommended by Coley and colleagues [35] did also reveal no significant interactions for the IDDD (p=0.340) and the PRPP (p=0.785), details are provided as supplementary online material. Tables 3 and 4 show mean, standard deviation and group difference including 95%-confidence intervals of an ANOVA for all outcomes. Patients' daily functioning did not significantly change over 26 weeks in either the experimental and control group. In the postal 52 weeks follow up, the patients' need for assistance increased in both groups, and accordingly the carer's hours of care for basic ADL were higher. Two patients of the COTiD group were placed to nursing homes 33 and 44 weeks after baseline and one patient of the control group after 33 weeks.

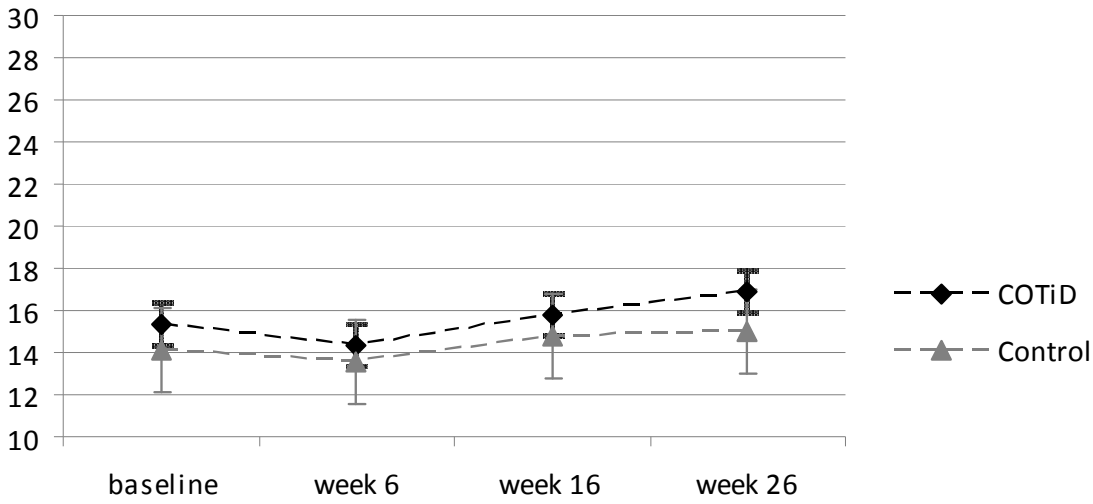
To address the problem of missing data in single measurement instruments, we performed a multiple data imputation. We calculated a MANOVA over four measurement time points for all primary and secondary outcomes for all 104 completers. Ten different data imputations did not reveal any significant time group interaction effects.

Figure 2: ADL task performance of Alzheimer patients following intense occupational therapy compared with a single session control intervention; means and 95%-confidence intervals of the PRPP independence scale (N=104 completers; range: 100=no errors to 0=all errors)



We also tested for study sites differences at baseline and found no significant differences in a MANOVA with the factors *study sites* and *intervention groups* (F(66, 432)=1.079, p=0.323). Furthermore, no study site effect was found in the primary outcome analysing IDDD and PRPP data of baseline, week 6, 16 and 26 (IDDD: F(6, 90)=0.724, p=0.631; PRPP: F(6, 90)=1.758, p=0.117).

Figure 3: Need for assistance in ADL of Alzheimer patients following intense occupational therapy compared with a single session control intervention; means and 95%-confidence intervals of the IDDD performance scale (N=104 completers; range: 0=never needed assistance to 44=always needed assistance)



Harms

There were no differences between intervention and control group, neither in the number of adverse events nor in their severity. The study site physicians judged all adverse events as unrelated to trial treatment or assessment contacts. In the total sample of all randomised participants (n=141), two deaths of patients (both in the control group) and one death of carer (in the COTiD group) were reported. In the COTiD group, 14 patients were admitted to hospital for an average of 15 nights; and 10 patients in the control group, for an average of 18 nights. There was no difference between the two groups in average number of nights admitted to hospital (F(1, 97)=2.785, p=0.1). All events were unrelated to the occupational therapy sessions.

Table 3: Patients' outcomes following intense occupational therapy compared with a single session control intervention in Alzheimer patients and their carers

	Sample size		Baseline		6 weeks			16 weeks			26 weeks			52 weeks (postal carer rating)		
	COTiD	Control	COTiD	Control	COTiD	Control	Group Diff.	COTiD	Control	Group Diff.	COTiD	Control	Group Diff.	COTiD	Control	Group Diff.
	N	N	mean (SD)	mean (SD)	mean (SD)	mean (SD)	mean [95%CI]	mean (SD)	mean (SD)	mean [95%CI]	mean (SD)	mean (SD)	mean [95%CI]	mean (SD)	mean (SD)	mean [95%CI]
PRPP independence 100 to 0*	54	50	62.1 (26.8)	64.6 (23.1)	72.0 (27.1)	66.7 (26.1)	-5.3 [-15.7 to 5.1]	65.2 (30.3)	67.4 (28.2)	2.2 [-9.2 to 13.6]	67.8 (30.1)	71.1 (29.4)	3.3 [-8.3 to 14.9]	-	-	-
IDDD performance 44 to 0*	54	50	15.4 (9.9)	14.1 (10.1)	14.3 (9.5)	13.5 (10.3)	-0.8 [-4.6 to 3.1]	15.8 (10.1)	14.8 (10.1)	-1.0 [-5.0 to 2.9]	16.9 (10.1)	15.0 (10.3)	-1.9 [-5.8 to 2.1]	21.1 (11.9)	18.7 (11.6)	-2.4 [-7.1 to 2.3]
IDDD initiative 0 to 36*	54	50	16.0 (8.7)	15.9 (8.4)	15.0 (8.1)	14.4 (8.7)	-0.6 [-3.9 to 2.7]	15.5 (8.2)	16.4 (9.1)	0.9 [-2.5 to 4.3]	16.1 (8.6)	16.7 (9.3)	0.6 [-2.9 to 4.1]	20.1 (9.9)	19.1 (10.1)	-1.0 [-5.0 to 3.0]
CSDD 0 to 38*	41	37	13.2 (7.6)	10.4 (6.3)	12.7 (7.8)	10.3 (6.1)	-2.4 [-5.5 to 0.8]	11.4 (7.2)	11.3 (6.6)	-0.1 [-3.2 to 3.0]	12.3 (6.8)	10.9 (6.3)	-1.3 [-4.3 to 1.6]	13.8 (6.7)	11.7 (6.7)	-2.0 [-5.1 to 1.0]
DQoL overall 5 to 1*	49	45	2.8 (0.8)	3.1 (0.8)	2.9 (0.9)	3.1 (0.6)	0.3 [-0.04 to 0.6]	2.8 (0.8)	3.1 (0.9)	0.3 [-0.02 to 0.6]	2.9 (0.8)	3.0 (0.8)	0.2 [-0.1 to 0.5]	-	-	-
SF-12 physical 100 to 0*	47	45	42.7 (10.0)	45.0 (9.4)	42.4 (11.4)	45.4 (11.0)	3.0 [-1.7 to 7.6]	41.8 (9.2)	45.1 (11.6)	3.3 [-1.0 to 7.6]	41.8 (11.3)	44.8 (11.1)	3.0 [-1.6 to 7.6]	-	-	-
SF-12 mental 100 to 0*	47	45	49.3 (11.0)	52.2 (9.3)	50.3 (12.3)	51.2 (9.9)	0.9 [-3.7 to 5.6]	51.8 (10.1)	52.8 (9.5)	1.1 [-3.0 to 5.1]	53.1 (9.0)	52.3 (10.6)	-0.8 [-4.9 to 3.3]	-	-	-

*Range: positive to negative, COTiD: Community Occupational Therapy in Dementia Programme, PRPP: Perceive, Recall, Plan and Perform System of Task Analysis, IDDD: Interview for Deterioration in Daily Living Activities in Dementia, CSDD: Cornell Scale for Depression in Dementia, DQoL: Dementia Quality of Life Instrument

Table 4: Carers' outcomes following intense occupational therapy compared with a single session control intervention in Alzheimer patients and their carers

	Sample size		Baseline		6 weeks			16 weeks			26 weeks			52 weeks (postal carer rating)		
	COTiD	Control	COTiD	Control	COTiD	Control	Group Diff.	COTiD	Control	Group Diff.	COTiD	Control	Group Diff.	COTiD	Control	Group Diff.
	N	N	mean (SD)	mean (SD)	mean (SD)	mean (SD)	mean [95%CI]	mean (SD)	mean (SD)	mean [95%CI]	mean (SD)	mean (SD)	mean [95%CI]	mean (SD)	mean (SD)	mean [95%CI]
SCQ 135 to 27*	50	47	100,8 (17,4)	107,0 (16,4)	103,0 (18,7)	108,6 (17,2)	5,7 [-1,6 to 12,9]	102,7 (18,2)	107,3 (17,8)	4,6 [-2,6 to 11,9]	104,7 (17,0)	107,9 (17,4)	3,2 [-3,7 to 10,1]	99,8 (17,8)	103,6 (18,6)	3,8 [-3,5 to 11,2]
CES-D 0 to 60*	52	46	12,1 (7,7)	11,3 (5,9)	10,6 (7,1)	10,9 (6,9)	0,3 [-2,6 to 3,1]	10,6 (7,7)	10,8 (7,3)	0,3 [-2,8 to 3,3]	10,0 (7,9)	10,0 (6,9)	0,0 [-3,0 to 3,0]	14,3 (10,3)	12,9 (7,7)	-1,4 [-5,1 to 2,3]
DQoL overall 5 to 1*	51	48	3,1 (0,8)	3,1 (0,7)	3,0 (0,6)	3,1 (0,7)	0,0 [-0,2 to 0,3]	3,1 (0,7)	3,0 (0,8)	0,0 [-0,3 to 0,3]	3,0 (0,7)	3,2 (0,8)	0,2 [-0,1 to 0,5]	2,8 (0,8)	3,0 (0,8)	0,2 [-0,1 to 0,5]
SF-12 physical 100 to 0*	40	38	42,4 (11,5)	43,5 (11,3)	45,8 (10,0)	44,0 (10,0)	-1,8 [-6,3 to 2,7]	44,1 (10,8)	46,2 (9,2)	2,1 [-2,5 to 6,6]	45,4 (10,7)	45,0 (10,5)	-0,4 [-5,2 to 4,4]	42,7 (10,7)	41,6 (11,7)	-1,0 [-6,1 to 4,0]
SF-12 mental 100 to 0*	40	38	50,9 (9,1)	49,8 (10,7)	50,6 (11,0)	50,0 (8,7)	-0,6 [-5,1 to 3,9]	52,3 (8,6)	48,5 (11,8)	-3,9 [-8,5 to 0,8]	50,2 (9,1)	50,1 (10,7)	0,0 [-4,5 to 4,4]	49,5 (11,9)	47,7 (10,7)	-1,7 [-6,9 to 3,4]
Basic ADL-care by primary carer (hours per day)	52	43	0.5 (0.8)	0.8 (1.3)	0.8 (1.8)	0.9 (1.4)	0.1 [-0.5 to 0.8]	0.7 (1.2)	1.0 (1.4)	0.2 [-0.3 to 0.7]	0.8 (1.2)	1.0 (1.5)	0.2 [-0.3 to 0.8]	1.6 (2.2)	1.8 (2.2)	0.1 [-0.8 to 1.0]
IADL-care by primary carer (hours per day)	52	45	2.1 (2.7)	2.5 (2.6)	1.9 (2.5)	2.9 (3.0)	1.1 [-0.04 to 2.2]	2.3 (2.6)	2.9 (2.8)	0.6 [-0.5 to 1.7]	2.2 (2.2)	3.2 (2.8)	1.0 [0.0 to 2.0]	2.7 (2.2)	3.2 (2.8)	0.5 [-0.6 to 1.6]

*Range: positive to negative, COTiD: Community Occupational Therapy in Dementia Programme, SCQ: Sense of Competence Questionnaire, CES-D: Center for Epidemiologic Depression Scale, DQoL: Dementia Quality of Life Instrument, ADL: Activities of Daily Living, IADL: Instrumental Activities of Daily Living

DISCUSSION

In the results of this study, a ten-session community occupational therapy in dementia programme (COTiD) was found to be no more beneficial than a one-session consultation concerning short- and middle-term effects on patients' daily functioning. In both groups, the need for assistance in basic and instrumental activities of daily living and the performance of a self-chosen daily living task remained stable up to six months after baseline. No significant group differences could be found on secondary outcomes, which were quality of life and mood of patient and primary carer; patient's initiative in daily activities; carer's sense of competence in interaction with the patient; carer's hours of daily care; and the patient's nursing home placement. There were no adverse events associated with experimental or control intervention.

Limitations

Despite an elaborate study design, there are some limitations in this study. We analysed only 104 completer dyads from 141 recruited pairs (74 %). However, (1) baseline data of completers and non-completers did not show imbalance; (2) dyads were maintained, whose data were valid, and for whom treatment was intended but not received in the complete ITT-analysis; (3) an additional mixed model analysis of all randomised patients did also not reveal significant differences; and (4) the analysis of the reduced patient sample with valid data did not show even a tendency towards significant group differences. Thus the hypothesis of group differences must be rejected, because the analysis of completers usually favours results in the direction of group differences.

A second shortcoming was that following the common introductory seminar the start of the study differed amongst the sites due to different time lines in administrative

matters and approval of the local ethic commissions. Therefore, a common repetition seminar for the interventionists could not be arranged after the pilot training. This may have led to some heterogeneity in the intervention, especially because in Germany eleven newly introduced interventionists performed the treatment compared to two experienced experts in the original Dutch trial. We addressed this problem with feedback on videos of treatment sessions the interventionists sent in. Furthermore, we arranged telephone supervision on demand.

We consider the contamination of the control intervention with knowledge from the experimental intervention to be low, because any specific intervention such as activity selection, simplification or training was precluded by the limited time to carry out the control intervention.

Comparison

The Dutch RCT on the COTiD with waiting-control-group design showed large effect sizes in the IDDD performance scale at six and twelve weeks after baseline (d=2.3 and 2.4, respectively).[6] Since the Dutch COTiD programme demonstrated such highly positive effects, we judged it as appropriate to conduct not an identical replication, but a twofold transfer from the source to the target country and from a mono-centre RCT design with high expertise of interventionists to a pragmatic multi-centre RCT design in routine care [35]. The Dutch and the German sample did not differ remarkably in cognition at baseline (MMSE: 19 v 20), but did differ in the need of assistance (IDDD performance: 24 v 15). The German patients showed a low need of assistance at the beginning of the study. This was comparable to the IDDD values of the Dutch patients at the end of the treatment. This may have caused a floor effect on the IDDD. Another mono-centre RCT in the USA compared community occupational therapy and a less intensive telephone consultation in patients with probable dementia (MMSE: 13).[37] The authors found a small effect size in daily

functioning (d=0.21). The initial need of assistance in both studies was higher than in the German sample. A systematic review of community programmes in dementia [38] reported one study on exercise and behavioural management with beneficial effects on daily functioning of patients with moderate dementia (MMSE: 17); one trial on occupational therapy with heterogeneous effects; and two studies on occupational therapy and music therapy with no significant effects. A current German health technology assessment on non-drug therapies in Alzheimer's disease did not identify further community occupational therapy trials [39]. The comparison of community intervention trials reveals that study samples with a lower MMSE and a higher need of assistance benefit more than those with initial higher cognitive and daily functioning. Similarly, a standardized synopsis of ADL outcomes in pharmacological dementia trials indicated that samples with an MMSE between 17 and 10 benefit most in ADL while samples with higher MMSE scores showed less effects.[40] However, different baseline scores of cognitive and daily functioning alone cannot explain the major difference between the findings in this German study and the positive results of the Dutch RCT. Detailed process evaluation and exploratory analyses of the study data might show whether variations in study site context and treatment performance influenced the intervention's effectiveness.

Clinical and research implications

Published evidence for the effectiveness of community occupational therapy in dementia is heterogeneous as indicated by a Dutch trial with large positive effects on daily functioning; a few USA trials with no or small positive effects on ADL and this German study showing that ten sessions were not superior to one consultation. A preventative one-session consultation might be hypothesised as beneficial for people with mild dementia and an improved 10-session programme more specifically adapted to the German health care system as beneficial for dementia patients with

moderate need of assistance in ADL, as was shown in the Dutch study in which most people with dementia had moderate to high need for assistance at baseline.

Although we had expected smaller effect sizes than in the Dutch original trial due to changed study design with (1) the introduction of an active control group, (2) a variance in treatment performance in several centres, (3) a prolonged follow up time and (4) rigorous reduction of the analysed sample to participants with valid data, it remains surprising that significant group difference could not be found in any of the primary or secondary outcomes.

This study has shown that careful cross-national comparisons are greatly needed, especially in complex interventions, before they can be considered evidence based and implemented effectively in other health care systems. Therefore, further analyses must investigate the role of interventionists' expertise and treatment performance, and the role of participants' needs and utilisation of health care resources, before conclusions on international implementation of this intense occupational therapy intervention can be drawn.

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Competing interests: SVR, RL, KS, JB, AF, MG and MVD non declared. FJ membership in DSMB of AC-immune; payment for lectures from Pfizer, Esai and Novartis. BM payment for lectures from various pharmaceutical companies. RD consultancy, grants, payment for lectures, patents, meeting

expenses from various pharmaceutical companies; royalities and patents from University of Marburg. GE grants from AC-immune and Janssen-AL. MOR consultancy for Jansen-Cilag and Numico. MH grants from Wyeth, Pfizer and Medivation, payment for lectures from Wyeth, Pfizer and Merz.

Data sharing statement: Complete data sets can be provided on request for research fellows in scope of collaborative projects and publications.

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Supplementary material: Results of the linear mixed-effects models procedure.

Table I: Descriptive results

	N	Mean (SD)	Missings (%)
PRPP			
Week 0	107	63,1 (25,2)	34 (24)
Week 6	107	69,8 (26,4)	34 (24)
Week 16	107	66,5 (29,0)	34 (24)
Week 26	107	69,5 (29,4)	34 (24)
Week 52	not applied		
IDDD performance			
Week 0	141	14,8 (10,2)	0 (0)
Week 6	131	14,5 (10,3)	10 (7)
Week 16	120	15,4 (10,3)	21 (15)
Week 26	116	16,4 (10,5)	25 (18)
Week 52	111	20,2 (12,3)	30 (21)

PRPP: Perceive, Recall, Plan and Perform System of Task Analysis, range: 100=no errors to 0=all errors
IDDD: Interview for Deterioration in Daily Living Activities in Dementia, performance scale, range: 0=never needed assistance to 44=always needed assistance

Table II: F-Values

	F-Value	p
PRPP		
Constant term	417.210	<0.001
Repeated measure	2.048	0.154
Group	0.041	0.840
Group * repeated measure	0.074	0.785
IDDD performance		
Constant term	181.379	<0.001
Repeated measure	0.827	0.364
Group	12.543	<0.001
Group * repeated measure	0.911	0.340

CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	3
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	5+6
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	7+8
	2b	Specific objectives or hypotheses	8
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	8
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	9
Participants	4a	Eligibility criteria for participants	9
	4b	Settings and locations where the data were collected	9+10
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	10+11+12
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	12+13+14
	6b	Any changes to trial outcomes after the trial commenced, with reasons	13
Sample size	7a	How sample size was determined	14
	7b	When applicable, explanation of any interim analyses and stopping guidelines	14
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	14
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	14
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	15
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	15
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those	15

		assessing outcomes) and how	
	11b	If relevant, description of the similarity of interventions	10+11
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	15+16
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	16
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	17
	13b	For each group, losses and exclusions after randomisation, together with reasons	17
Recruitment	14a	Dates defining the periods of recruitment and follow-up	16
	14b	Why the trial ended or was stopped	16
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	18
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	19+22
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	22
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	19+20
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	21
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	23+24
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	24+25
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	24+25
Other information			
Registration	23	Registration number and name of trial registry	9
Protocol	24	Where the full trial protocol can be accessed, if available	9
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	26

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.