



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

Journal:	<i>BMJ Open</i>
Manuscript ID:	bmjopen-2011-000096
Article Type:	Research
Date Submitted by the Author:	08-Feb-2011
Complete List of Authors:	Voigt-Radloff, Sebastian; University Hospital Freiburg, Centre of Geriatric Medicine and Gerontology Freiburg Graff, Maud; Radboud University Nijmegen Medical Centre, Alzheimer Centre Nijmegen Leonhart, Rainer; University of Freiburg, Department of Social Psychology and Methodology Schornstein, Katrin; University of Freiburg, Department of Social Psychology and Methodology Jessen, Frank; University of Bonn, Department of Psychiatry and Psychotherapy Bohlken, Jens; Private Practice for Neurology, Psychiatry and Psychotherapy Metz, Brigitte; Centre of Geriatric Medicine and Geriatric Clinic at Diakonissenkrankenhaus Karlsruhe-Rüppurr Fellgiebel, Andreas; University Medical Center Mainz, Department of Psychiatry and Psychotherapy Dodel, Richard; Philipps-University Marburg, Department of Neurology Eschweiler, Gerhard; Eberhard-Karls University Tuebingen, Department of Psychiatry and Psychotherapy Vernooij-Dassen, Myrra; Radboud University Nijmegen Medical Centre, Alzheimer Centre Nijmegen Olde Rikkert, Marcel; Radboud University Nijmegen Medical Centre, Alzheimer Centre Nijmegen Hüll, Michael; University Hospital Freiburg, Centre of Geriatric Medicine and Gerontology Freiburg
Subject Heading:	Neurology
Keywords:	Dementia < NEUROLOGY, Quality in health care < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, REHABILITATION

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60



SCHOLARONE™
Manuscripts

For peer review only

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

Sebastian Voigt-Radloff, Maud Graff, Rainer Leonhart, Katrin Schornstein, Frank Jessen, Jens Bohlken, Brigitte Metz, Andreas Fellgiebel, Richard Dodel, Gerhard Eschweiler, Myrra Vernooij-Dassen, Marcel Olde Rikkert, Michael Hüll

Department of Occupational Therapy, Centre of Geriatric Medicine and Gerontology Freiburg, University Hospital Freiburg, Lehener Str. 88, 79106 Freiburg, Germany Sebastian Voigt-Radloff *scientific researcher in allied healthcare research*

Alzheimer Centre Nijmegen, Scientific Institute for Quality in Health Care and Dept of Rehabilitation-Occupational Therapy, Radboud University Nijmegen Medical Centre, PO Box 9101, 6500 HB Nijmegen, The Netherlands Maud Graff *senior researcher in allied healthcare research and research on psychosocial interventions in dementia*

Department of Social Psychology and Methodology, University of Freiburg, Engelbergerstr. 41, 79085 Freiburg, Germany Rainer Leonhart *senior researcher in statistics and psychology*

Department of Social Psychology and Methodology, University of Freiburg, Engelbergerstr. 41, 79085 Freiburg, Germany Katrin Schornstein *researcher in statistics and psychology*

Department of Psychiatry and Psychotherapy, University of Bonn, Sigmund-Freud-Str. 25, 53105 Bonn, Germany Frank Jessen *professor in psychiatry*

Private Practice for Neurology, Psychiatry and Psychotherapy, Klosterstr. 34, 13581 Berlin, Germany Jens Bohlken *clinical psychiatrist*

Centre of Geriatric Medicine and Geriatric Clinic at Diakonissenkrankenhaus Karlsruhe-Rüppurr, Diakonissenstr. 28, 76199 Karlsruhe, Germany Brigitte Metz *clinical geriatrician*

Department of Psychiatry and Psychotherapy, University Medical Center Mainz, Untere Zahlbacher Str. 8, 55131 Mainz, Germany Andreas Fellgiebel *clinical psychiatrist*

Department of Neurology, Philipps-University Marburg, Rudolf-Bultmannstr. 8, 35039 Marburg, Germany Richard Dodel *professor in neurology*

Department of Psychiatry and Psychotherapy, Eberhard-Karls University Tuebingen, Osianderstr. 24, 72076 Tübingen Germany Gerhard Eschweiler *professor in psychiatry*

Alzheimer Centre Nijmegen, Scientific Institute for Quality in Health Care, Radboud University Nijmegen Medical Centre, Kalorama Foundation, PO Box 9101, 6525 JV Nijmegen, The Netherlands Myrra Vernooij-Dassen *professor in psychosocial interventions in frail elderly*

Alzheimer Centre Nijmegen, Department of Geriatrics, Radboud University Nijmegen Medical Centre, PO Box 9101, 6500 HB Nijmegen, The Netherlands Marcel Olde Rikkert *professor in geriatrics*

Section of Gerontopsychiatry and Neuropsychology, Centre of Geriatric Medicine and Gerontology Freiburg, University Hospital Freiburg, Lehener Str. 88, 79106 Freiburg, Germany Michael Hüll *professor in psychiatry*

Correspondence to: sebastian.voigt@uniklinik-freiburg.de

Keywords: Alzheimer Disease – Occupational Therapy – Randomized Controlled Trial

Words: 3,913

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

1
2
3 improving the patient's physical and social environment and by tailoring the
4
5 intervention to patient's capability.[12-15]
6
7

8 Until October 2010, there was no systematic review on community occupational
9
10 therapy for people with Alzheimer's disease but two research groups had
11
12 conducted RCTs in this subject. In the USA study, occupational therapy
13
14 demonstrated beneficial effects on patients' challenging behaviour but not on
15
16 ADL. No information on adverse events were given.[14, 16-18] In the
17
18 Netherlands, occupational therapy tailored to the needs of patients and carers
19
20 showed benefits on the patient's ADL, mood, health status and quality of life
21
22 and on the carer's sense of competence, mood, quality of life and costs of
23
24 informal care. No adverse events were reported in either intervention or control
25
26 group.[6, 19-20]
27
28
29
30

31 In the current randomised trial we tested the hypothesis that the Dutch ten-
32
33 session Community Occupational Therapy in Dementia Programme (COTiD)
34
35 would significantly better improve or stabilise the functioning in everyday life of
36
37 people with mild or moderate dementia than a one-session Community
38
39 Occupational Therapy Consultation (COTC). Secondary research questions
40
41 were whether these interventions show a difference in their effect on patient's
42
43 and primary carer's quality of life and mood; on the carer's sense of
44
45 competence in the interaction with the patient; and on long-term nursing home
46
47 placements.
48
49
50
51
52
53
54

55 **METHODS**

56 **Design**

57
58 In order to evaluate the superiority of COTiD, we used a seven-centre single-
59
60 blind, active-controlled design with a 1:1 randomisation for two parallel groups.

1
2
3 There was no modification in design or eligibility criteria from the study protocol
4 available at <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2761388/>. The study
5
6 was registered at the German register of clinical trials, which is connected to the
7
8 International Clinical Trials Registry Platform (<http://apps.who.int/trialsearch/> =>
9
10 DRKS00000053).
11
12
13
14
15
16

17 **Participants and Setting**

18
19 Patients were eligible to participate in the study if they had mild to moderate
20 dementia (MMSE 14-24) and were diagnosed as having Alzheimer's disease or
21
22 mixed type dementia, according to ICD-10 criteria, by physicians with more than
23
24 five years of experience in dementia diagnosis. Participants had to dwell in the
25
26 community either together with their primary carer or with involvement of a carer
27
28 providing care at least twice a week. Patients with a major need of physical
29
30 nursing care and a score above 12 on the 30-items Geriatric Depression Scale
31
32 were excluded. Unstable medical conditions or severe behavioural
33
34 disturbances, which did not allow participation in the study as judged by the
35
36 study physicians were criteria for exclusion as well as for discontinuation. Stop
37
38 criteria were death of patient or primary carer or a long-term nursing home
39
40 placement of the patient during the treatment phase. The patient gave written
41
42 informed consent and the carer assented in written form to join and support the
43
44 treatment procedures.
45
46
47
48
49
50
51

52
53 Patients were recruited from five outpatient memory centres at university
54
55 hospitals (in Bonn, Freiburg, Mainz, Marburg and Tübingen); one municipal
56
57 hospital in Karlsruhe specialising in geriatric medicine and one neurological
58
59 private practice in Berlin specialising in neuropsychiatry and collaborating with
60
an occupational therapy private practice. The seven participating centres are

1
2
3 located throughout Germany in urban regions with catchment areas from about
4
5 70,000 to 700,000 inhabitants. They had all provided outpatient dementia care
6
7 for three to fifteen years. Their standard service comprised diagnostic work-up
8
9 for dementia and related diagnoses as well as recommendation of risk
10
11 reduction, dementia medication and non-pharmacological treatments. Principal
12
13 investigators of the centres were psychiatrists, neurologists or geriatricians with
14
15 six to thirteen years of experience in dementia care.
16
17
18
19
20
21

22 **Interventions**

23
24 The experimental intervention (COTiD) was designed to improve the patient's
25
26 and the primary carer's daily functioning, and was based on an evidence-based
27
28 treatment manual.[6, 19-23] COTiD consisted of ten occupational therapy
29
30 sessions of one hour duration held over five weeks at each patient's home. In
31
32 the diagnostic phase, comprising of 3 to 4 sessions, the occupational therapist
33
34 explored (1) the patient's preferences and history of daily activities, (2) her or
35
36 his ability to perform activities and to use compensatory strategies within the
37
38 familiar environment, (3) the possibilities of modifying the patient's home, (4) the
39
40 carer's activity preferences, problems in care giving, coping strategies and
41
42 abilities to supervise and (5) the interaction between carer and patient. In a
43
44 shared decision-making process during the goal setting session, the patient and
45
46 the carer selected one or two most meaningful activities out of a list of their
47
48 preferences for daily activities to work on in occupational therapy. During the
49
50 treatment phase of 5 to 6 sessions, the occupational therapist defined together
51
52 with the patient and the carer more effective compensatory and environmental
53
54 strategies to adapt both the environment and the selected activities to the
55
56 patient's habits and cognitive abilities. Patient and carer were taught how to use
57
58
59
60

1
2
3 these suggested adaptations within strategies, activities and the environment, in
4
5 order to improve their performance of daily activities. In addition, the carer
6
7 received practical and emotional support and was coached in effective
8
9 supervision, problem solving and coping strategies by means of cognitive-
10
11 behavioural interventions. Detailed description of the experimental intervention
12
13 has been published elsewhere.[23]
14
15

16
17 For the trial in Germany, MG taught the content of the translated treatment
18
19 manual to 14 study participant occupational therapists in 16 hours of seminars
20
21 using presentation, videos and role play with feedback and group discussion.
22
23 After the seminar and before the study started, they needed to complete a full
24
25 treatment series for at least one pilot dyad of patient and carer. In the study
26
27 phase, the interventionists spent about 20 hours per patient for a full treatment
28
29 series including ten treatment sessions, travel, reports and multidisciplinary
30
31 briefing. In Germany, a series of ten to thirty sessions is within the normal range
32
33 of time that occupational therapists use for the treatment of older outpatients
34
35 diagnosed with other diseases, such as stroke or rheumatoid arthritis.
36
37

38
39 The control group received one hour occupational therapy consultation (COTC)
40
41 at the patient's home conducted by the same study interventionists. Based on
42
43 material of the German Alzheimer Society, two occupational therapists with
44
45 more than five years of experience in dementia care had prepared a leaflet of
46
47 ten pages.[24-25] The semi-structured consultation was half a talk on individual
48
49 problems that arose from patient's and carer's needs and half an hour
50
51 explanation of this leaflet. This included encouragement to stay active in
52
53 everyday life, to maintain social contacts and to use dementia services in the
54
55 region for which local addresses were listed in the leaflet. Occupational
56
57 therapists were taught the control intervention within a 4-hours seminar.
58
59
60

1
2
3 Consultations of 30 minutes up to one hour duration about such issues are
4
5 common in German dementia care. Detailed description of the control
6
7 intervention as well as means of quality assurance in experimental and control
8
9 intervention has been published elsewhere.[26]
10
11
12
13

14 **Outcome measures**

15
16 The primary endpoint was the patients' change of daily functioning from
17
18 baseline to follow-up time points at week 6, 16 and 26 measured with the
19
20 performance scale of the Interview for Deterioration in Daily Living Activities in
21
22 Dementia (IDDD).[27] This scale records carer rating of the patient's need of
23
24 assistance in the performance of (1) washing oneself, (2) making tea or coffee,
25
26 (3) dressing, (4) combing one's hair and brushing one's teeth, (5) eating, (6)
27
28 using the toilet, (7) shopping, (8) using the telephone, (9) preparing a meal, (10)
29
30 cleaning the house or doing minor repair work and (11) handling finances. Each
31
32 item is rated never=0, seldom=1, sometimes=2, often=3 or always=4. The sum
33
34 of scores ranged from 0 to 44. Higher scores indicated higher need for
35
36 assistance. Since carer rating could not be masked, daily functioning was
37
38 additionally evaluated by external assessors fully masked to the group
39
40 assignment. They rated video tapes of a challenging daily living task and used
41
42 the Perceive, Recall, Plan and Perform System of Task Analysis (PRPP).[28]
43
44 For the PRPP, assessors had to define single steps of the performed activity,
45
46 and they identified any activity step in which errors of accuracy, omission,
47
48 repetition or timing occurred. The number of activity steps rated as incorrectly
49
50 performed was divided by the total number of activity steps, resulting in an
51
52 independence-score indicated in a percentage (100% = all steps are error-free).
53
54
55
56
57
58
59
60

Table 1: Measurements of secondary endpoints²⁶

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.

1
2
3 Indicators of harm were defined as patient or carer death, number of patients
4 with admission to hospital and number of nights in hospital. These indicators
5 were recorded in interviews with the carer in intervals of 5 to 7 weeks over 52
6 weeks. Study sites had to report severe adverse events to the study centre
7 immediately when each occurred.
8
9
10
11
12
13
14
15
16

17 **Sample size calculation**

18
19 A sample size of 42 participants per group was calculated to be necessary to
20 detect an effect size of $f = 0.10$ on the IDDD performance scale in an analysis of
21 variance of two groups and four time points, using a two-sided 5% significance
22 level, a power of 80%, and a correlation of 0.7 between the measurement time
23 points. According to the Dutch original RCT, we expected a dropout rate of 10%
24 at week 16, which was extrapolated to 40% at week 52. In sum, we anticipated
25 a 9-month inclusion period to recruit the necessary number of 140 patients.
26 Although the Dutch original RCT found effect sizes of $d\text{-value}=2.4$ in the IDDD
27 performance scale at week 12, we calculated the power much more
28 conservatively. This was because we (1) introduced an active control group, (2)
29 investigated the programme effects under varying care conditions in seven
30 centres with interventionists who were introduced in this new treatment and
31 were far not as experienced as the Dutch study therapists and (3) we prolonged
32 the follow up period. Interim analyses were not planned.
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54

55 **Randomisation and masking**

56
57 The random allocation sequence was computer-generated with blocking by
58 centre and groups of two persons, without stratification and in a ratio of 1:1 by a
59 statistician from a distant site. After enrolment, study site physicians requested
60

1
2
3 randomisation via e-mail. The statistician e-mailed the individual allocation to
4
5 COTiD or COTC exclusively to the site interventionist and stored the allocation
6
7 list at his distant site not available to any study site staff. The interventionist
8
9 scheduled treatment sessions, faxed records to the distant coordinating study
10
11 centre and kept all documents strictly separated from any other site staff, in
12
13 order to avoid contamination. Since the numbers of home visits differed in the
14
15 experimental and control groups, masking of patients and carers was not
16
17 possible. However, study information did not include any preference for a
18
19 special treatment arm. Patients and carers were asked to avoid any talks about
20
21 the treatment with any study staff, except the interventionist. The procedure of
22
23 external video rating ensured the full 'blinding' of the assessors. Independent
24
25 research assistants cleaned the videotapes from any hint of group assignment,
26
27 before they were rated by Dutch assessors not involved in the trial treatment.
28
29 Agreement between the actual and the assessor estimation of group
30
31 assignment was 61%, and thus slightly over the expected 50% agreement by
32
33 chance. Data analysts were not blinded to the group assignment. However,
34
35 measurement time points and outcomes had been published before data were
36
37 available for analysis [26] and any decision to remove patients from the
38
39 analyses is reported here.
40
41
42
43
44
45
46
47
48
49

50 **Statistical methods**

51
52 Data were entered via special MS Access entry masks automatically controlling
53
54 for data plausibility. In addition, sections of entered data were checked for
55
56 typing errors by hand, in order to ensure an error rate lower than 0.2%.
57
58

59
60 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

1
2
3 primary outcomes, we performed a multivariate analysis of variance (MANOVA)
4
5 with repeated measures with two groups and four measurement time points at
6
7 baseline, week 6, 16 and 26. In this primary analysis, we did not adjust for
8
9 baseline values or any other co-variate. A univariate ANOVA with five
10
11 measurement time points (+ week 52) was carried out for the secondary
12
13 outcomes.
14
15

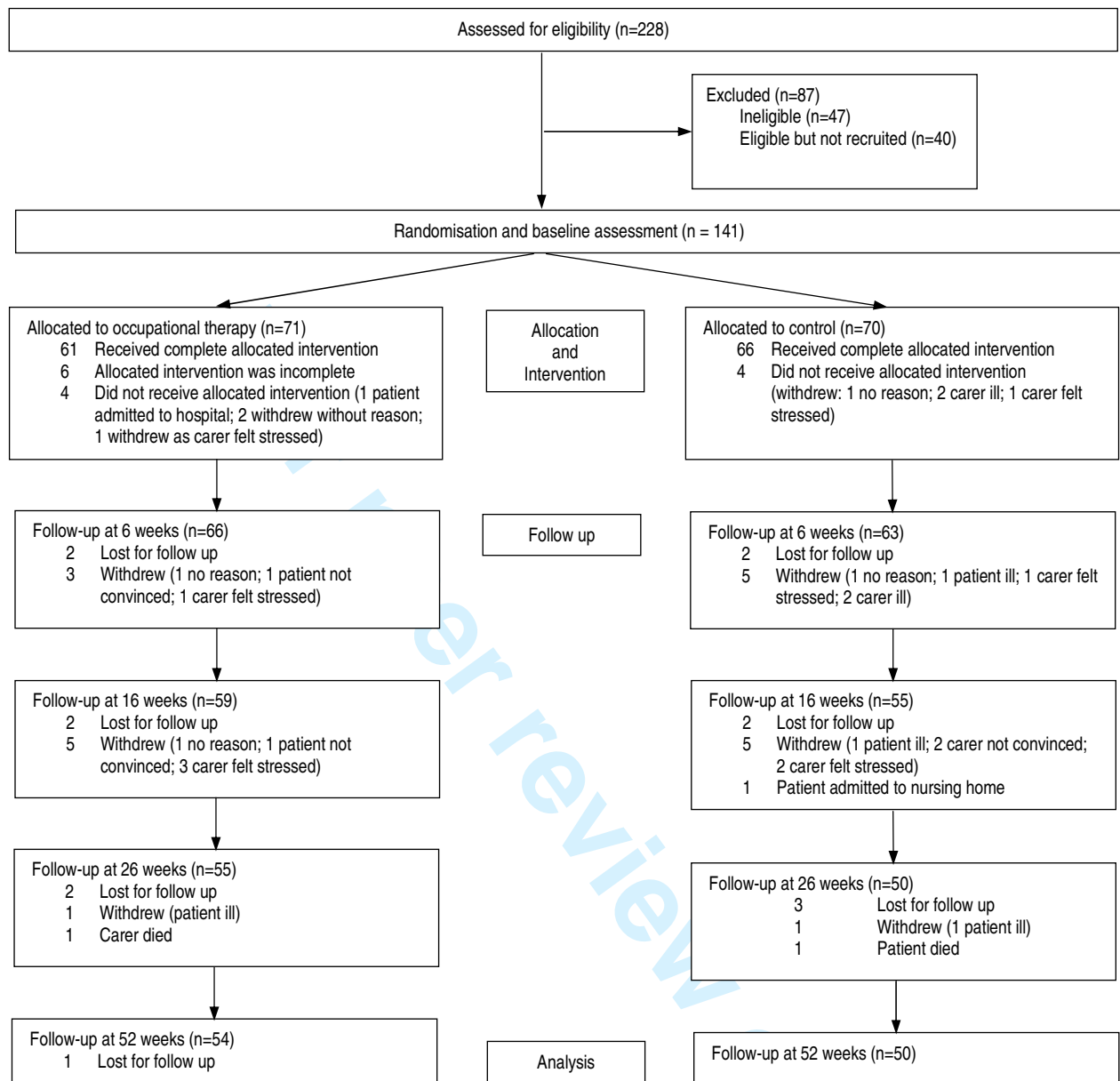
16
17 In order to deal with missing data, we performed secondary intention-to-treat
18
19 analyses with multiple data imputation using the Full Information Maximum
20
21 Likelihood (FIML) method.[31] All statistical tests were two-sided on an alpha
22
23 level of 0.05. Subgroup analyses were not planned.
24
25
26
27

28 29 **RESULTS**

30 31 **Recruitment and participant flow**

32
33 We prolonged the planned recruitment period from August 2008 to April 2009
34
35 for one additional month up to May 2009. This was in order to recruit the
36
37 intended sample size. The 52-week follow up was closed in May 2010. 141
38
39 participants were recruited. The flow chart (Figure 1) shows that attrition
40
41 following randomisation did not lead to significant group differences.
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

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

1
2
3 as 78% in the COTiD arm and 80% in the control group. Interventionists rated
4 the patient's adherence in 67 cases of the COTiD group, from 15 as hindering
5 the delivery of treatment; 26 as neutral and 26 as facilitating. Ratings of carers'
6 adherence were 5 hindering; 15 neutral; and 47 facilitating. The adherence of
7 the participants in the control group could not be rated, because interventionists
8 had no further contact after the consultation. Carers and patients were asked to
9 rate their satisfaction with treatment on a 5-point Likert-scale with 1=very
10 content and 5=very discontent. Mean (SD) satisfaction scores of 63 carers in
11 the COTiD group were 1.4 (0.5) and scores of 44 patients were 1.7 (0.6). 62
12 carers in the control group scored similarly: 1.7 (0.5), 34 patients scored 2.0
13 (0.7), respectively.
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31

32 **Outcomes**

33
34 The MANOVA in 104 completers (COTiD: n=54; control: n=50) revealed no
35 significant group time interaction effect in any of the outcome data, neither in
36 primary outcome measurements of patients' daily functioning (Figures 2 and 3)
37 nor in secondary outcomes of patients or carers (results not shown). Tables 3
38 and 4 show mean, standard deviation and group difference including 95%-
39 confidence intervals for all outcomes. Patients' daily functioning did not
40 significantly change over 26 weeks in either the experimental and control group.
41 In the 52 weeks follow up, the patients' need for assistance increased in both
42 groups, and accordingly the carer's hours of care for basic ADL were higher.
43 Two patients of the COTiD group were placed to nursing homes 33 and 44
44 weeks after baseline and one patient of the control group after 33 weeks.
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60 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=errorless to 0=errorful)

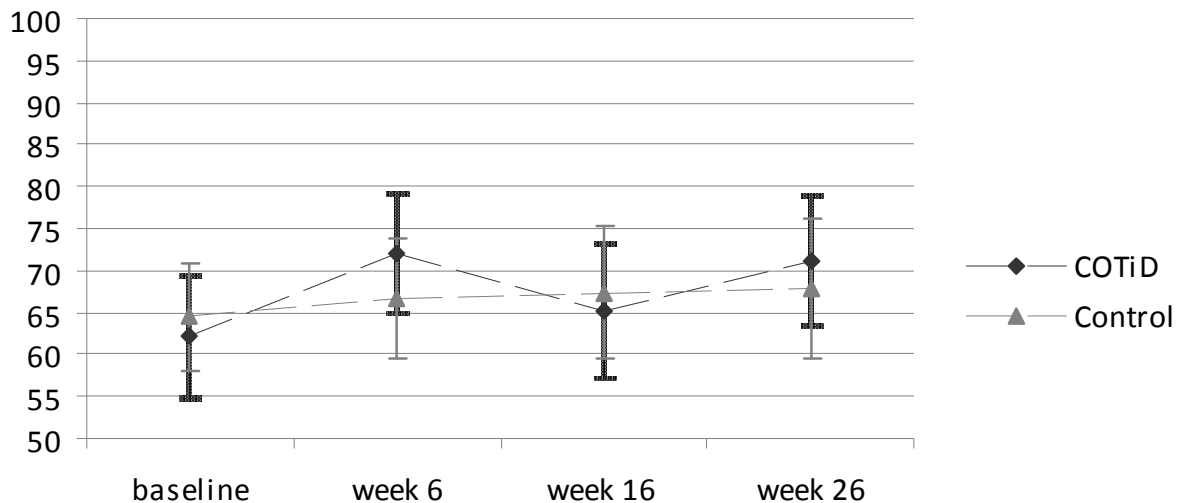
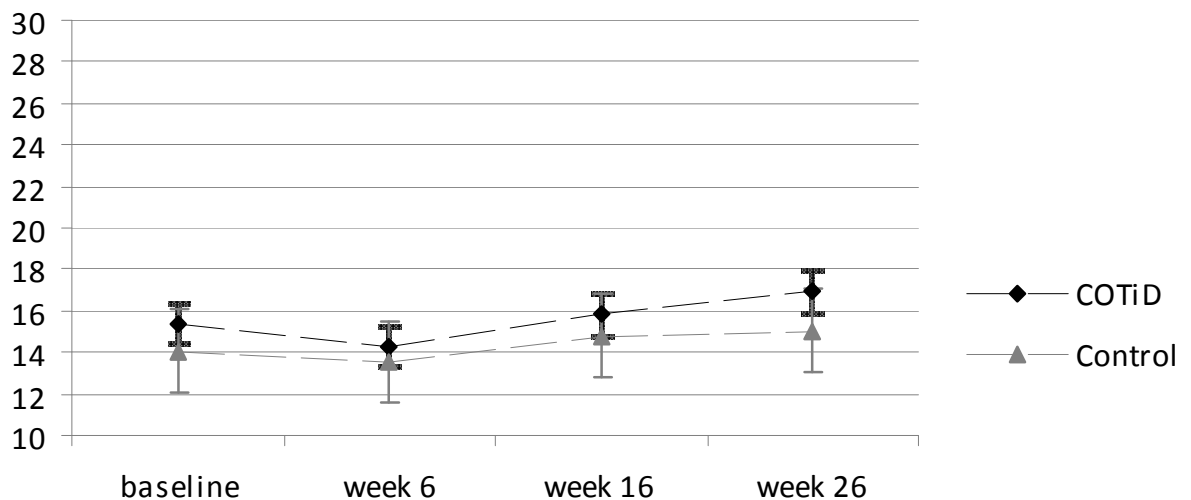


Figure 3: Need for assistance in ADL of Alzheimer patients following intense occupational therapy compared with a single session control intervention (IDDD performance, Range: 0=never assistance to 44=always assistance)



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

1
2
3 feedback on videos of treatment sessions the interventionists sent in. Further, we
4
5 arranged telephone supervision on demand. However, it is difficult to judge whether
6
7 these measures could compensate for the potential influence of different educational
8
9 backgrounds of Dutch and German occupational therapists. In the Netherlands,
10
11 occupational therapy education takes four years and is more psychosocial oriented
12
13 than the three years curriculum in Germany.
14
15

16 17 18 **Comparison**

19
20 The Dutch RCT on the COTiD with waiting-control-group design showed large effect
21
22 sizes in the IDDD performance scale at six and twelve weeks after baseline ($d=2.3$
23
24 and 2.4 , respectively).[6] The Dutch and the German sample did not differ
25
26 remarkably in cognition at baseline (MMSE: 19 v 20), but did differ in the need of
27
28 assistance (IDDD performance: 24 v 15). The German patients showed a low need of
29
30 assistance already at study start comparable to the IDDD values of the Dutch
31
32 patients at the end of the treatment. This may have caused a floor effect on the
33
34 IDDD. Another USA mono-centre RCT compared community occupational therapy
35
36 and a less intensive telephone consultation in patients with probable dementia
37
38 (MMSE: 13).[33] The authors found a small effect size in daily functioning ($d=0.21$).
39
40 The initial need of assistance in both studies was higher than in the German sample.
41
42 A systematic review of community programmes in dementia [34] reported one study
43
44 on exercise and behavioural management with beneficial effects on daily functioning
45
46 of patients with moderate dementia (MMSE: 17),[35] one trial on occupational
47
48 therapy with heterogeneous effects [16] and two studies on occupational therapy [36]
49
50 and music therapy [37] with no significant effects. A current German health
51
52 technology assessment on non-drug therapies in Alzheimer's disease did not identify
53
54 further community occupational therapy trials.[38] The comparison of community
55
56 intervention trials reveals that study samples with a lower MMSE and a higher need
57
58
59
60

1
2
3 of assistance benefit more than those with initial higher cognitive and daily
4 functioning. Similarly, a standardized synopsis of ADL outcomes in pharmacological
5 dementia trials pointed out that samples with an MMSE between 17 and 10 benefit
6 most in ADL while samples with higher MMSE scores showed less effects.[39]
7
8 However, different baseline scores of cognitive and daily functioning alone cannot
9 explain the major difference between our findings and the positive results of the
10 Dutch RCT. Detailed process evaluation and exploratory analyses of our study data
11 might show whether variations in study site context and treatment performance has
12 influenced the intervention's effectiveness.
13
14
15
16
17
18
19
20
21
22
23
24

25 **Clinical and research implications**

26
27 Published evidence for the effectiveness of community occupational therapy in
28 dementia is heterogeneous as indicated by a Dutch trial with large positive effects on
29 daily functioning; a few USA trials with no or small positive effects on ADL and this
30 German study showing that ten sessions were not superior to one consultation.
31
32 Given the high burden of Alzheimer's disease for patients and carers, a
33 comprehensive one-session consultation may be recommended as standard
34 occupational therapy intervention in the German health care system. This may have
35 a stabilizing effect on functional performance and carer burden over time, as was
36 found in both intervention and control groups. This study has shown that careful
37 cross-national comparisons are highly needed before complex interventions may be
38 considered evidence based in other health care systems. Therefore, further analyses
39 must investigate the role of interventionists' expertise and treatment performance and
40 the role of participants' needs and utilisation of health care resources before
41 conclusions on international implementation of this intense occupational therapy
42 intervention can be drawn.
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3 **Acknowledgement:** We thank all participants and interventionists for their contribution. We
4
5 acknowledge Professor Chris Mayers, Research Fellow, Faculty of Health & Life Sciences, York St
6
7 John University, UK, for critical reading and English correction.
8

9 **Funding:** German Federal Ministry of Health, Reference Number: IIA5-2508FSB111/44-004.
10

11 **Contributors:** SVR, MG, RL, GE and MH contributed to study conception and design. FJ, JB, BM, AF,
12
13 RD, GE and MH acquired data. SVR and KS participated in data and study management and
14
15 prepared the statistical analysis. RL performed the statistical analysis. SVR drafted the manuscript.
16
17 RL, MG, FJ, JB, BM, AF, RD, GE, MOR, MVD and MH revised the manuscript critically for important
18
19 intellectual content. All authors read and approved the final manuscript.
20

21 **Competing interests:** SVR, RL, KS, JB, AF, MG and MVD non declared. FJ membership in DSMB of
22
23 AC-immune; payment for lectures from Pfizer, Esai and Novartis. BM payment for lectures from
24
25 various pharmaceutical companies. RD consultancy, grants, payment for lectures, patents, meeting
26
27 expenses from various pharmaceutical companies; royalties and patents from University of Marburg.
28
29 GE grants from AC-immune and Janssen-AL. MOR consultancy for Jansen-Cilag and Numico. MH
30
31 grants from Wyeth, Pfizer and Medivation, payment for lectures from Wyeth, Pfizer and Merz.
32

33 **Ethical approval:** Medical Ethics Committee of the University Hospital Freiburg (no. 110/08).
34
35

36
37 “The Corresponding Author has the right to grant on behalf of all authors and does grant on behalf of
38
39 all authors, an exclusive licence (or non-exclusive for government employees) on a worldwide basis to
40
41 the BMJ Group and co-owners or contracting owning societies (where published by the BMJ Group on
42
43 their behalf), and its Licensees to permit this article (if accepted) to be published in the BMJ open and
44
45 any other BMJ Group products and to exploit all subsidiary rights, as set out in our licence.”
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

References

- 1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
- ¹ Wancata J, Musalek M, Alexandrowicz R, Krautgartner M. Number of dementia sufferers in Europe between the years 2000 and 2050. *Eur Psychiatry*. 2003;18:306-313.
 - ² Wimo A, Jonsson L, Winblad B. An estimate of the worldwide prevalence and direct costs of dementia in 2003. *Dement Geriatr Cogn Disord*. 2006;21(3):175-81.
 - ³ European Medicines Agency. Guideline on Medicinal Products for the Treatment of Alzheimer's Disease and other Dementias [Internet]. London: 2008. Doc. Ref. CPMP/EWP/553/95 Rev. 1 [cited 2010 Oct 26]. Available from: <http://www.emea.europa.eu/pdfs/human/ewp/055395en.pdf>
 - ⁴ Georges J, Jansen S, Jackson J, Meyrieux A, Sadowska A, Selmes M. Alzheimer's disease in real life--the dementia carer's survey. *Int J Geriatr Psychiatry*. 2008 May;23(5):546-51
 - ⁵ Voigt-Radloff S, Hüll M. Daily functioning in dementia: Pharmacological and non-pharmacological interventions demonstrate small effects on heterogeneous scales – a synopsis of four health technology assessments of the German Institute for Quality and Efficiency in Health Care regarding the endpoint activities of daily living. *Psychiatr Prax*. Accepted. German.
 - ⁶ Graff MJ, Vernooij-Dassen MJ, Thijssen M, Dekker J, Hoefnagels WH, Rikkert MG. Community based occupational therapy for patients with dementia and their care givers: randomised controlled trial. *BMJ*. 2006;333(7580):1196.
 - ⁷ National Collaborating Centre for Mental Health (commissioned by the Social Care Institute for Excellence and the National Institute for Health and Clinical Excellence). Dementia. A NICE-SCIE Guideline on supporting people with dementia and their carers in health and social care. National clinical practice guideline, number 42. London, The British Psychological Society and Gaskell 2007
 - ⁸ German Society for Psychiatry, Psychotherapy and Neurology and German Society for Neurology. Consented Guideline "Dementia" [Internet]. 2009. [cited 2010 Oct 26]. Available from: <http://media.dgppn.de/mediadb/media/dgppn/pdf/leitlinien/s3-leitlinie-demenz-lf.pdf>
 - ⁹ Work Group on Alzheimer's Disease and other dementias. Practice Guideline for the Treatment of Patients With Alzheimer's Disease and Other Dementias [Internet]. 2007. [cited 2010 Oct 26]. Available from: <http://www.psychiatryonline.com/pracGuide/PracticePDFs/AlzPG101007.pdf>

- 1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
- ¹⁰ Steultjens EM, Dekker J, Bouter LM, Leemrijse CJ, van den Ende CH. Evidence of the efficacy of occupational therapy in different conditions: an overview of systematic reviews. *Clin Rehabil*. 2005 May;19(3):247-54.
- ¹¹ Voigt-Radloff S. Occupational therapy in dementia. In: Haberstroh J, Pantel J (Ed). Psychosocial treatment in dementia. AKA Verlag Heidelberg: 2011. German
- ¹² World Health Organization: International Classification of Functioning, Disability and Health (ICF) [Internet]. Geneva: 2001. [cited 2010 Oct 26]. Available from: <http://www3.who.int/icf/icfitem>
- ¹³ Giovannetti T, Bettcher BM, Libon DJ, Brennan L, Sestito N, Kessler RK. Environmental adaptations improve everyday action performance in Alzheimer's disease: empirical support from performance-based assessment. *Neuropsychology*. 2007;21(4):448-57.
- ¹⁴ Gitlin LN, Winter L, Burke J, Chernett N, Dennis MP, Hauck WW. Tailored activities to manage neuropsychiatric behaviors in persons with dementia and reduce caregiver burden: a randomized pilot study. *Am J Geriatr Psychiatry*. 2008;16(3):229-39.
- ¹⁵ Mittelman MS, Haley WE, Clay OJ, Roth DL. Improving caregiver well-being delays nursing home placement of patients with Alzheimer disease. *Neurology*. 2006;67(9):1592-9.
- ¹⁶ Gitlin LN, Corcoran M, Winter L, Boyce A, Hauck WW. A randomized, controlled trial of a home environmental intervention: effect on efficacy and upset in caregivers and on daily function of persons with dementia. *Gerontologist*. 2001 Feb;41(1):4-14.
- ¹⁷ Gitlin LN, Hauck WW, Dennis MP, Winter L. Maintenance of effects of the home environmental skill-building program for family caregivers and individuals with Alzheimer's disease and related disorders. *J Gerontol A Biol Sci Med Sci*. 2005 Mar;60(3):368-74.
- ¹⁸ Gitlin LN, Winter L, Vause Earland T, Adel Herge E, Chernett NL, Piersol CV, Burke JP. The Tailored Activity Program to reduce behavioral symptoms in individuals with dementia: feasibility, acceptability, and replication potential. *Gerontologist*. 2009 Jun;49(3):428-39.
- ¹⁹ Graff MJ, Vernooij-Dassen MJ, Thijssen M, Dekker J, Hoefnagels WH, Olderikkert MG. Effects of community occupational therapy on quality of life, mood, and health status in dementia patients and their caregivers: a randomized controlled trial. *J Gerontol A Biol Sci Med Sci*. 2007;62(9):1002-9.
- ²⁰ Graff MJ, Adang EM, Vernooij-Dassen MJ, Dekker J, Jönsson L, Thijssen M, Hoefnagels WH, Rikkert MG. Community occupational therapy for older patients with dementia and their care givers: cost effectiveness study. *BMJ*. 2008;336(7636):134-8.

- 1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
- ²¹ Graff MJL, Melick van MBM: The development, testing and implementation of an occupational therapy guideline. The guideline for the OT diagnosis and treatment of older persons with cognitive impairments. *Nederlands Tijdschrift voor Ergotherapie*. 2000;28:169-74. Dutch
- ²² Graff MJL, Vernooij-Dassen MJFJ, Hoefnagels WHL, Dekker J, Witte de LP. Occupational therapy at home for older individuals with mild to moderate cognitive impairments and their primary caregivers: a pilot study. *Occupational Therapy Journal of Research*. 2003;23:155-63.
- ²³ Graff MJL, Vernooij-Dassen MJ, Zajec J, Olde Rikkert MGM, Hoefnagels WHL, Dekker J. How can occupational therapy improve the daily performance and communication of an older patient with dementia and his primary caregiver? A case study. *Dementia*. 2006;5:503-32.
- ²⁴ German Alzheimer Society. *Leben mit Demenzkranken*. Berlin: 2003. German
- ²⁵ German Alzheimer Society. *Ratgeber Häusliche Versorgung Demenzkranker*. Berlin: 2006. German
- ²⁶ Voigt-Radloff S, Graff M, Leonhart R, Schornstein K, Vernooij-Dassen M, Olde-Rikkert M, Hüll M. WHEDA study: effectiveness of occupational therapy at home for older people with dementia and their caregivers--the design of a pragmatic randomised controlled trial evaluating a Dutch programme in seven German centres. *BMC Geriatr*. 2009 Oct 2;9:44.
- ²⁷ Teunisse S, Derix MM. The interview for deterioration in daily living activities in dementia: agreement between primary and secondary caregivers. *Int Psychogeriatr*. 1997;9(Suppl 1):155-62.
- ²⁸ Chapparo C, Ranka J. *The PRPP System of Task Analysis: User's Training Manual*. In Research Edition Sydney: OP Network; 2006.
- ²⁹ Moniz-Cook E, Vernooij-Dassen M, Woods R, Verhey F, Chattat R, De Vugt M, Mountain G, O'Connell M, Harrison J, Vasse E, Dröes RM, Orrell M; INTERDEM group. A European consensus on outcome measures for psychosocial intervention research in dementia care. *Aging Ment Health*. 2008 Jan;12(1):14-29.
- ³⁰ Wolfson C, Moride Y, Perrault A, Momoli F, Demers L, Oremus M. Drug treatments for Alzheimer's disease. II. A review of outcome measures in clinical trials. Ottawa: Canadian Coordinating Office for Health Technology Assessment (CCOHTA); 2000.
- ³¹ Allison P. *Missing data*. Thousand Oaks: Sage; 2002.
- ³² Plassman BL, Williams JW Jr, Burke JR, Holsinger T, Benjamin S. Systematic review: factors associated with risk for and possible prevention of cognitive decline in later life. *Ann Intern Med*. 2010 Aug 3;153(3):182-93.

- 1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
- ³³ Gitlin LN, Winter L, Dennis MP, Hodgson N, Hauck WW. A biobehavioral home-based intervention and the well-being of patients with dementia and their caregivers: the COPE randomized trial. *JAMA*. 2010 Sep 1;304(9):983-91.
- ³⁴ Smits CH, de Lange J, Dröes RM, Meiland F, Vernooij-Dassen M, Pot AM. Effects of combined intervention programmes for people with dementia living at home and their caregivers: a systematic review. *Int J Geriatr Psychiatry*. 2007 Dec;22(12):1181-93.
- ³⁵ Teri L, Gibbons LE, McCurry SM, Logsdon RG, Buchner DM, Barlow WE, Kukull WA, LaCroix AZ, McCormick W, Larson EB. Exercise plus behavioural management in patients with Alzheimer disease. A randomized controlled trial. *JAMA*. 2003;290:2015-22.
- ³⁶ Gitlin LN, Winter L, Corcoran M, Dennis MP, Schinfeld S, Hauck WW. Effects of the home environmental skill-building program on the caregiver-care recipient dyad: 6-month outcomes from the Philadelphia REACH Initiative. *Gerontologist*. 2003 Aug;43(4):532-46.
- ³⁷ Berger G, Bernhardt T, Schramm U, Müller R, Landsiedel-Anders S, Peters J, Kratzsch T, Frolich L. No effects of a combination of caregivers support group and memory training/music therapy in dementia patients from a memory clinic population. *Int J Geriatr Psychiatry*. 2004 Mar;19(3):223-31.
- ³⁸ Rieckmann N, Schwarzbach C, Nocon M, Roll S, Vauth C, Willich SN, Greiner W. Concepts of care for people with dementia [Internet]. *GMS Health Technol Assess* 2009;5:Doc01. [cited 2010 Oct 26]. Available from: <http://www.egms.de/static/en/journals/hta/2009-5/hta000063.shtml>. German
- ³⁹ Gauthier S, Lopez OL, Waldemar G, Jones RW, Cummings J, Zhang R, Schindler R, Schwam E. Effects of donepezil on activities of daily living: integrated analysis of patient data from studies in mild, moderate and severe Alzheimer's disease. *Int Psychogeriatr*. 2010 Sep;22(6):973-83.



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

1		assessing outcomes) and how		
2	11b	If relevant, description of the similarity of interventions	10+11	
3	Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	15+16
4		12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	16
5				
6	Results			
7	Participant flow (a	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and	17
8	diagram is strongly		were analysed for the primary outcome	
9	recommended)	13b	For each group, losses and exclusions after randomisation, together with reasons	17
10	Recruitment	14a	Dates defining the periods of recruitment and follow-up	16
11		14b	Why the trial ended or was stopped	16
12	Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	18
13	Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was	19+22
14			by original assigned groups	
15	Outcomes and	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its	22
16	estimation		precision (such as 95% confidence interval)	
17		17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	
18	Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing	19+20
19			pre-specified from exploratory	
20	Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	21
21				
22	Discussion			
23	Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	23+24
24	Generalisability	21	Generalisability (external validity, applicability) of the trial findings	24+25
25	Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	24+25
26				
27	Other information			
28	Registration	23	Registration number and name of trial registry	9
29	Protocol	24	Where the full trial protocol can be accessed, if available	9
30	Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	26
31				
32				
33				
34				
35				
36				
37				
38				
39				
40				
41				
42				
43				
44				
45				
46				
47				

*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.

Journal:	<i>BMJ Open</i>
Manuscript ID:	bmjopen-2011-000096.R1
Article Type:	Research
Date Submitted by the Author:	30-Mar-2011
Complete List of Authors:	Voigt-Radloff, Sebastian; University Hospital Freiburg, Centre of Geriatric Medicine and Gerontology Freiburg Graff, Maud; Radboud University Nijmegen Medical Centre, Alzheimer Centre Nijmegen Leonhart, Rainer; University of Freiburg, Department of Social Psychology and Methodology Schorstein, Katrin; University of Freiburg, Department of Social Psychology and Methodology Jessen, Frank; University of Bonn, Department of Psychiatry and Psychotherapy Bohlken, Jens; Private Practice for Neurology, Psychiatry and Psychotherapy Metz, Brigitte; Centre of Geriatric Medicine and Geriatric Clinic at Diakonissenkrankenhaus Karlsruhe-Rüppurr Fellgiebel, Andreas; University Medical Center Mainz, Department of Psychiatry and Psychotherapy Dodel, Richard; Philipps-University Marburg, Department of Neurology Eschweiler, Gerhard; Eberhard-Karls University Tuebingen, Department of Psychiatry and Psychotherapy Vernooij-Dassen, Myrra; Radboud University Nijmegen Medical Centre, Alzheimer Centre Nijmegen Olde Rikkert, Marcel; Radboud University Nijmegen Medical Centre, Alzheimer Centre Nijmegen Hüll, Michael; University Hospital Freiburg, Centre of Geriatric Medicine and Gerontology Freiburg
Subject Heading:	Neurology
Keywords:	Dementia < NEUROLOGY, Quality in health care < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, REHABILITATION MEDICINE

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

SCHOLARONE™
Manuscripts

For peer review only

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

Sebastian Voigt-Radloff, Maud Graff, Rainer Leonhart, Katrin Schornstein, Frank Jessen, Jens Bohlken, Brigitte Metz, Andreas Fellgiebel, Richard Dodel, Gerhard Eschweiler, Myrra Vernooij-Dassen, Marcel Olde Rikkert, Michael Hüll

Department of Occupational Therapy, Centre of Geriatric Medicine and Gerontology Freiburg, University Hospital Freiburg, Lehener Str. 88, 79106 Freiburg, Germany Sebastian Voigt-Radloff *scientific researcher in allied healthcare research*

Alzheimer Centre Nijmegen, Scientific Institute for Quality in Health Care and Dept of Rehabilitation-Occupational Therapy, Radboud University Nijmegen Medical Centre, PO Box 9101, 6500 HB Nijmegen, The Netherlands, Maud Graff *senior researcher in allied healthcare research and research on psychosocial interventions in dementia*

Department of Social Psychology and Methodology, University of Freiburg, Engelbergerstr. 41, 79085 Freiburg, Germany Rainer Leonhart *senior researcher in statistics and psychology*

Department of Social Psychology and Methodology, University of Freiburg, Engelbergerstr. 41, 79085 Freiburg, Germany Katrin Schornstein *researcher in statistics and psychology*

Department of Psychiatry and Psychotherapy, University of Bonn, Sigmund-Freud-Str. 25, 53105 Bonn, Germany Frank Jessen *professor in psychiatry*

Private Practice for Neurology, Psychiatry and Psychotherapy, Klosterstr. 34, 13581 Berlin, Germany Jens Bohlken *clinical psychiatrist*

Centre of Geriatric Medicine and Geriatric Clinic at Diakonissenkrankenhaus Karlsruhe-Rüppurr, Diakonissenstr. 28, 76199 Karlsruhe, Germany Brigitte Metz *clinical geriatrician*

Department of Psychiatry and Psychotherapy, University Medical Center Mainz, Untere Zahlbacher Str. 8, 55131 Mainz, Germany Andreas Fellgiebel *professor in psychiatry*

Department of Neurology, Philipps-University Marburg, Rudolf-Bultmannstr. 8, 35039 Marburg, Germany Richard Dodel *professor in neurology*

Department of Psychiatry and Psychotherapy, Eberhard-Karls University Tuebingen, Osianderstr. 24, 72076 Tübingen Germany, Gerhard Eschweiler *professor in psychiatry*

Alzheimer Centre Nijmegen, Scientific Institute for Quality in Health Care, Radboud University Nijmegen Medical Centre, Kalorama Foundation, PO Box 9101, 6525 JV Nijmegen, The Netherlands, Myrra Vernooij-Dassen *professor in psychosocial interventions in frail elderly*

Alzheimer Centre Nijmegen, Department of Geriatrics, Radboud University Nijmegen Medical Centre, PO Box 9101, 6500 HB Nijmegen, The Netherlands, Marcel Olde Rikkert *professor in geriatrics*

Section of Gerontopsychiatry and Neuropsychology, Centre of Geriatric Medicine and Gerontology Freiburg, University Hospital Freiburg, Lehener Str. 88, 79106 Freiburg, Germany, Michael Hüll *professor in psychiatry*

Correspondence to: sebastian.voigt@uniklinik-freiburg.de

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.

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

1
2
3 improving the patient's physical and social environment and by tailoring the
4
5 intervention to the patient's capability.[12-15]
6

7
8 Until March 2011, there was no systematic review on community occupational
9
10 therapy for people with Alzheimer's disease but two research groups had
11
12 conducted RCTs in this subject. In the USA study, occupational therapy
13
14 demonstrated beneficial effects on patients' challenging behaviours but not on
15
16 ADL. No information on adverse events were given.[14, 16-18] In the
17
18 Netherlands, occupational therapy, tailored to the needs of patients and carers
19
20 showed benefits on the patient's ADL, mood, health status and quality of life
21
22 and on the carer's sense of competence, mood, quality of life and costs of
23
24 informal care. No adverse events were reported in either intervention or control
25
26 group.[6, 19-20]
27
28
29
30

31
32 In the current randomised trial we tested the hypothesis that the Dutch ten-
33
34 session Community Occupational Therapy in Dementia Programme (COTiD)
35
36 would significantly improve the daily functioning of people with mild or moderate
37
38 dementia, more so than a one-session Community Occupational Therapy
39
40 Consultation (COTC). Secondary research questions were whether these
41
42 interventions would show a difference in their effect on patient's and primary
43
44 carer's quality of life and mood; on the carer's sense of competence in the
45
46 interaction with the patient; and on long-term nursing home placements.
47
48
49
50

51 52 53 **METHODS**

54 55 56 **Design**

57
58 In order to evaluate the superiority of COTiD, we used a seven-centre single-
59
60 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

1
2
3 available at <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2761388/>. The study
4
5 was registered at the German register of clinical trials, which is connected to the
6
7 International Clinical Trials Registry Platform (<http://apps.who.int/trialsearch/> =>
8
9 DRKS00000053). The Medical Ethics Committee of the University Hospital
10
11 Freiburg gave ethical approval (no. 110/08).
12
13
14
15
16

17 **Participants and Setting**

18
19 Patients were eligible to participate in the study if they had mild to moderate
20
21 dementia (MMSE 14-24) and were diagnosed as having Alzheimer's disease or
22
23 mixed type dementia, according to ICD-10 criteria, by physicians with more than
24
25 five years of experience in dementia diagnosis. Participants had to dwell in the
26
27 community either together with their primary carer or with involvement of a carer
28
29 providing care at least twice a week. Patients with a score above 12 on the 30-
30
31 items Geriatric Depression Scale or a major need of physical nursing care of
32
33 more than 120 min per day (level 2 or higher according to the German Long-
34
35 Term Care Insurance Act) were excluded. Unstable medical conditions or
36
37 severe behavioural disturbances, which did not allow participation in the study
38
39 as judged by the study physicians were criteria for exclusion as well as for
40
41 discontinuation. Long-term nursing home placements of the patients during the
42
43 treatment phase or death of patient or primary carer were criteria for
44
45 discontinuation. The patient gave written informed consent and the carer
46
47 consented by written format to join and support the treatment procedures.
48
49
50
51 Patients were recruited from five outpatient memory centres at university
52
53 hospitals (in Bonn, Freiburg, Mainz, Marburg and Tübingen); one municipal
54
55 hospital in Karlsruhe specialising in geriatric medicine; and one neurological
56
57 private practice in Berlin specialising in neuropsychiatry and collaborating with
58
59
60

1
2
3 an occupational therapy private practice. The seven participating centres are
4 located throughout Germany in urban regions with catchment areas of about
5 70,000 to 700,000 inhabitants. They had all provided outpatient dementia care
6 for three to fifteen years. Their standard service comprised diagnostic work-up
7 for dementia and related diagnoses as well as recommendation of risk
8 reduction, dementia medication and non-pharmacological treatments. Principal
9 investigators of the centres were psychiatrists, neurologists or geriatricians with
10 six to thirteen years of experience in dementia care.
11
12
13
14
15
16
17
18
19
20
21
22
23

24 **Interventions**

25
26 The experimental intervention (COTiD) was designed to improve the patient's
27 and the primary carer's daily functioning, and was based on an evidence-based
28 treatment manual.[6, 19-23] COTiD consisted of ten occupational therapy
29 sessions of one hour duration held over five weeks at each patient's home. In
30 the diagnostic phase, comprising of 3 to 4 sessions, the occupational therapist
31 explored (1) the patient's preferences and history of daily activities, (2) her or
32 his ability to perform activities and to use compensatory strategies within the
33 familiar environment, (3) the possibilities of modifying the patient's home, (4) the
34 carer's activity preferences, problems in care giving, coping strategies and
35 abilities to supervise and (5) the interaction between carer and patient. In a
36 shared decision-making process during the goal setting session, the patient and
37 the carer selected the one or two most meaningful activities out of a list of their
38 preferences for daily activities to work on in occupational therapy. During the
39 treatment phase of 5 to 6 sessions, the occupational therapist defined, together
40 with the patient and the carer, more effective compensatory and environmental
41 strategies to adapt both the environment and the selected activities to the
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3 patient's habits and cognitive abilities. Patient and carer were taught how to use
4 these suggested adaptations within strategies, activities and the environment in
5 order to improve their performance of daily activities. In addition, the carer
6 received practical and emotional support and was coached in effective
7 supervision, problem solving and coping strategies by means of cognitive-
8 behavioural interventions. Detailed description of the experimental intervention
9 has been published elsewhere.[23]

10
11 For the German RCT, MG taught the content of the translated treatment manual
12 to 14 study participant occupational therapists in 16 hours of seminars using
13 presentation, videos and role play with feedback and group discussion. After the
14 seminar and before the study started, they needed to complete a full treatment
15 series for at least one pilot dyad of patient and carer. In the study phase, the
16 interventionists spent about 20 hours per patient for a full treatment series
17 including ten treatment sessions, travel, reports and multidisciplinary briefing. In
18 Germany, a series of ten to thirty sessions is within the normal range of time
19 that occupational therapists use for the treatment of older outpatients diagnosed
20 with other diseases, such as stroke or rheumatoid arthritis.

21
22 The control group received one hour occupational therapy consultation (COTC)
23 at the patient's home conducted by the same study interventionists. Based on
24 material of the German Alzheimer Society, two occupational therapists with
25 more than five years of experience in dementia care had prepared a leaflet of
26 ten pages.[24-25] The semi-structured consultation was an explanation of 30
27 min of this leaflet and a talk of 30 min on individual problems that arose from
28 patient's and carer's needs. This included encouragement to stay active in
29 everyday life, to maintain social contacts and to use dementia services in the
30 region for which local addresses were listed in the leaflet. Occupational
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3 therapists were taught the control intervention within a 4-hour seminar.
4
5 Consultations of 30 minutes up to one hour duration about such issues are
6
7 common in German dementia care. Detailed description of the control
8
9 intervention as well as means of quality assurance in experimental and control
10
11 intervention has been published elsewhere.[26]
12
13
14
15
16

17 **Outcome measures**

18
19 The primary endpoint was the patients' change of daily functioning from
20
21 baseline to follow-up time points at week 6, 16 and 26 measured with the
22
23 performance scale of the Interview for Deterioration in Daily Living Activities in
24
25 Dementia (IDDD).[27] This scale records carer rating of the patient's need of
26
27 assistance in the performance of (1) washing oneself, (2) making tea or coffee,
28
29 (3) dressing, (4) combing one's hair and brushing one's teeth, (5) eating, (6)
30
31 using the toilet, (7) shopping, (8) using the telephone, (9) preparing a meal, (10)
32
33 cleaning the house or doing minor repair work and (11) handling finances. Each
34
35 item is rated never=0, seldom=1, sometimes=2, often=3 or always=4. The sum
36
37 of scores ranged from 0 to 44. Higher scores indicated higher need for
38
39 assistance. Since carer rating could not be 'masked', daily functioning was
40
41 additionally evaluated by external **raters** fully 'blind' to the group assignment.
42
43 They rated video tapes of a challenging daily living task and used the Perceive,
44
45 Recall, Plan and Perform System of Task Analysis (PRPP).[28] For the PRPP,
46
47 **raters** had to define single steps of the performed activity, and they identified
48
49 any activity step in which errors of accuracy, omission, repetition or timing
50
51 occurred. The number of activity steps rated as incorrectly performed was
52
53 divided by the total number of activity steps, resulting in an independence-score
54
55 indicated in a percentage (100% = all steps are error-free).
56
57
58
59
60

Table 1: Measurements of secondary endpoints²⁶

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

1
2
3 all translators. There was no need to translate the PRPP because, because it
4
5 was established in the Netherlands and applied by Dutch raters. There was one
6
7 protocol amendment before recruitment started. The Assessment of Motor and
8
9 Process Skills (AMPS) was replaced by the PRPP, because the AMPS was not
10
11 available in the German language within the planned schedule.
12
13

14
15 Indicators of harm were defined as patient or carer death, number of patients
16
17 with admission to hospital and number of nights in hospital. These indicators
18
19 were recorded in interviews with the carer at intervals of 5 to 7 weeks over 52
20
21 weeks. Study sites had to report severe adverse events to the study centre
22
23 immediately when each occurred. We did not assume a direct association
24
25 between the defined harms and either the experimental or the control
26
27 intervention. However, increased daily activities in the interventions group might
28
29 have resulted in a higher risk of falls or accidents and thus may indirectly have
30
31 led to more nights in hospital or in the worst case to death.
32
33
34
35
36
37
38

39 **Sample size calculation**

40
41 A sample size of 42 participants per group was calculated to be necessary to
42
43 detect an effect size of $f = 0.10$ on the IDDD performance scale in an analysis of
44
45 variance of two groups and four time points; using a two-sided 5% significance
46
47 level, a power of 80%, and a correlation of 0.7 between the measurement time
48
49 points [31]. According to the Dutch original RCT, we expected a dropout rate of
50
51 10% at week 16, which was extrapolated to 40% at week 52. A nine-month
52
53 inclusion period was anticipated as necessary in order to recruit the 140
54
55 patients. Although the Dutch original RCT found effect sizes of $d\text{-value}=2.4$ in
56
57 the IDDD performance scale at week 12, for this study the power was
58
59 calculated much more conservatively. This was because we (1) introduced an
60

1
2
3 active control group, (2) investigated the programme effects under varying care
4 conditions in seven centres with interventionists who were introduced in this
5 new treatment and were far not as experienced as the Dutch study therapists
6 and (3) we prolonged the follow up period. Interim analyses were not planned.
7
8
9
10
11

12 13 14 15 **Randomisation and masking**

16
17 The random allocation sequence was computer-generated with blocking by
18 centre and groups of two persons, without stratification and in a ratio of 1:1 by a
19 statistician from a distant site. After enrolment, study site physicians requested
20 randomisation via e-mail. The statistician e-mailed the individual allocation to
21 COTiD or COTC exclusively to the site interventionist and stored the allocation
22 list at his distant site which was not available to any study site staff. The
23 interventionist scheduled treatment sessions, faxed records to the distant
24 coordinating study centre and kept all documents strictly separated from any
25 other site staff. This was in order to avoid contamination. Since the numbers of
26 home visits differed in the experimental and control groups, masking of patients
27 and carers was not possible. However, study information did not include any
28 preference for a special treatment 'arm'. Patients and carers were asked to give
29 no information about their treatment package to assessors or study physicians.
30 All study personal was 'blind' for group assignment, except the interventionists.
31 Agreement between the assessors' estimation of group assignment and the
32 actual group assignment was 61%, and thus slightly over the expected 50% of
33 agreement by chance. The procedure of external video rating ensured the full
34 'blinding' of the external raters for the PRPP primary outcome measure.
35
36 Independent research assistants cleaned the videotapes of any hint of group
37 assignment before they were rated by two Dutch raters not involved in the trial
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3 treatment. In order to establish the inter-rater reliability, we tested ten double
4
5 ratings of the same video by the two raters and found an intra-class correlation
6
7 coefficient of 0.9. Data analysts were not 'blind' for the group assignment.
8
9
10 However, measurement time points and outcomes had been published before
11
12 data were available for analysis [26] and any decision to remove patients from
13
14 the analyses is reported in the present publication.
15
16
17
18
19

20 **Statistical methods**

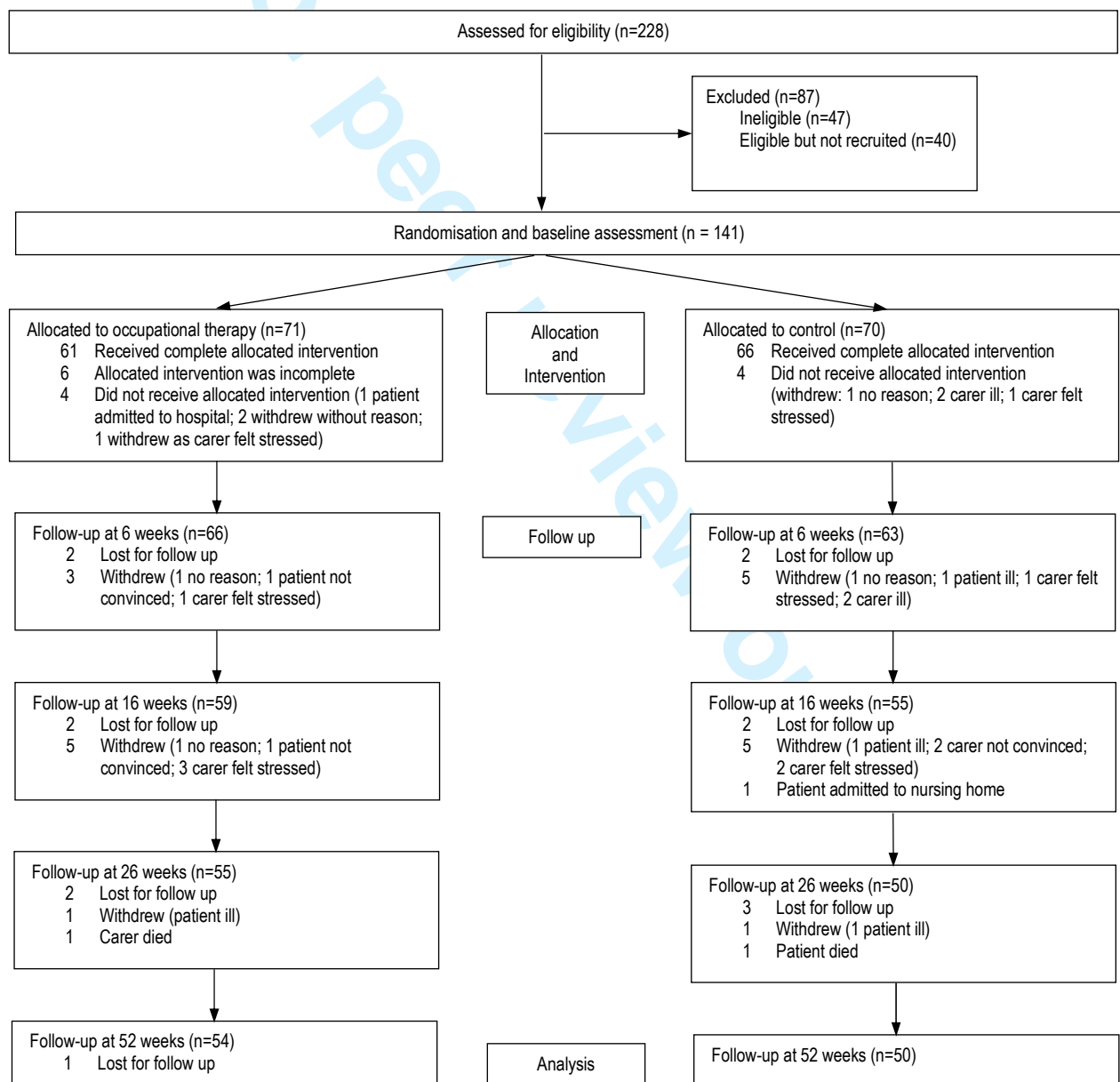
21
22 Data were entered via special MS Access entry masks automatically controlling
23
24 for data plausibility. In addition, sections of entered data were checked for
25
26 typing errors by hand, in order to ensure an error rate lower than 0.2%. The
27
28 primary intention-to-treat analysis included all allocated participants with valid
29
30 data whether they did or did not receive the complete intervention. For the
31
32 primary outcomes, we performed a multivariate analysis of variance (MANOVA)
33
34 with repeated measures with two groups and four measurement time points at
35
36 baseline, week 6, 16 and 26. In this primary analysis, we did not adjust for
37
38 baseline values or any other co-variate. A univariate ANOVA with five
39
40 measurement time points (+ week 52) was carried out for the secondary
41
42 outcomes. In order to deal with missing data, we performed secondary
43
44 intention-to-treat analyses with multiple data imputation using the Full
45
46 Information Maximum Likelihood (FIML) method.[32] We imputed data for all
47
48 secondary outcome measurements and all time points using SPSS (version 19).
49
50
51
52
53 All statistical tests were two-sided on an alpha level of 0.05. Subgroup analyses
54
55 were not planned.
56
57
58
59
60

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

1
2
3 lost before intervention. Six patient-carer dyads in the COTiD had less than 10
4 sessions. Interventionists rated the delivery of 20 pre-defined treatment sub-
5 processes, ranging from interviewing patient and carer to training of simplified
6 activities or supporting the carer in supervision. They scored treatment delivery
7 as 78% in the COTiD group and 80% in the control group. Interventionists rated
8 the patient's adherence in 67 cases of the COTiD group, from 15 as hindering
9 the delivery of treatment; 26 as neutral and 26 as facilitating. Rating criteria
10 were the patient's cooperation during interview, goal setting and training; the
11 daily changing mental capacity; collaboration with the carer; and the acceptance
12 of innovations. Ratings of carers' adherence were 5 hindering; 15 neutral; and
13 47 facilitating. The carer adherence was assessed with regard to the
14 cooperation during scheduling, interview, goal setting and training to supervise;
15 the encouragement of the patient; the acceptance of support service; and the
16 implementation of innovations. The adherence of the participants in the control
17 group could not be rated, because interventionists had no further contact after
18 the consultation.

43 Outcomes

44
45 The MANOVA in 104 completers (COTiD: n=54; control: n=50) revealed no
46 significant group time interaction effect in the primary outcome measurements
47 of patients' daily functioning (Figures 2 and 3). Tables 3 and 4 show mean,
48 standard deviation and group difference including 95%-confidence intervals of
49 an ANOVA for all outcomes. Patients' daily functioning did not significantly
50 change over 26 weeks in either the experimental and control group. In the
51 postal 52 weeks follow up, the patients' need for assistance increased in both
52 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)

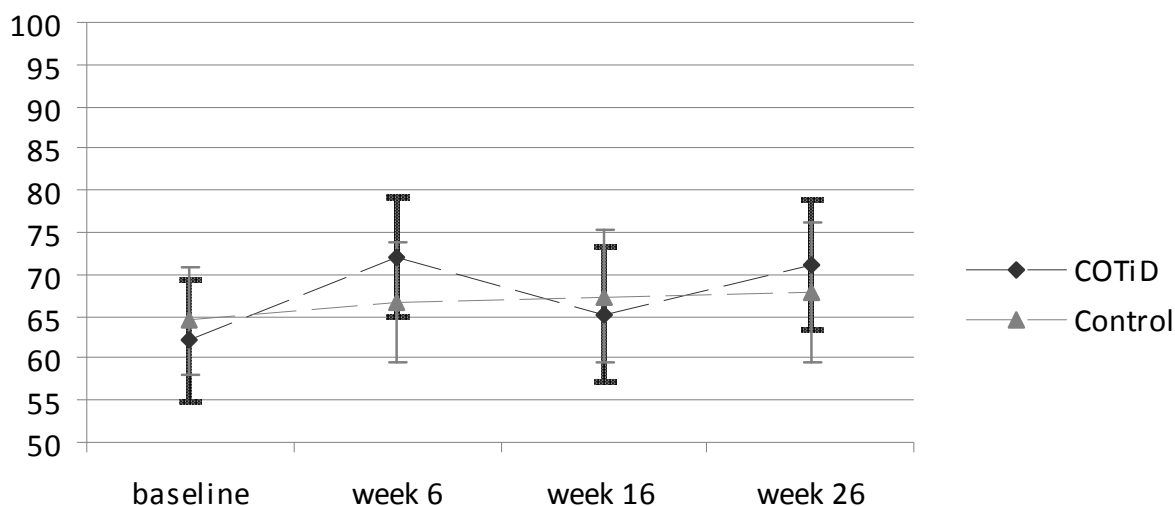
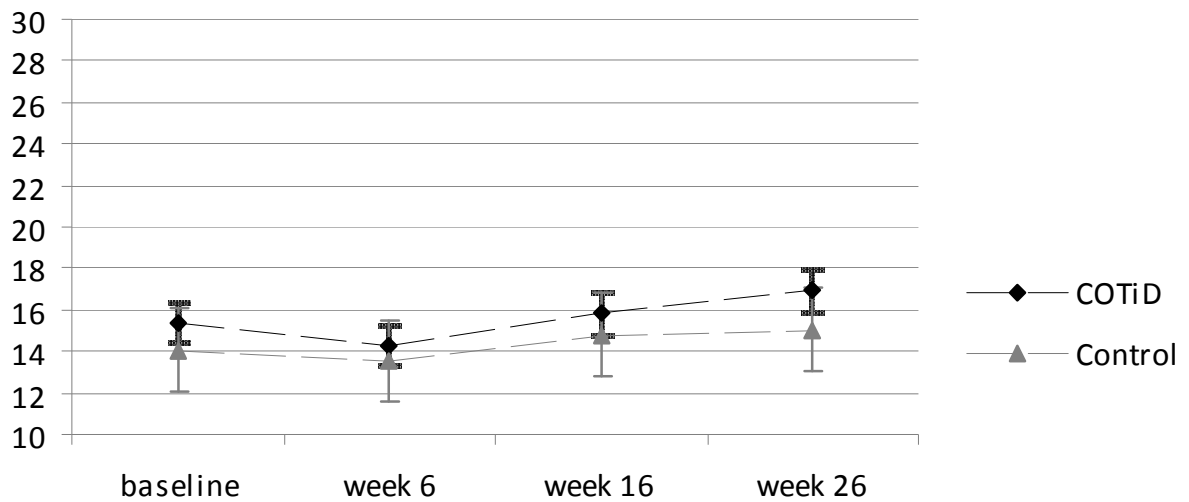


Figure 3: Need for assistance in ADL of Alzheimer patients following intense occupational therapy compared with a single session control intervention; means and 95%-confidence intervals of the IDDD performance scale (range: 0=never needed assistance to 44=always needed assistance)



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

1
2
3 matters and approval of the local ethic commissions. Therefore, a common repetition
4 seminar for the interventionists could not be arranged after the pilot training. This
5 may have led to some heterogeneity in the intervention, especially because in
6 Germany eleven newly introduced interventionists performed the treatment
7 compared to two experienced experts in the original Dutch trial. We addressed this
8 problem with feedback on videos of treatment sessions the interventionists sent in.
9 Furthermore, we arranged telephone supervision on demand. However, it is difficult
10 to judge whether these measures could compensate for the potential influence of
11 different educational backgrounds of Dutch and German occupational therapists. In
12 the Netherlands, occupational therapy education takes four years and is more
13 psychosocial oriented than the three years curriculum in Germany.
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28

29 **We consider the contamination of the control intervention with knowledge from the**
30 **experimental intervention to be low, because any specific intervention such as**
31 **activity selection, simplification or training was precluded by the limited time to carry**
32 **out the control intervention.**
33
34
35
36
37
38

39 **Comparison**

40
41 The Dutch RCT on the COTiD with waiting-control-group design showed large effect
42 sizes in the IDDD performance scale at six and twelve weeks after baseline ($d=2.3$
43 and 2.4 , respectively).[6] The Dutch and the German sample did not differ
44 remarkably in cognition at baseline (MMSE: 19 v 20), but did differ in the need of
45 assistance (IDDD performance: 24 v 15). The German patients showed a low need of
46 assistance at the beginning of the study. This was comparable to the IDDD values of
47 the Dutch patients at the end of the treatment. This may have caused a floor effect
48 on the IDDD. Another mono-centre RCT in the USA compared community
49 occupational therapy and a less intensive telephone consultation in patients with
50 probable dementia (MMSE: 13).[34] The authors found a small effect size in daily
51
52
53
54
55
56
57
58
59
60

1
2
3 functioning ($d=0.21$). The initial need of assistance in both studies was higher than in
4
5 the German sample. A systematic review of community programmes in dementia [35]
6
7 reported one study on exercise and behavioural management with beneficial effects
8
9 on daily functioning of patients with moderate dementia (MMSE: 17) [36]; one trial on
10
11 occupational therapy with heterogeneous effects [16]; and two studies on
12
13 occupational therapy [37] and music therapy [38] with no significant effects. A current
14
15 German health technology assessment on non-drug therapies in Alzheimer's disease
16
17 did not identify further community occupational therapy trials.[39] The comparison of
18
19 community intervention trials reveals that study samples with a lower MMSE and a
20
21 higher need of assistance benefit more than those with initial higher cognitive and
22
23 daily functioning. Similarly, a standardized synopsis of ADL outcomes in
24
25 pharmacological dementia trials indicated that samples with an MMSE between 17
26
27 and 10 benefit most in ADL while samples with higher MMSE scores showed less
28
29 effects.[40] However, different baseline scores of cognitive and daily functioning
30
31 alone cannot explain the major difference between the findings in this German study
32
33 and the positive results of the Dutch RCT. Detailed process evaluation and
34
35 exploratory analyses of the study data might show whether variations in study site
36
37 context and treatment performance influenced the intervention's effectiveness.
38
39
40
41
42
43
44
45

46 **Clinical and research implications**

47
48 Published evidence for the effectiveness of community occupational therapy in
49
50 dementia is heterogeneous as indicated by a Dutch trial with large positive effects on
51
52 daily functioning; a few USA trials with no or small positive effects on ADL and this
53
54 German study showing that ten sessions were not superior to one consultation. **A**
55
56 **preventative one-session consultation might be hypothesised as beneficial for people**
57
58 **with mild dementia and an improved 10-session programme more specifically**
59
60 **adapted to the German health care system as beneficial for dementia patients with**

1
2
3 moderate need of assistance in ADL, as was shown in the Dutch study in which most
4
5 people with dementia had moderate to high need for assistance at baseline.
6
7

8 Although we had expected smaller effect sizes than in the Dutch original trial due to
9
10 changed study design with (1) the introduction of an active control group, (2) a
11
12 variance in treatment performance in several centres, (3) a prolonged follow up time
13
14 and (4) rigorous reduction of the analysed sample to participants with valid data, it
15
16 remains surprising that significant group difference could not be found in any of the
17
18 primary or secondary outcomes.
19
20
21

22 This study has shown that careful cross-national comparisons are greatly needed,
23
24 especially in complex interventions, before they can be considered evidence based
25
26 and implemented effectively in other health care systems. Therefore, further analyses
27
28 must investigate the role of interventionists' expertise and treatment performance,
29
30 and the role of participants' needs and utilisation of health care resources, before
31
32 conclusions on international implementation of this intense occupational therapy
33
34 intervention can be drawn.
35
36
37
38
39

40 **Acknowledgement:** We thank all participants and interventionists for their contribution. We
41
42 acknowledge Professor Chris Mayers, Research Fellow, Faculty of Health & Life Sciences, York St
43
44 John University, UK, for critical reading and English correction.
45

46 **Funding:** German Federal Ministry of Health, Reference Number: IIA5-2508FSB111/44-004.

47
48 **Contributors:** SVR, MG, RL, GE and MH contributed to study conception and design. FJ, JB, BM, AF,
49
50 RD, GE and MH acquired data. SVR and KS participated in data and study management and
51
52 prepared the statistical analysis. RL performed the statistical analysis. SVR drafted the manuscript.
53
54 RL, MG, FJ, JB, BM, AF, RD, GE, MOR, MVD and MH revised the manuscript critically for important
55
56 intellectual content. All authors read and approved the final manuscript.
57

58 **Competing interests:** SVR, RL, KS, JB, AF, MG and MVD non declared. FJ membership in DSMB of
59
60 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

1
2
3 expenses from various pharmaceutical companies; royalties and patents from University of Marburg.
4
5 GE grants from AC-immune and Janssen-AL. MOR consultancy for Jansen-Cilag and Numico. MH
6
7 grants from Wyeth, Pfizer and Medivation, payment for lectures from Wyeth, Pfizer and Merz.
8
9

10
11 **Data sharing statement:** Complete data sets can be provided on request for research fellows in
12
13 **scope of collaborative projects and publications.**
14

15
16
17 “The Corresponding Author has the right to grant on behalf of all authors and does grant on behalf of
18
19 all authors, an exclusive licence (or non-exclusive for government employees) on a worldwide basis to
20
21 the BMJ Group and co-owners or contracting owning societies (where published by the BMJ Group on
22
23 their behalf), and its Licensees to permit this article (if accepted) to be published in the BMJ open and
24
25 any other BMJ Group products and to exploit all subsidiary rights, as set out in our licence.”
26
27

28 29 References

- 30
31 ¹ Wancata J, Musalek M, Alexandrowicz R, Krautgartner M. Number of dementia sufferers in Europe
32
33 between the years 2000 and 2050. *Eur Psychiatry*. 2003;18:306-313.
34
35 ² Wimo A, Jonsson L, Winblad B. An estimate of the worldwide prevalence and direct costs of
36
37 dementia in 2003. *Dement Geriatr Cogn Disord*. 2006;21(3):175-81.
38
39 ³ European Medicines Agency. Guideline on Medicinal Products for the Treatment of Alzheimer’s
40
41 Disease and other Dementias [Internet]. London: 2008. Doc. Ref. CPMP/EWP/553/95 Rev. 1
42
43 [cited 2010 Oct 26]. Available from: <http://www.emea.europa.eu/pdfs/human/ewp/055395en.pdf>
44
45 ⁴ Georges J, Jansen S, Jackson J, Meyrieux A, Sadowska A, Selmes M. Alzheimer's disease in real
46
47 life--the dementia carer's survey. *Int J Geriatr Psychiatry*. 2008 May;23(5):546-51
48
49 ⁵ Voigt-Radloff S, Hüll M. Daily functioning in dementia: Pharmacological and non-pharmacological
50
51 interventions demonstrate small effects on heterogeneous scales – a synopsis of four health
52
53 technology assessments of the German Institute for Quality and Efficiency in Health Care
54
55 regarding the endpoint activities of daily living. *Psychiatr Prax*. Accepted. German.
56
57 ⁶ Graff MJ, Vernooij-Dassen MJ, Thijssen M, Dekker J, Hoefnagels WH, Rikkert MG. Community
58
59 based occupational therapy for patients with dementia and their care givers: randomised
60
controlled trial. *BMJ*. 2006;333(7580):1196.

- 1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
- ⁷ National Collaborating Centre for Mental Health (commissioned by the Social Care Institute for Excellence and the National Institute for Health and Clinical Excellence). Dementia. A NICE-SCIE Guideline on supporting people with dementia and their carers in health and social care. National clinical practice guideline, number 42. London, The British Psychological Society and Gaskell 2007
- ⁸ German Society for Psychiatry, Psychotherapy and Neurology and German Society for Neurology. Consented Guideline "Dementia" [Internet]. 2009. [cited 2010 Oct 26]. Available from: <http://media.dgppn.de/mediadb/media/dgppn/pdf/leitlinien/s3-leitlinie-demenz-lf.pdf>
- ⁹ Work Group on Alzheimer's Disease and other dementias. Practice Guideline for the Treatment of Patients With Alzheimer's Disease and Other Dementias [Internet]. 2007. [cited 2010 Oct 26]. Available from: <http://www.psychiatryonline.com/pracGuide/PracticePDFs/AlzPG101007.pdf>
- ¹⁰ Steultjens EM, Dekker J, Bouter LM, Leemrijse CJ, van den Ende CH. Evidence of the efficacy of occupational therapy in different conditions: an overview of systematic reviews. *Clin Rehabil*. 2005 May;19(3):247-54.
- ¹¹ Voigt-Radloff S. Occupational therapy in dementia. In: Haberstroh J, Pantel J (Ed). Psychosocial treatment in dementia. AKA Verlag Heidelberg: 2011. German
- ¹² World Health Organization: International Classification of Functioning, Disability and Health (ICF) [Internet]. Geneva: 2001. [cited 2010 Oct 26]. Available from: <http://www3.who.int/icf/icfem>
- ¹³ Giovannetti T, Bettcher BM, Libon DJ, Brennan L, Sestito N, Kessler RK. Environmental adaptations improve everyday action performance in Alzheimer's disease: empirical support from performance-based assessment. *Neuropsychology*. 2007;21(4):448-57.
- ¹⁴ Gitlin LN, Winter L, Burke J, Chernett N, Dennis MP, Hauck WW. Tailored activities to manage neuropsychiatric behaviors in persons with dementia and reduce caregiver burden: a randomized pilot study. *Am J Geriatr Psychiatry*. 2008;16(3):229-39.
- ¹⁵ Mittelman MS, Haley WE, Clay OJ, Roth DL. Improving caregiver well-being delays nursing home placement of patients with Alzheimer disease. *Neurology*. 2006;67(9):1592-9.
- ¹⁶ Gitlin LN, Corcoran M, Winter L, Boyce A, Hauck WW. A randomized, controlled trial of a home environmental intervention: effect on efficacy and upset in caregivers and on daily function of persons with dementia. *Gerontologist*. 2001 Feb;41(1):4-14.

- 1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
- ¹⁷ Gitlin LN, Hauck WW, Dennis MP, Winter L. Maintenance of effects of the home environmental skill-building program for family caregivers and individuals with Alzheimer's disease and related disorders. *J Gerontol A Biol Sci Med Sci*. 2005 Mar;60(3):368-74.
- ¹⁸ Gitlin LN, Winter L, Vause Earland T, Adel Herge E, Chernett NL, Piersol CV, Burke JP. The Tailored Activity Program to reduce behavioral symptoms in individuals with dementia: feasibility, acceptability, and replication potential. *Gerontologist*. 2009 Jun;49(3):428-39.
- ¹⁹ Graff MJ, Vernooij-Dassen MJ, Thijssen M, Dekker J, Hoefnagels WH, Olderikkert MG. Effects of community occupational therapy on quality of life, mood, and health status in dementia patients and their caregivers: a randomized controlled trial. *J Gerontol A Biol Sci Med Sci*. 2007;62(9):1002-9.
- ²⁰ Graff MJ, Adang EM, Vernooij-Dassen MJ, Dekker J, Jönsson L, Thijssen M, Hoefnagels WH, Rikkert MG. Community occupational therapy for older patients with dementia and their caregivers: cost effectiveness study. *BMJ*. 2008;336(7636):134-8.
- ²¹ Graff MJL, Melick van MBM: The development, testing and implementation of an occupational therapy guideline. The guideline for the OT diagnosis and treatment of older persons with cognitive impairments. *Nederlands Tijdschrift voor Ergotherapie*. 2000;28:169-74. Dutch
- ²² Graff MJL, Vernooij-Dassen MJFJ, Hoefnagels WHL, Dekker J, Witte de LP. Occupational therapy at home for older individuals with mild to moderate cognitive impairments and their primary caregivers: a pilot study. *Occupational Therapy Journal of Research*. 2003;23:155-63.
- ²³ Graff MJL, Vernooij-Dassen MJ, Zajec J, Olde Rikkert MGM, Hoefnagels WHL, Dekker J. How can occupational therapy improve the daily performance and communication of an older patient with dementia and his primary caregiver? A case study. *Dementia*. 2006;5:503-32.
- ²⁴ German Alzheimer Society. *Leben mit Demenzkranken*. Berlin: 2003. German
- ²⁵ German Alzheimer Society. *Ratgeber Häusliche Versorgung Demenzkranker*. Berlin: 2006. German
- ²⁶ Voigt-Radloff S, Graff M, Leonhart R, Schornstein K, Vernooij-Dassen M, Olde-Rikkert M, Hüll M. WHEDA study: effectiveness of occupational therapy at home for older people with dementia and their caregivers--the design of a pragmatic randomised controlled trial evaluating a Dutch programme in seven German centres. *BMC Geriatr*. 2009 Oct 2;9:44.
- ²⁷ Teunisse S, Derix MM. The interview for deterioration in daily living activities in dementia: agreement between primary and secondary caregivers. *Int Psychogeriatr*. 1997;9(Suppl 1):155-62.

- 1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
- ²⁸ Chapparo C, Ranka J. The PRPP System of Task Analysis: User's Training Manual. In Research Edition Sydney: OP Network; 2006.
- ²⁹ Moniz-Cook E, Vernooij-Dassen M, Woods R, Verhey F, Chattat R, De Vugt M, Mountain G, O'Connell M, Harrison J, Vasse E, Dröes RM, Orrell M; INTERDEM group. A European consensus on outcome measures for psychosocial intervention research in dementia care. *Aging Ment Health*. 2008 Jan;12(1):14-29.
- ³⁰ Wolfson C, Moride Y, Perrault A, Momoli F, Demers L, Oremus M. Drug treatments for Alzheimer's disease. II. A review of outcome measures in clinical trials. Ottawa: Canadian Coordinating Office for Health Technology Assessment (CCOHTA); 2000.
- ³¹ Faul F, Erdfelder E, Lang AG, Buchner A. G*Power 3: A flexible statistical power analysis for the social, behavioral, and biomedical sciences. *Behavior Research Methods*. 2007;39:175-91.
- ³² Allison P. Missing data. Thousand Oaks: Sage; 2002.
- ³³ Plassman BL, Williams JW Jr, Burke JR, Holsinger T, Benjamin S. Systematic review: factors associated with risk for and possible prevention of cognitive decline in later life. *Ann Intern Med*. 2010 Aug 3;153(3):182-93.
- ³⁴ Gitlin LN, Winter L, Dennis MP, Hodgson N, Hauck WW. A biobehavioral home-based intervention and the well-being of patients with dementia and their caregivers: the COPE randomized trial. *JAMA*. 2010 Sep 1;304(9):983-91.
- ³⁵ Smits CH, de Lange J, Dröes RM, Meiland F, Vernooij-Dassen M, Pot AM. Effects of combined intervention programmes for people with dementia living at home and their caregivers: a systematic review. *Int J Geriatr Psychiatry*. 2007 Dec;22(12):1181-93.
- ³⁶ Teri L, Gibbons LE, McCurry SM, Logsdon RG, Buchner DM, Barlow WE, Kukull WA, LaCroix AZ, McCormick W, Larson EB. Exercise plus behavioural management in patients with Alzheimer disease. A randomized controlled trial. *JAMA*. 2003;290:2015-22.
- ³⁷ Gitlin LN, Winter L, Corcoran M, Dennis MP, Schinfeld S, Hauck WW. Effects of the home environmental skill-building program on the caregiver-care recipient dyad: 6-month outcomes from the Philadelphia REACH Initiative. *Gerontologist*. 2003 Aug;43(4):532-46.
- ³⁸ Berger G, Bernhardt T, Schramm U, Müller R, Landsiedel-Anders S, Peters J, Kratzsch T, Frolich L. No effects of a combination of caregivers support group and memory training/music therapy in dementia patients from a memory clinic population. *Int J Geriatr Psychiatry*. 2004 Mar;19(3):223-31.

- 1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
- ³⁹ Rieckmann N, Schwarzbach C, Nocon M, Roll S, Vauth C, Willich SN, Greiner W. Concepts of care for people with dementia [Internet]. *GMS Health Technol Assess* 2009;5:Doc01. [cited 2010 Oct 26]. Available from: <http://www.egms.de/static/en/journals/hta/2009-5/hta000063.shtml>. German
- ⁴⁰ Gauthier S, Lopez OL, Waldemar G, Jones RW, Cummings J, Zhang R, Schindler R, Schwam E. Effects of donepezil on activities of daily living: integrated analysis of patient data from studies in mild, moderate and severe Alzheimer's disease. *Int Psychogeriatr*. 2010 Sep;22(6):973-83.

For peer review only



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.



Journal:	<i>BMJ Open</i>
Manuscript ID:	bmjopen-2011-000096.R2
Article Type:	Research
Date Submitted by the Author:	17-May-2011
Complete List of Authors:	Voigt-Radloff, Sebastian; University Hospital Freiburg, Centre of Geriatric Medicine and Gerontology Freiburg Graff, Maud; Radboud University Nijmegen Medical Centre, Alzheimer Centre Nijmegen Leonhart, Rainer; University of Freiburg, Department of Social Psychology and Methodology Schorstein, Katrin; University of Freiburg, Department of Social Psychology and Methodology Jessen, Frank; University of Bonn, Department of Psychiatry and Psychotherapy Bohlken, Jens; Private Practice for Neurology, Psychiatry and Psychotherapy Metz, Brigitte; Centre of Geriatric Medicine and Geriatric Clinic at Diakonissenkrankenhaus Karlsruhe-Rüppurr Fellgiebel, Andreas; University Medical Center Mainz, Department of Psychiatry and Psychotherapy Dodel, Richard; Philipps-University Marburg, Department of Neurology Eschweiler, Gerhard; Eberhard-Karls University Tuebingen, Department of Psychiatry and Psychotherapy Vernooij-Dassen, Myrra; Radboud University Nijmegen Medical Centre, Alzheimer Centre Nijmegen Olde Rikkert, Marcel; Radboud University Nijmegen Medical Centre, Alzheimer Centre Nijmegen Hüll, Michael; University Hospital Freiburg, Centre of Geriatric Medicine and Gerontology Freiburg
Subject Heading:	Neurology
Keywords:	Dementia < NEUROLOGY, Quality in health care < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, REHABILITATION MEDICINE

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

SCHOLARONE™
Manuscripts

For peer review only

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

Sebastian Voigt-Radloff, Maud Graff, Rainer Leonhart, Katrin Schornstein, Frank Jessen, Jens Bohlken, Brigitte Metz, Andreas Fellgiebel, Richard Dodel, Gerhard Eschweiler, Myrra Vernooij-Dassen, Marcel Olde Rikkert, Michael Hüll

Department of Occupational Therapy, Centre of Geriatric Medicine and Gerontology Freiburg, University Hospital Freiburg, Lehener Str. 88, 79106 Freiburg, Germany Sebastian Voigt-Radloff *scientific researcher in allied healthcare research*

Alzheimer Centre Nijmegen, Scientific Institute for Quality in Health Care and Dept of Rehabilitation-Occupational Therapy, Radboud University Nijmegen Medical Centre, PO Box 9101, 6500 HB Nijmegen, The Netherlands, Maud Graff *senior researcher in allied healthcare research and research on psychosocial interventions in dementia*

Department of Social Psychology and Methodology, University of Freiburg, Engelbergerstr. 41, 79085 Freiburg, Germany Rainer Leonhart *senior researcher in statistics and psychology*

Department of Social Psychology and Methodology, University of Freiburg, Engelbergerstr. 41, 79085 Freiburg, Germany Katrin Schornstein *researcher in statistics and psychology*

Department of Psychiatry and Psychotherapy, University of Bonn, Sigmund-Freud-Str. 25, 53105 Bonn, Germany Frank Jessen *professor in psychiatry*

Private Practice for Neurology, Psychiatry and Psychotherapy, Klosterstr. 34, 13581 Berlin, Germany Jens Bohlken *clinical psychiatrist*

Centre of Geriatric Medicine and Geriatric Clinic at Diakonissenkrankenhaus Karlsruhe-Rüppurr, Diakonissenstr. 28, 76199 Karlsruhe, Germany Brigitte Metz *clinical geriatrician*

Department of Psychiatry and Psychotherapy, University Medical Center Mainz, Untere Zahlbacher Str. 8, 55131 Mainz, Germany Andreas Fellgiebel *professor in psychiatry*

Department of Neurology, Philipps-University Marburg, Rudolf-Bultmannstr. 8, 35039 Marburg, Germany Richard Dodel *professor in neurology*

Department of Psychiatry and Psychotherapy, Eberhard-Karls University Tuebingen, Osianderstr. 24, 72076 Tübingen Germany, Gerhard Eschweiler *professor in psychiatry*

Alzheimer Centre Nijmegen, Scientific Institute for Quality in Health Care, Radboud University Nijmegen Medical Centre, Kalorama Foundation, PO Box 9101, 6525 JV Nijmegen, The Netherlands, Myrra Vernooij-Dassen *professor in psychosocial interventions in frail elderly*

Alzheimer Centre Nijmegen, Department of Geriatrics, Radboud University Nijmegen Medical Centre, PO Box 9101, 6500 HB Nijmegen, The Netherlands, Marcel Olde Rikkert *professor in geriatrics*

Section of Gerontopsychiatry and Neuropsychology, Centre of Geriatric Medicine and Gerontology Freiburg, University Hospital Freiburg, Lehener Str. 88, 79106 Freiburg, Germany, Michael Hüll *professor in psychiatry*

Correspondence to: sebastian.voigt@uniklinik-freiburg.de

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

1
2
3 randomised patients did not reveal significant differences. Consequently, the
4
5 hypothesis of better effects within the experimental group must be rejected.
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For peer review only

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

1
2
3 improving the patient's physical and social environment and by tailoring the
4 intervention to the patient's capability.[12-15]
5
6

7
8 Until March 2011, there was no systematic review on community occupational
9 therapy for people with Alzheimer's disease but two research groups had
10 conducted RCTs in this subject. In the USA study, occupational therapy
11 demonstrated beneficial effects on patients' challenging behaviours but not on
12 ADL. No information on adverse events were given.[14, 16-18] In the
13 Netherlands, occupational therapy, tailored to the needs of patients and carers
14 showed benefits on the patient's ADL, mood, health status and quality of life
15 and on the carer's sense of competence, mood, quality of life and costs of
16 informal care. No adverse events were reported in either intervention or control
17 group.[6, 19-20]
18
19
20
21
22
23
24
25
26
27
28
29
30

31 In the current randomised trial we tested the hypothesis that the Dutch ten-
32 session Community Occupational Therapy in Dementia Programme (COTiD)
33 would significantly improve the daily functioning of people with mild or moderate
34 dementia, more so than a one-session Community Occupational Therapy
35 Consultation (COTC). Secondary research questions were whether these
36 interventions would show a difference in their effect on patient's and primary
37 carer's quality of life and mood; on the carer's sense of competence in the
38 interaction with the patient; and on long-term nursing home placements.
39
40
41
42
43
44
45
46
47
48
49
50

51 52 53 **METHODS**

54 55 56 **Design**

57 In order to evaluate the superiority of COTiD, we used a seven-centre single-
58 blind, active-controlled design with a 1:1 randomisation for two parallel groups.
59
60 There was no modification in design or eligibility criteria from the study protocol

1
2
3 available at <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2761388/>. The study
4
5 was registered at the German register of clinical trials, which is connected to the
6
7 International Clinical Trials Registry Platform (<http://apps.who.int/trialsearch/> =>
8
9 DRKS00000053). The Medical Ethics Committee of the University Hospital
10
11 Freiburg gave ethical approval (no. 110/08).
12
13
14
15

16 17 **Participants and Setting**

18
19 Patients were eligible to participate in the study if they had mild to moderate
20
21 dementia (MMSE 14-24) and were diagnosed as having Alzheimer's disease or
22
23 mixed type dementia, according to ICD-10 criteria, by physicians with more than
24
25 five years of experience in dementia diagnosis. Participants had to dwell in the
26
27 community either together with their primary carer or with involvement of a carer
28
29 providing care at least twice a week. Patients with a score above 12 on the 30-
30
31 items Geriatric Depression Scale or a major need of physical nursing care of
32
33 more than 120 min per day (level 2 or higher according to the German Long-
34
35 Term Care Insurance Act) were excluded. Unstable medical conditions or
36
37 severe behavioural disturbances, which did not allow participation in the study
38
39 as judged by the study physicians were criteria for exclusion as well as for
40
41 discontinuation. Long-term nursing home placements of the patients during the
42
43 treatment phase or death of patient or primary carer were criteria for
44
45 discontinuation. The patient gave written informed consent and the carer
46
47 consented by written format to join and support the treatment procedures.
48
49
50
51
52

53
54 Patients were recruited from five outpatient memory centres at university
55
56 hospitals (in Bonn, Freiburg, Mainz, Marburg and Tübingen); one municipal
57
58 hospital in Karlsruhe specialising in geriatric medicine; and one neurological
59
60 private practice in Berlin specialising in neuropsychiatry and collaborating with

1
2
3 an occupational therapy private practice. The seven participating centres are
4 located throughout Germany in urban regions with catchment areas of about
5 70,000 to 700,000 inhabitants. They had all provided outpatient dementia care
6 for three to fifteen years. Their standard service comprised diagnostic work-up
7 for dementia and related diagnoses as well as recommendation of risk
8 reduction, dementia medication and non-pharmacological treatments. Principal
9 investigators of the centres were psychiatrists, neurologists or geriatricians with
10 six to thirteen years of experience in dementia care.
11
12
13
14
15
16
17
18
19
20
21
22
23
24

25 **Interventions**

26
27 The experimental intervention (COTiD) was designed to improve the patient's
28 and the primary carer's daily functioning, and was based on an evidence-based
29 treatment manual.[6, 19-23] COTiD consisted of ten occupational therapy
30 sessions of one hour duration held over five weeks at each patient's home. In
31 the diagnostic phase, comprising of 3 to 4 sessions, the occupational therapist
32 explored (1) the patient's preferences and history of daily activities, (2) her or
33 his ability to perform activities and to use compensatory strategies within the
34 familiar environment, (3) the possibilities of modifying the patient's home, (4) the
35 carer's activity preferences, problems in care giving, coping strategies and
36 abilities to supervise and (5) the interaction between carer and patient. In a
37 shared decision-making process during the goal setting session, the patient and
38 the carer selected the one or two most meaningful activities out of a list of their
39 preferences for daily activities to work on in occupational therapy. During the
40 treatment phase of 5 to 6 sessions, the occupational therapist defined, together
41 with the patient and the carer, more effective compensatory and environmental
42 strategies to adapt both the environment and the selected activities to the
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3 patient's habits and cognitive abilities. Patient and carer were taught how to use
4 these suggested adaptations within strategies, activities and the environment in
5 order to improve their performance of daily activities. In addition, the carer
6 received practical and emotional support and was coached in effective
7 supervision, problem solving and coping strategies by means of cognitive-
8 behavioural interventions. Detailed description of the experimental intervention
9 has been published elsewhere.[23]

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

20 The control group received one hour occupational therapy consultation (COTC)
21 at the patient's home conducted by the same study interventionists. Based on
22 material of the German Alzheimer Society, two occupational therapists with
23 more than five years of experience in dementia care had prepared a leaflet of
24 ten pages.[24-25] The semi-structured consultation was an explanation of 30
25 min of this leaflet and a talk of 30 min on individual problems that arose from
26 patient's and carer's needs. This included encouragement to stay active in
27 everyday life, to maintain social contacts and to use dementia services in the
28 region for which local addresses were listed in the leaflet. Occupational
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3 therapists were taught the control intervention within a 4-hour seminar.
4
5 Consultations of 30 minutes up to one hour duration about such issues are
6
7 common in German dementia care. Detailed description of the control
8
9 intervention as well as means of quality assurance in experimental and control
10
11 intervention has been published elsewhere.[26]
12
13
14
15
16

17 **Outcome measures**

18
19 The primary endpoint was the patients' change of daily functioning from
20
21 baseline to follow-up time points at week 6, 16 and 26 measured with the
22
23 performance scale of the Interview for Deterioration in Daily Living Activities in
24
25 Dementia (IDDD).[27] This scale records carer rating of the patient's need of
26
27 assistance in the performance of (1) washing oneself, (2) making tea or coffee,
28
29 (3) dressing, (4) combing one's hair and brushing one's teeth, (5) eating, (6)
30
31 using the toilet, (7) shopping, (8) using the telephone, (9) preparing a meal, (10)
32
33 cleaning the house or doing minor repair work and (11) handling finances. Each
34
35 item is rated never=0, seldom=1, sometimes=2, often=3 or always=4. The sum
36
37 of scores ranged from 0 to 44. Higher scores indicated higher need for
38
39 assistance. Since carer rating could not be 'masked', daily functioning was
40
41 additionally evaluated by external raters fully 'blind' to the group assignment.
42
43 They rated video tapes of a challenging daily living task and used the Perceive,
44
45 Recall, Plan and Perform System of Task Analysis (PRPP).[28] For the PRPP,
46
47 raters had to define single steps of the performed activity, and they identified
48
49 any activity step in which errors of accuracy, omission, repetition or timing
50
51 occurred. The number of activity steps rated as incorrectly performed was
52
53 divided by the total number of activity steps, resulting in an independence-score
54
55 indicated in a percentage (100% = all steps are error-free).
56
57
58
59
60

Table 1: Measurements of secondary endpoints²⁶

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

1
2
3 was established in the Netherlands and applied by Dutch raters. There was one
4
5 protocol amendment before recruitment started. The Assessment of Motor and
6
7 Process Skills (AMPS) was replaced by the PRPP, because the AMPS was not
8
9 available in the German language within the planned schedule.
10
11

12 Indicators of harm were defined as patient or carer death, number of patients
13
14 with admission to hospital and number of nights in hospital. These indicators
15
16 were recorded in interviews with the carer at intervals of 5 to 7 weeks over 52
17
18 weeks. Study sites had to report severe adverse events to the study centre
19
20 immediately when each occurred. We did not assume a direct association
21
22 between the defined harms and either the experimental or the control
23
24 intervention. However, increased daily activities in the interventions group might
25
26 have resulted in a higher risk of falls or accidents and thus may indirectly have
27
28 led to more nights in hospital or in the worst case to death.
29
30
31
32
33

34 35 36 **Sample size calculation**

37
38 A sample size of 42 participants per group was calculated to be necessary to
39
40 detect an effect size of $f = 0.10$ on the IDDD performance scale in an analysis of
41
42 variance of two groups and four time points; using a two-sided 5% significance
43
44 level, a power of 80%, and a correlation of 0.7 between the measurement time
45
46 points [31]. According to the Dutch original RCT, we expected a dropout rate of
47
48 10% at week 16, which was extrapolated to 40% at week 52. A nine-month
49
50 inclusion period was anticipated as necessary in order to recruit the 140
51
52 patients. Our assumed effect size of $f = 0.10$ is based on a group by time
53
54 interaction and compatible to Cohen's $d = 0.20$, which corresponds to a small
55
56 effect size and any d over 0.8 is large. Although the Dutch original RCT found
57
58
59
60

1
2
3 effect sizes of $d = 2.4$ in the IDDD performance scale at week 12, for this study
4
5 the power was calculated much more conservatively.
6

7
8 This was because we (1) introduced an active control group, (2) investigated
9
10 the programme effects under varying care conditions in seven centres with
11
12 interventionists who were introduced in this new treatment and were far not as
13
14 experienced as the Dutch study therapists and (3) we prolonged the follow up
15
16 period. Interim analyses were not planned.
17
18

21 22 **Randomisation and masking**

23
24 The random allocation sequence was computer-generated with blocking by
25
26 centre and groups of two persons, without stratification and in a ratio of 1:1 by a
27
28 statistician from a distant site. After enrolment, study site physicians requested
29
30 randomisation via e-mail. The statistician e-mailed the individual allocation to
31
32 COTiD or COTC exclusively to the site interventionist and stored the allocation
33
34 list at his distant site which was not available to any study site staff. The
35
36 interventionist scheduled treatment sessions, faxed records to the distant
37
38 coordinating study centre and kept all documents strictly separated from any
39
40 other site staff. This was in order to avoid contamination. Since the numbers of
41
42 home visits differed in the experimental and control groups, masking of patients
43
44 and carers was not possible. However, study information did not include any
45
46 preference for a special treatment 'arm'. Patients and carers were asked to give
47
48 no information about their treatment package to assessors or study physicians.
49
50 All study personal was 'blind' for group assignment, except the interventionists.
51
52 Agreement between the assessors' estimation of group assignment and the
53
54 actual group assignment was 61%, and thus slightly over the expected 50% of
55
56 agreement by chance. The procedure of external video rating ensured the full
57
58
59
60

1
2
3 'blinding' of the external raters for the PRPP primary outcome measure.
4
5 Independent research assistants cleaned the videotapes of any hint of group
6
7 assignment before they were rated by two Dutch raters not involved in the trial
8
9 treatment. In order to establish the inter-rater reliability, we tested ten double
10
11 ratings of the same video by the two raters and found an intra-class correlation
12
13 coefficient of 0.9. Data analysts were not 'blind' for the group assignment.
14
15 However, measurement time points and outcomes had been published before
16
17 data were available for analysis [26] and any decision to remove patients from
18
19 the analyses is reported in the present publication.
20
21
22
23
24
25
26

27 **Statistical methods**

28
29 Data were entered via special MS Access entry masks automatically controlling
30
31 for data plausibility. In addition, sections of entered data were checked for
32
33 typing errors by hand, in order to ensure an error rate lower than 0.2%. The
34
35 primary intention-to-treat analysis included all allocated participants with valid
36
37 data whether they did or did not receive the complete intervention. For the IDDD
38
39 and the PRPP measurements of the primary outcome, we performed a
40
41 multivariate analysis of variance (MANOVA) with repeated measures with two
42
43 groups and four measurement time points at baseline, week 6, 16 and 26. A
44
45 univariate ANOVA with five measurement time points (+ postal assessment in
46
47 week 52) was carried out for the secondary outcomes and the IDDD. We did not
48
49 adjust for baseline values, because we found no marked group differences. In
50
51 order to deal with missing data occurring not in the primary but in the secondary
52
53 outcomes, we performed secondary intention-to-treat analyses with multiple
54
55 data imputation using the Full Information Maximum Likelihood (FIML)
56
57 method.[32] We imputed data for all secondary outcome measurements and all
58
59
60

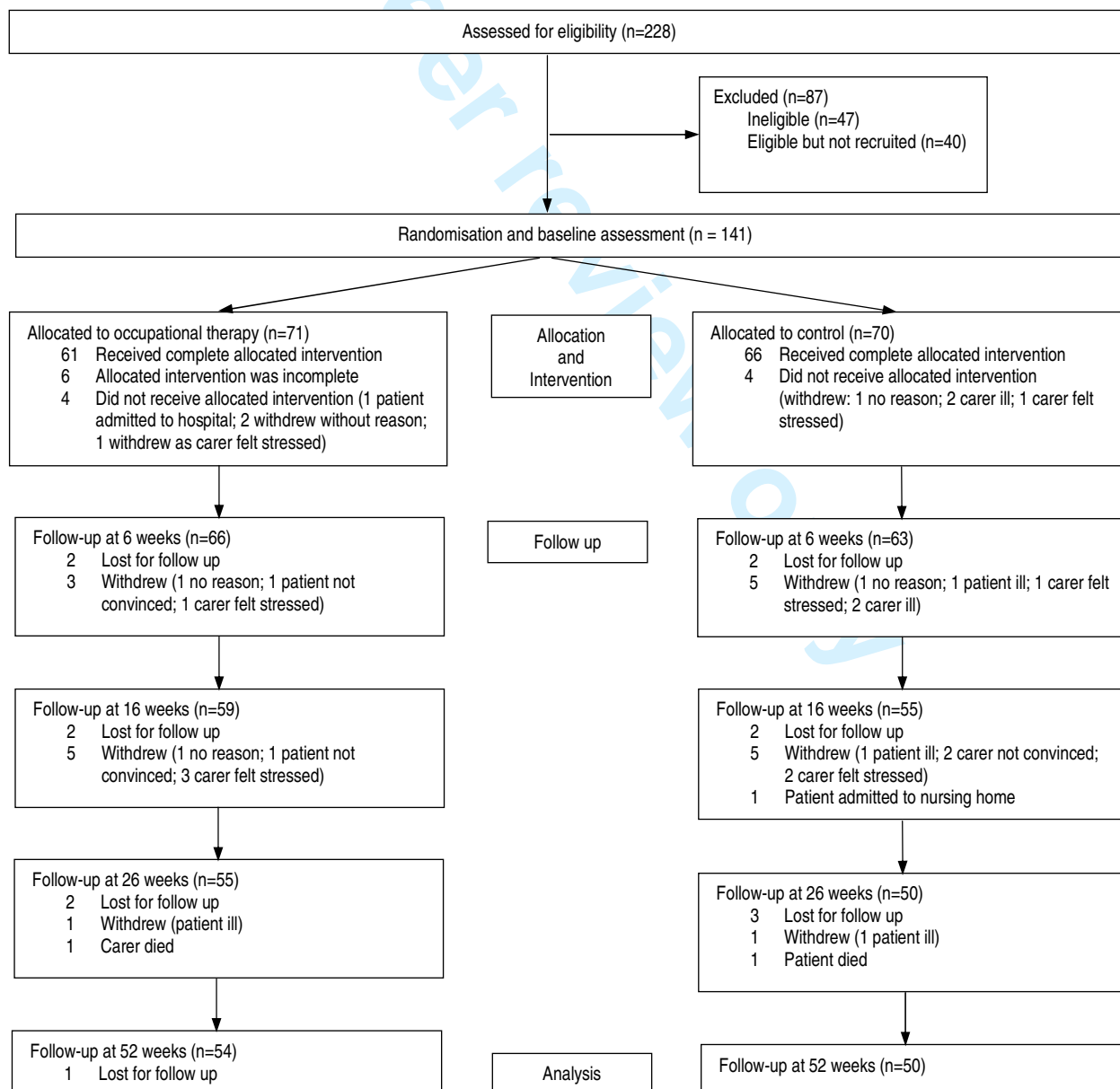
time points using SPSS (version 19). All statistical tests were two-sided on an alpha level of 0.05. Subgroup analyses were not planned.

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

1
2
3 lost before intervention. Six patient-carer dyads in the COTiD had less than 10
4 sessions. Interventionists rated the delivery of 20 pre-defined treatment sub-
5 processes, ranging from interviewing patient and carer to training of simplified
6 activities or supporting the carer in supervision. They scored treatment delivery
7 as 78% in the COTiD group and 80% in the control group. Interventionists rated
8 the patient's adherence in 67 cases of the COTiD group, from 15 as hindering
9 the delivery of treatment; 26 as neutral and 26 as facilitating. Rating criteria
10 were the patient's cooperation during interview, goal setting and training; the
11 daily changing mental capacity; collaboration with the carer; and the acceptance
12 of innovations. Ratings of carers' adherence were 5 hindering; 15 neutral; and
13 47 facilitating. The carer adherence was assessed with regard to the
14 cooperation during scheduling, interview, goal setting and training to supervise;
15 the encouragement of the patient; the acceptance of support service; and the
16 implementation of innovations. The adherence of the participants in the control
17 group could not be rated, because interventionists had no further contact after
18 the consultation.

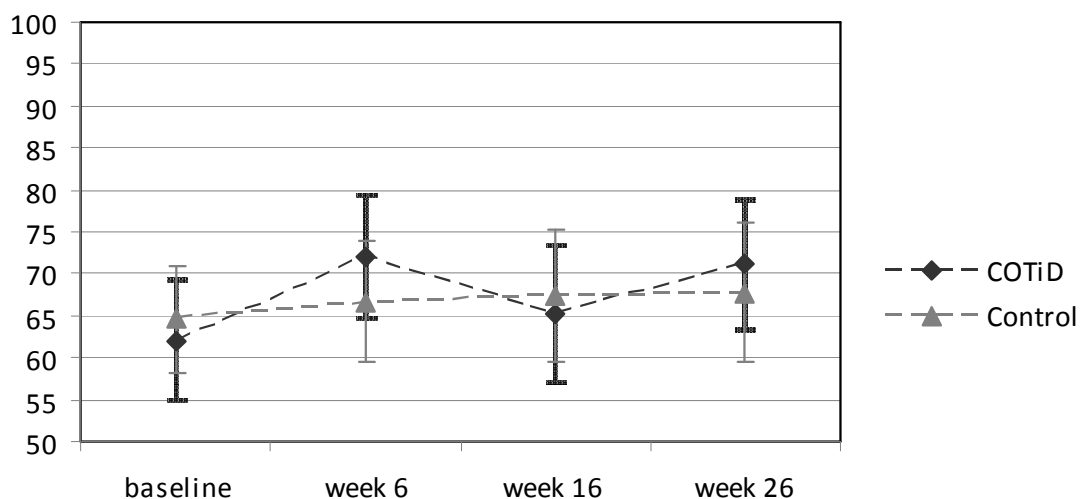
43 **Outcomes**

44
45 The MANOVA in 104 completers (COTiD: n=54; control: n=50) revealed no
46 significant group time interaction effect in the primary outcome measurements
47 of patients' daily functioning (Figures 2 and 3). Using the arcsine transform [34]
48 for the PRPR percentage did not change results (original: $p = 0.243$; arcsine-
49 transform: $p = 0.216$). An additional mixed models analysis of all randomised
50 patients (N=141) as recommended by Coley and colleagues [35] did reveal no
51 significant interactions for the IDDD ($p=0.340$) and the PRPP ($p=0.785$). Tables
52 3 and 4 show mean, standard deviation and group difference including 95%-
53
54
55
56
57
58
59
60

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.

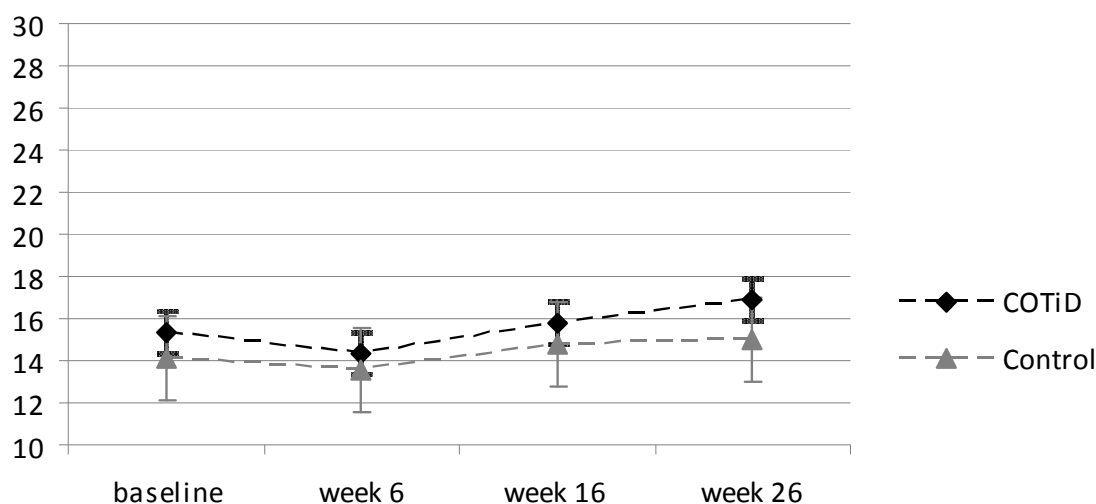
Figure 2: ADL task performance of Alzheimer patients following intense occupational therapy compared with a single session control intervention; means and 95%-confidence intervals of the PRPP independence scale (N=104 completers; range: 100=no errors to 0=all errors)



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

1
2
3 matters and approval of the local ethic commissions. Therefore, a common repetition
4 seminar for the interventionists could not be arranged after the pilot training. This
5 may have led to some heterogeneity in the intervention, especially because in
6 Germany eleven newly introduced interventionists performed the treatment
7 compared to two experienced experts in the original Dutch trial. We addressed this
8 problem with feedback on videos of treatment sessions the interventionists sent in.
9 Furthermore, we arranged telephone supervision on demand.

10 We consider the contamination of the control intervention with knowledge from the
11 experimental intervention to be low, because any specific intervention such as
12 activity selection, simplification or training was precluded by the limited time to carry
13 out the control intervention.
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29

30 **Comparison**

31
32 The Dutch RCT on the COTiD with waiting-control-group design showed large effect
33 sizes in the IDDD performance scale at six and twelve weeks after baseline ($d=2.3$
34 and 2.4 , respectively).[6] The Dutch and the German sample did not differ
35 remarkably in cognition at baseline (MMSE: 19 v 20), but did differ in the need of
36 assistance (IDDD performance: 24 v 15). The German patients showed a low need of
37 assistance at the beginning of the study. This was comparable to the IDDD values of
38 the Dutch patients at the end of the treatment. This may have caused a floor effect
39 on the IDDD. Another mono-centre RCT in the USA compared community
40 occupational therapy and a less intensive telephone consultation in patients with
41 probable dementia (MMSE: 13).[36] The authors found a small effect size in daily
42 functioning ($d=0.21$). The initial need of assistance in both studies was higher than in
43 the German sample. A systematic review of community programmes in dementia [37]
44 reported one study on exercise and behavioural management with beneficial effects
45 on daily functioning of patients with moderate dementia (MMSE: 17); one trial on
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3 occupational therapy with heterogeneous effects; and two studies on occupational
4 therapy and music therapy with no significant effects. A current German health
5 technology assessment on non-drug therapies in Alzheimer's disease did not identify
6 further community occupational therapy trials [38]. The comparison of community
7 intervention trials reveals that study samples with a lower MMSE and a higher need
8 of assistance benefit more than those with initial higher cognitive and daily
9 functioning. Similarly, a standardized synopsis of ADL outcomes in pharmacological
10 dementia trials indicated that samples with an MMSE between 17 and 10 benefit
11 most in ADL while samples with higher MMSE scores showed less effects.[39]
12
13 However, different baseline scores of cognitive and daily functioning alone cannot
14 explain the major difference between the findings in this German study and the
15 positive results of the Dutch RCT. Detailed process evaluation and exploratory
16 analyses of the study data might show whether variations in study site context and
17 treatment performance influenced the intervention's effectiveness.
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36

37 **Clinical and research implications**

38
39 Published evidence for the effectiveness of community occupational therapy in
40 dementia is heterogeneous as indicated by a Dutch trial with large positive effects on
41 daily functioning; a few USA trials with no or small positive effects on ADL and this
42 German study showing that ten sessions were not superior to one consultation. A
43 preventative one-session consultation might be hypothesised as beneficial for people
44 with mild dementia and an improved 10-session programme more specifically
45 adapted to the German health care system as beneficial for dementia patients with
46 moderate need of assistance in ADL, as was shown in the Dutch study in which most
47 people with dementia had moderate to high need for assistance at baseline.
48
49
50
51
52
53
54
55
56
57
58
59
60

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

1
2
3 variance in treatment performance in several centres, (3) a prolonged follow up time
4
5 and (4) rigorous reduction of the analysed sample to participants with valid data, it
6
7 remains surprising that significant group difference could not be found in any of the
8
9 primary or secondary outcomes.
10
11

12 This study has shown that careful cross-national comparisons are greatly needed,
13
14 especially in complex interventions, before they can be considered evidence based
15
16 and implemented effectively in other health care systems. Therefore, further analyses
17
18 must investigate the role of interventionists' expertise and treatment performance,
19
20 and the role of participants' needs and utilisation of health care resources, before
21
22 conclusions on international implementation of this intense occupational therapy
23
24 intervention can be drawn.
25
26
27
28
29
30

31 **Acknowledgement:** We thank all participants and interventionists for their contribution. We
32
33 acknowledge Professor Chris Mayers, Research Fellow, Faculty of Health & Life Sciences, York St
34
35 John University, UK, for critical reading and English correction.
36

37 **Funding:** German Federal Ministry of Health, Reference Number: IIA5-2508FSB111/44-004.
38

39 **Contributors:** SVR, MG, RL, GE and MH contributed to study conception and design. FJ, JB, BM, AF,
40
41 RD, GE and MH acquired data. SVR and KS participated in data and study management and
42
43 prepared the statistical analysis. RL performed the statistical analysis. SVR drafted the manuscript.
44
45 RL, MG, FJ, JB, BM, AF, RD, GE, MOR, MVD and MH revised the manuscript critically for important
46
47 intellectual content. All authors read and approved the final manuscript.
48

49 **Competing interests:** SVR, RL, KS, JB, AF, MG and MVD non declared. FJ membership in DSMB of
50
51 AC-immune; payment for lectures from Pfizer, Esai and Novartis. BM payment for lectures from
52
53 various pharmaceutical companies. RD consultancy, grants, payment for lectures, patents, meeting
54
55 expenses from various pharmaceutical companies; royalties and patents from University of Marburg.
56
57 GE grants from AC-immune and Janssen-AL. MOR consultancy for Jansen-Cilag and Numico. MH
58
59 grants from Wyeth, Pfizer and Medivation, payment for lectures from Wyeth, Pfizer and Merz.
60

1
2
3 **Data sharing statement:** Complete data sets can be provided on request for research fellows in
4 scope of collaborative projects and publications.
5
6
7

8
9 “The Corresponding Author has the right to grant on behalf of all authors and does grant on behalf of
10 all authors, an exclusive licence (or non-exclusive for government employees) on a worldwide basis to
11 the BMJ Group and co-owners or contracting owning societies (where published by the BMJ Group on
12 their behalf), and its Licensees to permit this article (if accepted) to be published in the BMJ open and
13 any other BMJ Group products and to exploit all subsidiary rights, as set out in our licence.”
14
15
16
17
18

19
20
21 **References**
22

- 23 ¹ Wancata J, Musalek M, Alexandrowicz R, Krautgartner M. Number of dementia sufferers in Europe
24 between the years 2000 and 2050. *Eur Psychiatry*. 2003;18:306-313.
25
26 ² Wimo A, Jonsson L, Winblad B. An estimate of the worldwide prevalence and direct costs of
27 dementia in 2003. *Dement Geriatr Cogn Disord*. 2006;21(3):175-81.
28
29 ³ European Medicines Agency. Guideline on Medicinal Products for the Treatment of Alzheimer's
30 Disease and other Dementias [Internet]. London: 2008. Doc. Ref. CPMP/EWP/553/95 Rev. 1
31 [cited 2010 Oct 26]. Available from: <http://www.emea.europa.eu/pdfs/human/ewp/055395en.pdf>
32
33 ⁴ Georges J, Jansen S, Jackson J, Meyrieux A, Sadowska A, Selmes M. Alzheimer's disease in real
34 life--the dementia carer's survey. *Int J Geriatr Psychiatry*. 2008 May;23(5):546-51
35
36 ⁵ Voigt-Radloff S, Hüll M. Daily functioning in dementia: Pharmacological and non-pharmacological
37 interventions demonstrate small effects on heterogeneous scales – a synopsis of four health
38 technology assessments of the German Institute for Quality and Efficiency in Health Care
39 regarding the endpoint activities of daily living. *Psychiatr Prax*. 2011 Mar 21. [Epub ahead of
40 print]. German.
41
42 ⁶ Graff MJ, Vernooij-Dassen MJ, Thijssen M, Dekker J, Hoefnagels WH, Rikkert MG. Community
43 based occupational therapy for patients with dementia and their care givers: randomised
44 controlled trial. *BMJ*. 2006;333(7580):1196.
45
46 ⁷ National Collaborating Centre for Mental Health (commissioned by the Social Care Institute for
47 Excellence and the National Institute for Health and Clinical Excellence). Dementia. A NICE-
48 SCIE Guideline on supporting people with dementia and their carers in health and social care.
49
50
51
52
53
54
55
56
57
58
59
60

- 1
2
3 National clinical practice guideline, number 42. London, The British Psychological Society and
4
5 Gaskell 2007
6
- 7⁸ German Society for Psychiatry, Psychotherapy and Neurology and German Society for Neurology.
8
9 Consented Guideline "Dementia" [Internet]. 2009. [cited 2010 Oct 26]. Available from:
10
11 <http://media.dgppn.de/mediadb/media/dgppn/pdf/leitlinien/s3-leitlinie-demenz-lf.pdf>
12
- 13⁹ Work Group on Alzheimer's Disease and other dementias. Practice Guideline for the Treatment of
14
15 Patients With Alzheimer's Disease and Other Dementias [Internet]. 2007. [cited 2010 Oct 26].
16
17 Available from: <http://www.psychiatryonline.com/pracGuide/PracticePDFs/AlzPG101007.pdf>
18
- 19¹⁰ Steultjens EM, Dekker J, Bouter LM, Leemrijse CJ, van den Ende CH. Evidence of the efficacy of
20
21 occupational therapy in different conditions: an overview of systematic reviews. *Clin Rehabil*.
22
23 2005 May;19(3):247-54.
24
- 25¹¹ Voigt-Radloff S. Occupational therapy in dementia. In: Haberstroh J, Pantel J (Ed). Psychosocial
26
27 treatment in dementia. AKA Verlag Heidelberg: 2011. German
28
- 29¹² World Health Organization: International Classification of Functioning, Disability and Health (ICF)
30
31 [Internet]. Geneva: 2001. [cited 2010 Oct 26]. Available from: <http://www3.who.int/icf/icfitem>
32
- 33¹³ Giovannetti T, Bettcher BM, Libon DJ, Brennan L, Sestito N, Kessler RK. Environmental adaptations
34
35 improve everyday action performance in Alzheimer's disease: empirical support from
36
37 performance-based assessment. *Neuropsychology*. 2007;21(4):448-57.
38
- 39¹⁴ Gitlin LN, Winter L, Burke J, Chernett N, Dennis MP, Hauck WW. Tailored activities to manage
40
41 neuropsychiatric behaviors in persons with dementia and reduce caregiver burden: a
42
43 randomized pilot study. *Am J Geriatr Psychiatry*. 2008;16(3):229-39.
44
- 45¹⁵ Mittelman MS, Haley WE, Clay OJ, Roth DL. Improving caregiver well-being delays nursing home
46
47 placement of patients with Alzheimer disease. *Neurology*. 2006;67(9):1592-9.
48
- 49¹⁶ Gitlin LN, Corcoran M, Winter L, Boyce A, Hauck WW. A randomized, controlled trial of a home
50
51 environmental intervention: effect on efficacy and upset in caregivers and on daily function of
52
53 persons with dementia. *Gerontologist*. 2001 Feb;41(1):4-14.
54
- 55¹⁷ Gitlin LN, Hauck WW, Dennis MP, Winter L. Maintenance of effects of the home environmental skill-
56
57 building program for family caregivers and individuals with Alzheimer's disease and related
58
59 disorders. *J Gerontol A Biol Sci Med Sci*. 2005 Mar;60(3):368-74.
60

- 1
2
3 18 Gitlin LN, Winter L, Vause Earland T, Adel Herge E, Chernett NL, Piersol CV, Burke JP. The
4
5 Tailored Activity Program to reduce behavioral symptoms in individuals with dementia:
6
7 feasibility, acceptability, and replication potential. *Gerontologist*. 2009 Jun;49(3):428-39.
8
9 19 Graff MJ, Vernooij-Dassen MJ, Thijssen M, Dekker J, Hoefnagels WH, Olderikkert MG. Effects of
10
11 community occupational therapy on quality of life, mood, and health status in dementia patients
12
13 and their caregivers: a randomized controlled trial. *J Gerontol A Biol Sci Med Sci*.
14
15 2007;62(9):1002-9.
16
17 20 Graff MJ, Adang EM, Vernooij-Dassen MJ, Dekker J, Jönsson L, Thijssen M, Hoefnagels WH,
18
19 Rikkert MG. Community occupational therapy for older patients with dementia and their care
20
21 givers: cost effectiveness study. *BMJ*. 2008;336(7636):134-8.
22
23 21 Graff MJL, Melick van MBM: The development, testing and implementation of an occupational
24
25 therapy guideline. The guideline for the OT diagnosis and treatment of older persons with
26
27 cognitive impairments. *Nederlands Tijdschrift voor Ergotherapie*. 2000;28:169-74. Dutch
28
29 22 Graff MJL, Vernooij-Dassen MJFJ, Hoefnagels WHL, Dekker J, Witte de LP. Occupational therapy
30
31 at home for older individuals with mild to moderate cognitive impairments and their primary
32
33 caregivers: a pilot study. *Occupational Therapy Journal of Research*. 2003;23:155-63.
34
35 23 Graff MJL, Vernooij-Dassen MJ, Zajec J, Olde Rikkert MGM, Hoefnagels WHL, Dekker J. How can
36
37 occupational therapy improve the daily performance and communication of an older patient with
38
39 dementia and his primary caregiver? A case study. *Dementia*. 2006;5:503-32.
40
41 24 German Alzheimer Society. *Leben mit Demenzkranken*. Berlin: 2003. German
42
43 25 German Alzheimer Society. *Ratgeber Häusliche Versorgung Demenzkranker*. Berlin: 2006. German
44
45 26 Voigt-Radloff S, Graff M, Leonhart R, Schornstein K, Vernooij-Dassen M, Olde-Rikkert M, Hüll M.
46
47 WHEDA study: effectiveness of occupational therapy at home for older people with dementia
48
49 and their caregivers--the design of a pragmatic randomised controlled trial evaluating a Dutch
50
51 programme in seven German centres. *BMC Geriatr*. 2009 Oct 2;9:44.
52
53 27 Teunisse S, Derix MM. The interview for deterioration in daily living activities in dementia:
54
55 agreement between primary and secondary caregivers. *Int Psychogeriatr*. 1997;9(Suppl 1):155-
56
57 62.
58
59 28 Chapparo C, Ranka J. The PRPP System of Task Analysis: User's Training Manual. In *Research*
60
Edition Sydney: OP Network; 2006.

- 1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
- ²⁹ Moniz-Cook E, Vernooij-Dassen M, Woods R, Verhey F, Chattat R, De Vugt M, Mountain G, O'Connell M, Harrison J, Vasse E, Dröes RM, Orrell M; INTERDEM group. A European consensus on outcome measures for psychosocial intervention research in dementia care. *Aging Ment Health*. 2008 Jan;12(1):14-29.
- ³⁰ Wolfson C, Moride Y, Perrault A, Momoli F, Demers L, Oremus M. Drug treatments for Alzheimer's disease. II. A review of outcome measures in clinical trials. Ottawa: Canadian Coordinating Office for Health Technology Assessment (CCOHTA); 2000.
- ³¹ Faul F, Erdfelder E, Lang AG, Buchner A. G*Power 3: A flexible statistical power analysis for the social, behavioral, and biomedical sciences. *Behavior Research Methods*. 2007;39:175-91.
G*POWER free software available from <http://www.psych.uni-duesseldorf.de/abteilungen/aap/gpower3/>
- ³² Allison P. Missing data. Thousand Oaks: Sage; 2002.
- ³³ Plassman BL, Williams JW Jr, Burke JR, Holsinger T, Benjamin S. Systematic review: factors associated with risk for and possible prevention of cognitive decline in later life. *Ann Intern Med*. 2010 Aug 3;153(3):182-93.
- ³⁴ Howell, DC (1997). Statistical methods for psychology. Fourth Edition. Wadsworth:Belmont,CA.
- ³⁵ Coley N, Gardette V, Cantet C, Gillette-Guyonnet S, Nourhashemi F, Vellas B, Andrieu S. How should we deal with missing data in clinical trials involving Alzheimer's disease patients? *Curr Alzheimer Res*. 2011 Jan 19. [Epub ahead of print]
- ³⁶ Gitlin LN, Winter L, Dennis MP, Hodgson N, Hauck WW. A biobehavioral home-based intervention and the well-being of patients with dementia and their caregivers: the COPE randomized trial. *JAMA*. 2010 Sep 1;304(9):983-91.
- ³⁷ Smits CH, de Lange J, Dröes RM, Meiland F, Vernooij-Dassen M, Pot AM. Effects of combined intervention programmes for people with dementia living at home and their caregivers: a systematic review. *Int J Geriatr Psychiatry*. 2007 Dec;22(12):1181-93.
- ³⁸ Rieckmann N, Schwarzbach C, Nocon M, Roll S, Vauth C, Willich SN, Greiner W. Concepts of care for people with dementia [Internet]. *GMS Health Technol Assess* 2009;5:Doc01. [cited 2010 Oct 26]. Available from: <http://www.egms.de/static/en/journals/hta/2009-5/hta000063.shtml>. German
- ³⁹ Gauthier S, Lopez OL, Waldemar G, Jones RW, Cummings J, Zhang R, Schindler R, Schwam E. Effects of donepezil on activities of daily living: integrated analysis of patient data from studies in mild, moderate and severe Alzheimer's disease. *Int Psychogeriatr*. 2010 Sep;22(6):973-83.



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.



Journal:	<i>BMJ Open</i>
Manuscript ID:	bmjopen-2011-000096.R3
Article Type:	Research
Date Submitted by the Author:	15-Jun-2011
Complete List of Authors:	Voigt-Radloff, Sebastian; University Hospital Freiburg, Centre of Geriatric Medicine and Gerontology Freiburg Graff, Maud; Radboud University Nijmegen Medical Centre, Alzheimer Centre Nijmegen Leonhart, Rainer; University of Freiburg, Department of Social Psychology and Methodology Schorstein, Katrin; University of Freiburg, Department of Social Psychology and Methodology Jessen, Frank; University of Bonn, Department of Psychiatry and Psychotherapy Bohlken, Jens; Private Practice for Neurology, Psychiatry and Psychotherapy Metz, Brigitte; Centre of Geriatric Medicine and Geriatric Clinic at Diakonissenkrankenhaus Karlsruhe-Rüppurr Fellgiebel, Andreas; University Medical Center Mainz, Department of Psychiatry and Psychotherapy Dodel, Richard; Philipps-University Marburg, Department of Neurology Eschweiler, Gerhard; Eberhard-Karls University Tuebingen, Department of Psychiatry and Psychotherapy Vernooij-Dassen, Myrra; Radboud University Nijmegen Medical Centre, Alzheimer Centre Nijmegen Olde Rikkert, Marcel; Radboud University Nijmegen Medical Centre, Alzheimer Centre Nijmegen Hüll, Michael; University Hospital Freiburg, Centre of Geriatric Medicine and Gerontology Freiburg
Primary Subject Heading:	Neurology
Keywords:	Dementia < NEUROLOGY, Quality in health care < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, REHABILITATION MEDICINE

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

SCHOLARONE™
Manuscripts

For peer review only

1
2
3 **A multi-centre RCT on community occupational therapy in Alzheimer's**
4 **disease: Ten sessions are not superior to one consultation.**
5
6

7 Sebastian Voigt-Radloff, Maud Graff, Rainer Leonhart, Katrin Schornstein, Frank Jessen, Jens
8 Bohlken, Brigitte Metz, Andreas Fellgiebel, Richard Dodel, Gerhard Eschweiler, Myrra Vernooij-
9 Dassen, Marcel Olde Rikkert, Michael Hüll

10
11 Department of Occupational Therapy, Centre of Geriatric Medicine and Gerontology Freiburg,
12 University Hospital Freiburg, Lehener Str. 88, 79106 Freiburg, Germany Sebastian Voigt-
13 Radloff *scientific researcher in allied healthcare research*

14
15 Alzheimer Centre Nijmegen, Scientific Institute for Quality in Health Care and Dept of
16 Rehabilitation-Occupational Therapy, Radboud University Nijmegen Medical Centre, PO Box
17 9101, 6500 HB Nijmegen, The Netherlands, Maud Graff *senior researcher in allied healthcare*
18 *research and research on psychosocial interventions in dementia*

19
20 Department of Social Psychology and Methodology, University of Freiburg, Engelbergerstr. 41,
21 79085 Freiburg, Germany Rainer Leonhart *senior researcher in statistics and psychology*

22
23 Department of Social Psychology and Methodology, University of Freiburg, Engelbergerstr. 41,
24 79085 Freiburg, Germany Katrin Schornstein *researcher in statistics and psychology*

25
26 Department of Psychiatry and Psychotherapy, University of Bonn, Sigmund-Freud-Str. 25,
27 53105 Bonn, Germany Frank Jessen *professor in psychiatry*

28
29 Private Practice for Neurology, Psychiatry and Psychotherapy, Klosterstr. 34, 13581 Berlin,
30 Germany Jens Bohlken *clinical psychiatrist*

31
32 Centre of Geriatric Medicine and Geriatric Clinic at Diakonissenkrankenhaus Karlsruhe-Rüppurr,
33 Diakonissenstr. 28, 76199 Karlsruhe, Germany Brigitte Metz *clinical geriatrician*

34
35 Department of Psychiatry and Psychotherapy, University Medical Center Mainz, Untere
36 Zahlbacher Str. 8, 55131 Mainz, Germany Andreas Fellgiebel *professor in psychiatry*

37
38 Department of Neurology, Philipps-University Marburg, Rudolf-Bultmannstr. 8, 35039 Marburg,
39 Germany Richard Dodel *professor in neurology*

40
41 Department of Psychiatry and Psychotherapy, Eberhard-Karls University Tuebingen,
42 Osianderstr. 24, 72076 Tübingen Germany, Gerhard Eschweiler *professor in psychiatry*

43
44 Alzheimer Centre Nijmegen, Scientific Institute for Quality in Health Care, Radboud University
45 Nijmegen Medical Centre, Kalorama Foundation, PO Box 9101, 6525 JV Nijmegen, The
46 Netherlands, Myrra Vernooij-Dassen *professor in psychosocial interventions in frail elderly*

47
48 Alzheimer Centre Nijmegen, Department of Geriatrics, Radboud University Nijmegen Medical
49 Centre, PO Box 9101, 6500 HB Nijmegen, The Netherlands, Marcel Olde Rikkert *professor in*
50 *geriatrics*

51
52 Section of Gerontopsychiatry and Neuropsychology, Centre of Geriatric Medicine and
53 Gerontology Freiburg, University Hospital Freiburg, Lehener Str. 88, 79106 Freiburg, Germany,
54 Michael Hüll *professor in psychiatry*

55 Correspondence to: sebastian.voigt@uniklinik-freiburg.de

56
57 Keywords: Alzheimer Disease – Occupational Therapy – Randomized Controlled Trial

58
59 Words: 3544

60
International Clinical Trials Registry Platform, DRKS00000053;

Funded by the German Federal Ministry of Health

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

1
2
3 randomised patients did not reveal significant differences. Consequently, the
4
5 hypothesis of better effects within the experimental group must be rejected.
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For peer review only

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

1
2
3 negative impact of cognitive deficits on activities can be diminished by
4
5 improving the patient's physical and social environment and by tailoring the
6
7 intervention to the patient's capability.[12-15]
8
9

10
11 Until March 2011, there was no systematic review on community occupational
12
13 therapy for people with Alzheimer's disease but two research groups had
14
15 conducted RCTs in this subject. In the USA study, occupational therapy
16
17 demonstrated beneficial effects on patients' challenging behaviours but not on
18
19 ADL. No information on adverse events were given.[14, 16-18] In the
20
21 Netherlands, occupational therapy, tailored to the needs of patients and carers
22
23 showed benefits on the patient's ADL, mood, health status and quality of life
24
25 and on the carer's sense of competence, mood, quality of life and costs of
26
27 informal care. No adverse events were reported in either intervention or control
28
29 group.[6, 19-20]
30
31
32

33
34 In the current randomised trial we tested the hypothesis that the Dutch ten-
35
36 session Community Occupational Therapy in Dementia Programme (COTiD)
37
38 would significantly improve the daily functioning of people with mild or moderate
39
40 dementia, more so than a one-session Community Occupational Therapy
41
42 Consultation (COTC). Secondary research questions were whether these
43
44 interventions would show a difference in their effect on patient's and primary
45
46 carer's quality of life and mood; on the carer's sense of competence in the
47
48 interaction with the patient; and on long-term nursing home placements.
49
50
51
52
53
54

55 **METHODS**

56 **Design**

57
58 In order to evaluate the superiority of COTiD, we used a seven-centre single-
59
60 blind, active-controlled design with a 1:1 randomisation for two parallel groups.

1
2
3 There was no modification in design or eligibility criteria from the study protocol
4 available at <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2761388/>. The study
5
6 was registered at the German register of clinical trials, which is connected to the
7
8 International Clinical Trials Registry Platform (<http://apps.who.int/trialsearch/> =>
9
10 DRKS00000053). The Medical Ethics Committee of the University Hospital
11
12 Freiburg gave ethical approval (no. 110/08).
13
14
15
16
17
18
19

20 **Participants and Setting**

21
22 Patients were eligible to participate in the study if they had mild to moderate
23
24 dementia (MMSE 14-24) and were diagnosed as having Alzheimer's disease or
25
26 mixed type dementia, according to ICD-10 criteria, by physicians with more than
27
28 five years of experience in dementia diagnosis. Participants had to dwell in the
29
30 community either together with their primary carer or with involvement of a carer
31
32 providing care at least twice a week. Patients with a score above 12 on the 30-
33
34 items Geriatric Depression Scale or a major need of physical nursing care of
35
36 more than 120 min per day (level 2 or higher according to the German Long-
37
38 Term Care Insurance Act) were excluded. Unstable medical conditions or
39
40 severe behavioural disturbances, which did not allow participation in the study
41
42 as judged by the study physicians were criteria for exclusion as well as for
43
44 discontinuation. Long-term nursing home placements of the patients during the
45
46 treatment phase or death of patient or primary carer were criteria for
47
48 discontinuation. The patient gave written informed consent and the carer
49
50 consented by written format to join and support the treatment procedures.
51
52
53
54
55
56

57 Patients were recruited from five outpatient memory centres at university
58
59 hospitals (in Bonn, Freiburg, Mainz, Marburg and Tübingen); one municipal
60
hospital in Karlsruhe specialising in geriatric medicine; and one neurological

1
2
3 private practice in Berlin specialising in neuropsychiatry and collaborating with
4 an occupational therapy private practice. The seven participating centres are
5 located throughout Germany in urban regions with catchment areas of about
6 70,000 to 700,000 inhabitants. They had all provided outpatient dementia care
7 for three to fifteen years. Their standard service comprised diagnostic work-up
8 for dementia and related diagnoses as well as recommendation of risk
9 reduction, dementia medication and non-pharmacological treatments. Principal
10 investigators of the centres were psychiatrists, neurologists or geriatricians with
11 six to thirteen years of experience in dementia care.
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26

27 **Interventions**

28
29 The experimental intervention (COTiD) was designed to improve the patient's
30 and the primary carer's daily functioning, and was based on an evidence-based
31 treatment manual.[6, 19-23] COTiD consisted of ten occupational therapy
32 sessions of one hour duration held over five weeks at each patient's home. In
33 the diagnostic phase, comprising of 3 to 4 sessions, the occupational therapist
34 explored (1) the patient's preferences and history of daily activities, (2) her or
35 his ability to perform activities and to use compensatory strategies within the
36 familiar environment, (3) the possibilities of modifying the patient's home, (4) the
37 carer's activity preferences, problems in care giving, coping strategies and
38 abilities to supervise and (5) the interaction between carer and patient. In a
39 shared decision-making process during the goal setting session, the patient and
40 the carer selected the one or two most meaningful activities out of a list of their
41 preferences for daily activities to work on in occupational therapy. During the
42 treatment phase of 5 to 6 sessions, the occupational therapist defined, together
43 with the patient and the carer, more effective compensatory and environmental
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3 strategies to adapt both the environment and the selected activities to the
4 patient's habits and cognitive abilities. Patient and carer were taught how to use
5 these suggested adaptations within strategies, activities and the environment in
6 order to improve their performance of daily activities. In addition, the carer
7 received practical and emotional support and was coached in effective
8 supervision, problem solving and coping strategies by means of cognitive-
9 behavioural interventions. Detailed description of the experimental intervention
10 has been published elsewhere.[23]

11
12 For the German RCT, MG taught the content of the translated treatment manual
13 to 14 study participant occupational therapists in 16 hours of seminars using
14 presentation, videos and role play with feedback and group discussion. After the
15 seminar and before the study started, they needed to complete a full treatment
16 series for at least one pilot dyad of patient and carer. In the study phase, the
17 interventionists spent about 20 hours per patient for a full treatment series
18 including ten treatment sessions, travel, reports and multidisciplinary briefing. In
19 Germany, a series of ten to thirty sessions is within the normal range of time
20 that occupational therapists use for the treatment of older outpatients diagnosed
21 with other diseases, such as stroke or rheumatoid arthritis.

22
23 The control group received one hour occupational therapy consultation (COTC)
24 at the patient's home conducted by the same study interventionists. Based on
25 material of the German Alzheimer Society, two occupational therapists with
26 more than five years of experience in dementia care had prepared a leaflet of
27 ten pages.[24-25] The semi-structured consultation was an explanation of 30
28 min of this leaflet and a talk of 30 min on individual problems that arose from
29 patient's and carer's needs. This included encouragement to stay active in
30 everyday life, to maintain social contacts and to use dementia services in the
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3 region for which local addresses were listed in the leaflet. Occupational
4
5 therapists were taught the control intervention within a 4-hour seminar.
6
7 Consultations of 30 minutes up to one hour duration about such issues are
8
9 common in German dementia care. Detailed description of the control
10
11 intervention as well as means of quality assurance in experimental and control
12
13 intervention has been published elsewhere.[26]
14
15
16
17
18
19

20 **Outcome measures**

21
22 The primary endpoint was the patients' change of daily functioning from
23
24 baseline to follow-up time points at week 6, 16 and 26 measured with the
25
26 performance scale of the Interview for Deterioration in Daily Living Activities in
27
28 Dementia (IDDD).[27] This scale records carer rating of the patient's need of
29
30 assistance in the performance of (1) washing oneself, (2) making tea or coffee,
31
32 (3) dressing, (4) combing one's hair and brushing one's teeth, (5) eating, (6)
33
34 using the toilet, (7) shopping, (8) using the telephone, (9) preparing a meal, (10)
35
36 cleaning the house or doing minor repair work and (11) handling finances. Each
37
38 item is rated never=0, seldom=1, sometimes=2, often=3 or always=4. The sum
39
40 of scores ranged from 0 to 44. Higher scores indicated higher need for
41
42 assistance. Since carer rating could not be 'masked', daily functioning was
43
44 additionally evaluated by external raters fully 'blind' to the group assignment.
45
46 They rated video tapes of a challenging daily living task and used the Perceive,
47
48 Recall, Plan and Perform System of Task Analysis (PRPP).[28] For the PRPP,
49
50 raters had to define single steps of the performed activity, and they identified
51
52 any activity step in which errors of accuracy, omission, repetition or timing
53
54 occurred. The number of activity steps rated as incorrectly performed was
55
56
57
58
59
60

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 endpoints²⁶

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

1
2
3 translations, analysis of discrepancies and final agreement by discussion with
4 all translators. There was no need to translate the PRPP because, because it
5 was established in the Netherlands and applied by Dutch raters. There was one
6 protocol amendment before recruitment started. The Assessment of Motor and
7 Process Skills (AMPS) was replaced by the PRPP, because the AMPS was not
8 available in the German language within the planned schedule.
9

10 Indicators of harm were defined as patient or carer death, number of patients
11 with admission to hospital and number of nights in hospital. These indicators
12 were recorded in interviews with the carer at intervals of 5 to 7 weeks over 52
13 weeks. Study sites had to report severe adverse events to the study centre
14 immediately when each occurred. We did not assume a direct association
15 between the defined harms and either the experimental or the control
16 intervention. However, increased daily activities in the interventions group might
17 have resulted in a higher risk of falls or accidents and thus may indirectly have
18 led to more nights in hospital or in the worst case to death.
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40

41 **Sample size calculation**

42 A sample size of 42 participants per group was calculated to be necessary to
43 detect an effect size of $f = 0.10$ on the IDDD performance scale in an analysis of
44 variance of two groups and four time points; using a two-sided 5% significance
45 level, a power of 80%, and a correlation of 0.7 between the measurement time
46 points [31]. According to the Dutch original RCT, we expected a dropout rate of
47 10% at week 16, which was extrapolated to 40% at week 52. A nine-month
48 inclusion period was anticipated as necessary in order to recruit the 140
49 patients. Our assumed effect size of $f = 0.10$ is based on a group by time
50 interaction and compatible to Cohen's $d = 0.20$, which corresponds to a small
51
52
53
54
55
56
57
58
59
60

1
2
3 effect size and any d over 0.8 is large. Although the Dutch original RCT found
4
5 effect sizes of $d = 2.4$ in the IDDD performance scale at week 12, for this study
6
7 the power was calculated much more conservatively.
8
9

10 This was because we (1) introduced an active control group, (2) investigated
11
12 the programme effects under varying care conditions in seven centres with
13
14 interventionists who were introduced in this new treatment and were far not as
15
16 experienced as the Dutch study therapists and (3) we prolonged the follow up
17
18 period. Interim analyses were not planned.
19
20
21

22 23 24 **Randomisation and masking**

25
26 The random allocation sequence was computer-generated with blocking by
27
28 centre and groups of two persons, without stratification and in a ratio of 1:1 by a
29
30 statistician from a distant site. After enrolment, study site physicians requested
31
32 randomisation via e-mail. The statistician e-mailed the individual allocation to
33
34 COTiD or COTC exclusively to the site interventionist and stored the allocation
35
36 list at his distant site which was not available to any study site staff. The
37
38 interventionist scheduled treatment sessions, faxed records to the distant
39
40 coordinating study centre and kept all documents strictly separated from any
41
42 other site staff. This was in order to avoid contamination. Since the numbers of
43
44 home visits differed in the experimental and control groups, masking of patients
45
46 and carers was not possible. However, study information did not include any
47
48 preference for a special treatment 'arm'. Patients and carers were asked to give
49
50 no information about their treatment package to assessors or study physicians.
51
52 All study personal was 'blind' for group assignment, except the interventionists.
53
54 Agreement between the assessors' estimation of group assignment and the
55
56 actual group assignment was 61%, and thus slightly over the expected 50% of
57
58
59
60

1
2
3 agreement by chance. The procedure of external video rating ensured the full
4
5 'blinding' of the external raters for the PRPP primary outcome measure.
6
7 Independent research assistants cleaned the videotapes of any hint of group
8
9 assignment before they were rated by two Dutch raters not involved in the trial
10
11 treatment. In order to establish the inter-rater reliability, we tested ten double
12
13 ratings of the same video by the two raters and found an intra-class correlation
14
15 coefficient of 0.9. Data analysts were not 'blind' for the group assignment.
16
17 However, measurement time points and outcomes had been published before
18
19 data were available for analysis [26] and any decision to remove patients from
20
21 the analyses is reported in the present publication.
22
23
24
25
26
27
28

29 **Statistical methods**

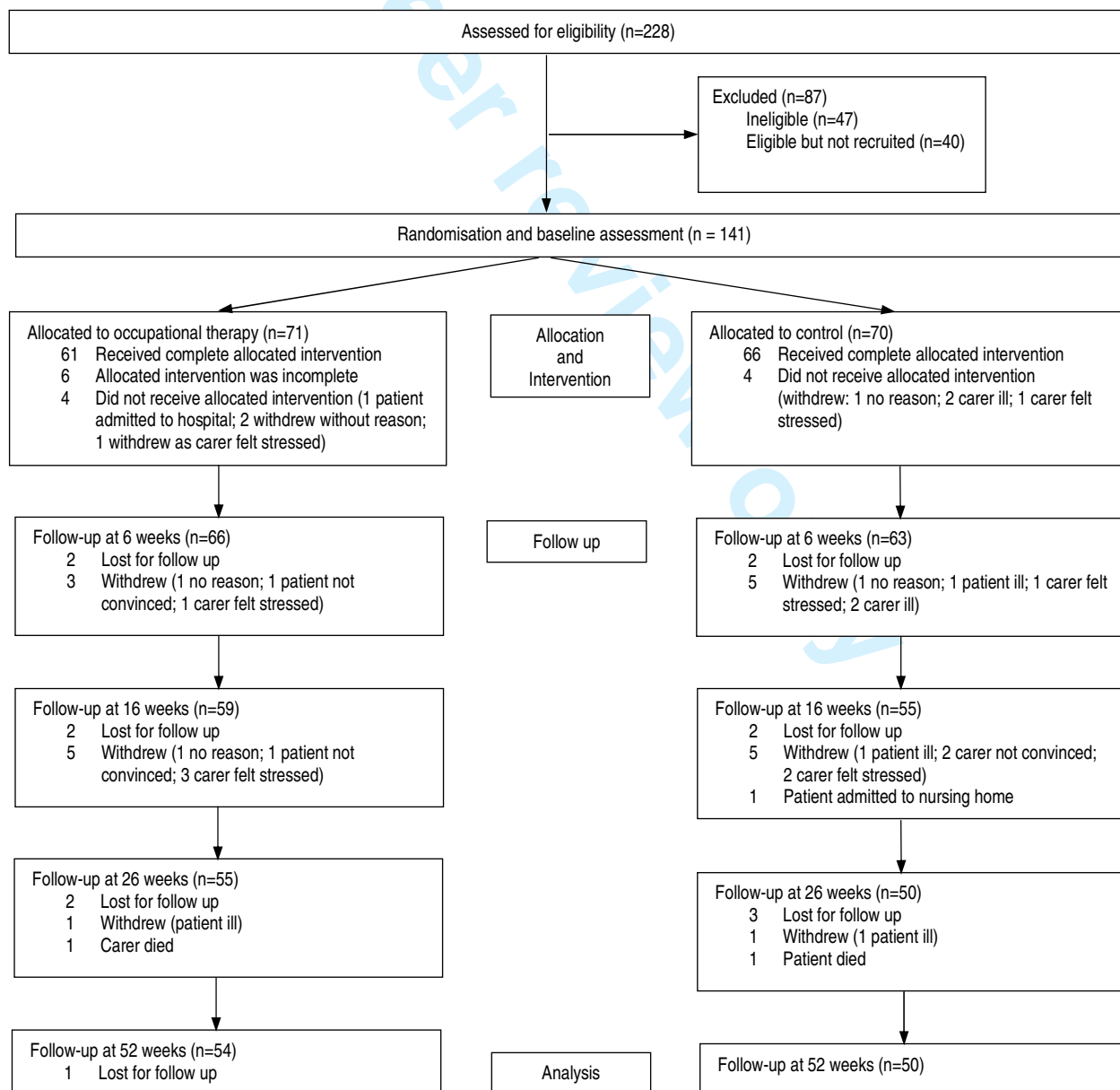
30
31 Data were entered via special MS Access entry masks automatically controlling
32
33 for data plausibility. In addition, sections of entered data were checked for
34
35 typing errors by hand, in order to ensure an error rate lower than 0.2%. The
36
37 primary intention-to-treat analysis included all allocated participants with valid
38
39 data whether they did or did not receive the complete intervention. For the IDDD
40
41 and the PRPP measurements of the primary outcome, we performed a
42
43 multivariate analysis of variance (MANOVA) with repeated measures with two
44
45 groups and four measurement time points at baseline, week 6, 16 and 26. A
46
47 univariate ANOVA with five measurement time points (+ postal assessment in
48
49 week 52) was carried out for the secondary outcomes and the IDDD. We did not
50
51 adjust for baseline values, because we found no marked group differences. In
52
53 order to deal with missing data occurring not in the primary but in the secondary
54
55 outcomes, we performed secondary intention-to-treat analyses with multiple
56
57 data imputation using the Full Information Maximum Likelihood (FIML)
58
59
60

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

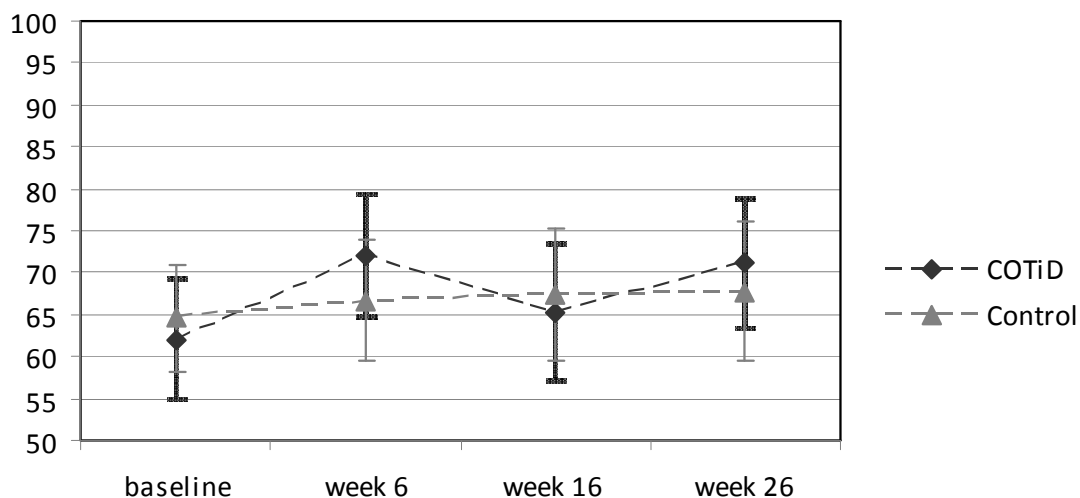
61 of 71 (86%) allocated patient-carer dyads received complete sessions in the COTiD group, 66 of 70 (94%) in the control group. In each group, 4 pairs were lost before intervention. Six patient-carer dyads in the COTiD had less than 10 sessions. Interventionists rated the delivery of 20 pre-defined 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

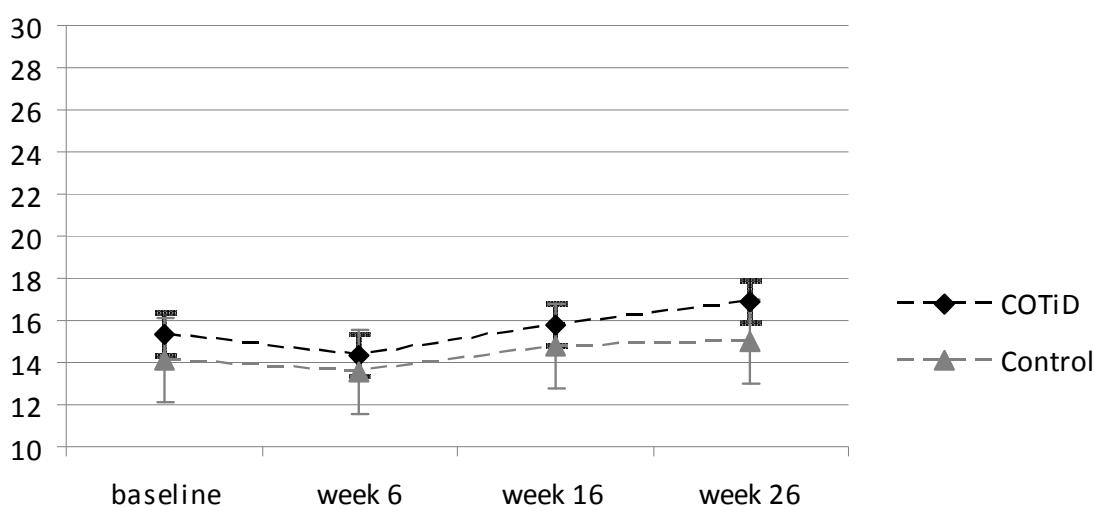
1
2
3 patients (N=141) as recommended by Coley and colleagues [35] did also reveal
4
5 no significant interactions for the IDDD ($p=0.340$) and the PRPP ($p=0.785$),
6
7 **details are provided as supplementary online material.** Tables 3 and 4 show
8
9 mean, standard deviation and group difference including 95%-confidence
10
11 intervals of an ANOVA for all outcomes. Patients' daily functioning did not
12
13 significantly change over 26 weeks in either the experimental and control group.
14
15 In the postal 52 weeks follow up, the patients' need for assistance increased in
16
17 both groups, and accordingly the carer's hours of care for basic ADL were
18
19 higher. Two patients of the COTiD group were placed to nursing homes 33 and
20
21 44 weeks after baseline and one patient of the control group after 33 weeks.
22
23 To address the problem of missing data in single measurement instruments, we
24
25 performed a multiple data imputation. We calculated a MANOVA over four
26
27 measurement time points for all primary and secondary outcomes for all 104
28
29 completers. Ten different data imputations did not reveal any significant time
30
31 group interaction effects.
32
33
34
35
36
37
38
39

40 Figure 2: ADL task performance of Alzheimer patients following intense occupational therapy compared
41 with a single session control intervention; means and 95%-confidence intervals of the PRPP
42 independence scale (N=104 completers; range: 100=no errors to 0=all errors)
43



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

1
2
3 matters and approval of the local ethic commissions. Therefore, a common repetition
4 seminar for the interventionists could not be arranged after the pilot training. This
5 may have led to some heterogeneity in the intervention, especially because in
6 Germany eleven newly introduced interventionists performed the treatment
7 compared to two experienced experts in the original Dutch trial. We addressed this
8 problem with feedback on videos of treatment sessions the interventionists sent in.
9 Furthermore, we arranged telephone supervision on demand.

10 We consider the contamination of the control intervention with knowledge from the
11 experimental intervention to be low, because any specific intervention such as
12 activity selection, simplification or training was precluded by the limited time to carry
13 out the control intervention.
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29

30 **Comparison**

31
32 The Dutch RCT on the COTiD with waiting-control-group design showed large effect
33 sizes in the IDDD performance scale at six and twelve weeks after baseline ($d=2.3$
34 and 2.4 , respectively).[6] Since the Dutch COTiD programme demonstrated such
35 highly positive effects, we judged it as appropriate to conduct not an identical
36 replication, but a twofold transfer from the source to the target country and from a
37 mono-centre RCT design with high expertise of interventionists to a pragmatic multi-
38 centre RCT design in routine care [35]. The Dutch and the German sample did not
39 differ remarkably in cognition at baseline (MMSE: 19 v 20), but did differ in the need
40 of assistance (IDDD performance: 24 v 15). The German patients showed a low need
41 of assistance at the beginning of the study. This was comparable to the IDDD values
42 of the Dutch patients at the end of the treatment. This may have caused a floor effect
43 on the IDDD. Another mono-centre RCT in the USA compared community
44 occupational therapy and a less intensive telephone consultation in patients with
45 probable dementia (MMSE: 13).[37] The authors found a small effect size in daily
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3 functioning (d=0.21). The initial need of assistance in both studies was higher than in
4
5 the German sample. A systematic review of community programmes in dementia [38]
6
7 reported one study on exercise and behavioural management with beneficial effects
8
9 on daily functioning of patients with moderate dementia (MMSE: 17); one trial on
10
11 occupational therapy with heterogeneous effects; and two studies on occupational
12
13 therapy and music therapy with no significant effects. A current German health
14
15 technology assessment on non-drug therapies in Alzheimer's disease did not identify
16
17 further community occupational therapy trials [39]. The comparison of community
18
19 intervention trials reveals that study samples with a lower MMSE and a higher need
20
21 of assistance benefit more than those with initial higher cognitive and daily
22
23 functioning. Similarly, a standardized synopsis of ADL outcomes in pharmacological
24
25 dementia trials indicated that samples with an MMSE between 17 and 10 benefit
26
27 most in ADL while samples with higher MMSE scores showed less effects.[40]
28
29 However, different baseline scores of cognitive and daily functioning alone cannot
30
31 explain the major difference between the findings in this German study and the
32
33 positive results of the Dutch RCT. Detailed process evaluation and exploratory
34
35 analyses of the study data might show whether variations in study site context and
36
37 treatment performance influenced the intervention's effectiveness.
38
39
40
41
42
43
44
45

46 **Clinical and research implications**

47
48 Published evidence for the effectiveness of community occupational therapy in
49
50 dementia is heterogeneous as indicated by a Dutch trial with large positive effects on
51
52 daily functioning; a few USA trials with no or small positive effects on ADL and this
53
54 German study showing that ten sessions were not superior to one consultation. A
55
56 preventative one-session consultation might be hypothesised as beneficial for people
57
58 with mild dementia and an improved 10-session programme more specifically
59
60 adapted to the German health care system as beneficial for dementia patients with

1
2
3 moderate need of assistance in ADL, as was shown in the Dutch study in which most
4
5 people with dementia had moderate to high need for assistance at baseline.
6
7

8 Although we had expected smaller effect sizes than in the Dutch original trial due to
9
10 changed study design with (1) the introduction of an active control group, (2) a
11
12 variance in treatment performance in several centres, (3) a prolonged follow up time
13
14 and (4) rigorous reduction of the analysed sample to participants with valid data, it
15
16 remains surprising that significant group difference could not be found in any of the
17
18 primary or secondary outcomes.
19
20

21
22 This study has shown that careful cross-national comparisons are greatly needed,
23
24 especially in complex interventions, before they can be considered evidence based
25
26 and implemented effectively in other health care systems. Therefore, further analyses
27
28 must investigate the role of interventionists' expertise and treatment performance,
29
30 and the role of participants' needs and utilisation of health care resources, before
31
32 conclusions on international implementation of this intense occupational therapy
33
34 intervention can be drawn.
35
36
37
38
39

40
41 **Acknowledgement:** We thank all participants and interventionists for their contribution. We
42
43 acknowledge Professor Chris Mayers, Research Fellow, Faculty of Health & Life Sciences, York St
44
45 John University, UK, for critical reading and English correction.

46
47 **Funding:** German Federal Ministry of Health, Reference Number: IIA5-2508FSB111/44-004.

48
49 **Contributors:** SVR, MG, RL, GE and MH contributed to study conception and design. FJ, JB, BM, AF,
50
51 RD, GE and MH acquired data. SVR and KS participated in data and study management and
52
53 prepared the statistical analysis. RL performed the statistical analysis. SVR drafted the manuscript.
54
55 RL, MG, FJ, JB, BM, AF, RD, GE, MOR, MVD and MH revised the manuscript critically for important
56
57 intellectual content. All authors read and approved the final manuscript.

58
59 **Competing interests:** SVR, RL, KS, JB, AF, MG and MVD non declared. FJ membership in DSMB of
60
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

1
2
3 expenses from various pharmaceutical companies; royalties and patents from University of Marburg.
4
5 GE grants from AC-immune and Janssen-AL. MOR consultancy for Jansen-Cilag and Numico. MH
6
7 grants from Wyeth, Pfizer and Medivation, payment for lectures from Wyeth, Pfizer and Merz.
8
9

10
11 **Data sharing statement:** Complete data sets can be provided on request for research fellows in
12
13 scope of collaborative projects and publications.
14
15

16
17 “The Corresponding Author has the right to grant on behalf of all authors and does grant on behalf of
18
19 all authors, an exclusive licence (or non-exclusive for government employees) on a worldwide basis to
20
21 the BMJ Group and co-owners or contracting owning societies (where published by the BMJ Group on
22
23 their behalf), and its Licensees to permit this article (if accepted) to be published in the BMJ open and
24
25 any other BMJ Group products and to exploit all subsidiary rights, as set out in our licence.”
26
27

28 29 References

- 30
31 ¹ Wancata J, Musalek M, Alexandrowicz R, Krautgartner M. Number of dementia sufferers in Europe
32
33 between the years 2000 and 2050. *Eur Psychiatry*. 2003;18:306-313.
34
35 ² Wimo A, Jonsson L, Winblad B. An estimate of the worldwide prevalence and direct costs of
36
37 dementia in 2003. *Dement Geriatr Cogn Disord*. 2006;21(3):175-81.
38
39 ³ European Medicines Agency. Guideline on Medicinal Products for the Treatment of Alzheimer’s
40
41 Disease and other Dementias [Internet]. London: 2008. Doc. Ref. CPMP/EWP/553/95 Rev. 1
42
43 [cited 2010 Oct 26]. Available from: <http://www.emea.europa.eu/pdfs/human/ewp/055395en.pdf>
44
45 ⁴ Georges J, Jansen S, Jackson J, Meyrieux A, Sadowska A, Selmes M. Alzheimer’s disease in real
46
47 life--the dementia carer’s survey. *Int J Geriatr Psychiatry*. 2008 May;23(5):546-51
48
49 ⁵ Voigt-Radloff S, Hüll M. Daily functioning in dementia: Pharmacological and non-pharmacological
50
51 interventions demonstrate small effects on heterogeneous scales – a synopsis of four health
52
53 technology assessments of the German Institute for Quality and Efficiency in Health Care
54
55 regarding the endpoint activities of daily living. *Psychiatr Prax*. 2011 Mar 21. [Epub ahead of
56
57 print]. German.
58
59 ⁶ Graff MJ, Vernooij-Dassen MJ, Thijssen M, Dekker J, Hoefnagels WH, Rikkert MG. Community
60
based occupational therapy for patients with dementia and their care givers: randomised
controlled trial. *BMJ*. 2006;333(7580):1196.

- 1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
- ⁷ National Collaborating Centre for Mental Health (commissioned by the Social Care Institute for Excellence and the National Institute for Health and Clinical Excellence). Dementia. A NICE-SCIE Guideline on supporting people with dementia and their carers in health and social care. National clinical practice guideline, number 42. London, The British Psychological Society and Gaskell 2007
- ⁸ German Society for Psychiatry, Psychotherapy and Neurology and German Society for Neurology. Consented Guideline "Dementia" [Internet]. 2009. [cited 2010 Oct 26]. Available from: <http://media.dgppn.de/mediadb/media/dgppn/pdf/leitlinien/s3-leitlinie-demenz-lf.pdf>
- ⁹ Work Group on Alzheimer's Disease and other dementias. Practice Guideline for the Treatment of Patients With Alzheimer's Disease and Other Dementias [Internet]. 2007. [cited 2010 Oct 26]. Available from: <http://www.psychiatryonline.com/pracGuide/PracticePDFs/AlzPG101007.pdf>
- ¹⁰ Steultjens EM, Dekker J, Bouter LM, Leemrijse CJ, van den Ende CH. Evidence of the efficacy of occupational therapy in different conditions: an overview of systematic reviews. *Clin Rehabil*. 2005 May;19(3):247-54.
- ¹¹ Voigt-Radloff S. Occupational therapy in dementia. In: Haberstroh J, Pantel J (Ed). Psychosocial treatment in dementia. AKA Verlag Heidelberg: 2011. German
- ¹² World Health Organization: International Classification of Functioning, Disability and Health (ICF) [Internet]. Geneva: 2001. [cited 2010 Oct 26]. Available from: <http://www3.who.int/icf/icfitem>
- ¹³ Giovannetti T, Bettcher BM, Libon DJ, Brennan L, Sestito N, Kessler RK. Environmental adaptations improve everyday action performance in Alzheimer's disease: empirical support from performance-based assessment. *Neuropsychology*. 2007;21(4):448-57.
- ¹⁴ Gitlin LN, Winter L, Burke J, Chernett N, Dennis MP, Hauck WW. Tailored activities to manage neuropsychiatric behaviors in persons with dementia and reduce caregiver burden: a randomized pilot study. *Am J Geriatr Psychiatry*. 2008;16(3):229-39.
- ¹⁵ Mittelman MS, Haley WE, Clay OJ, Roth DL. Improving caregiver well-being delays nursing home placement of patients with Alzheimer disease. *Neurology*. 2006;67(9):1592-9.
- ¹⁶ Gitlin LN, Corcoran M, Winter L, Boyce A, Hauck WW. A randomized, controlled trial of a home environmental intervention: effect on efficacy and upset in caregivers and on daily function of persons with dementia. *Gerontologist*. 2001 Feb;41(1):4-14.

- 1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
- ¹⁷ Gitlin LN, Hauck WW, Dennis MP, Winter L. Maintenance of effects of the home environmental skill-building program for family caregivers and individuals with Alzheimer's disease and related disorders. *J Gerontol A Biol Sci Med Sci*. 2005 Mar;60(3):368-74.
- ¹⁸ Gitlin LN, Winter L, Vause Earland T, Adel Herge E, Chernett NL, Piersol CV, Burke JP. The Tailored Activity Program to reduce behavioral symptoms in individuals with dementia: feasibility, acceptability, and replication potential. *Gerontologist*. 2009 Jun;49(3):428-39.
- ¹⁹ Graff MJ, Vernooij-Dassen MJ, Thijssen M, Dekker J, Hoefnagels WH, Olderikkert MG. Effects of community occupational therapy on quality of life, mood, and health status in dementia patients and their caregivers: a randomized controlled trial. *J Gerontol A Biol Sci Med Sci*. 2007;62(9):1002-9.
- ²⁰ Graff MJ, Adang EM, Vernooij-Dassen MJ, Dekker J, Jönsson L, Thijssen M, Hoefnagels WH, Rikkert MG. Community occupational therapy for older patients with dementia and their caregivers: cost effectiveness study. *BMJ*. 2008;336(7636):134-8.
- ²¹ Graff MJL, Melick van MBM: The development, testing and implementation of an occupational therapy guideline. The guideline for the OT diagnosis and treatment of older persons with cognitive impairments. *Nederlands Tijdschrift voor Ergotherapie*. 2000;28:169-74. Dutch
- ²² Graff MJL, Vernooij-Dassen MJFJ, Hoefnagels WHL, Dekker J, Witte de LP. Occupational therapy at home for older individuals with mild to moderate cognitive impairments and their primary caregivers: a pilot study. *Occupational Therapy Journal of Research*. 2003;23:155-63.
- ²³ Graff MJL, Vernooij-Dassen MJ, Zajec J, Olde Rikkert MGM, Hoefnagels WHL, Dekker J. How can occupational therapy improve the daily performance and communication of an older patient with dementia and his primary caregiver? A case study. *Dementia*. 2006;5:503-32.
- ²⁴ German Alzheimer Society. *Leben mit Demenzkranken*. Berlin: 2003. German
- ²⁵ German Alzheimer Society. *Ratgeber Häusliche Versorgung Demenzkranker*. Berlin: 2006. German
- ²⁶ Voigt-Radloff S, Graff M, Leonhart R, Schornstein K, Vernooij-Dassen M, Olde-Rikkert M, Hüll M. WHEDA study: effectiveness of occupational therapy at home for older people with dementia and their caregivers--the design of a pragmatic randomised controlled trial evaluating a Dutch programme in seven German centres. *BMC Geriatr*. 2009 Oct 2;9:44.
- ²⁷ Teunisse S, Derix MM. The interview for deterioration in daily living activities in dementia: agreement between primary and secondary caregivers. *Int Psychogeriatr*. 1997;9(Suppl 1):155-62.

- 1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
- ²⁸ Chapparo C, Ranka J. The PRPP System of Task Analysis: User's Training Manual. In Research Edition Sydney: OP Network; 2006.
- ²⁹ Moniz-Cook E, Vernooij-Dassen M, Woods R, Verhey F, Chattat R, De Vugt M, Mountain G, O'Connell M, Harrison J, Vasse E, Dröes RM, Orrell M; INTERDEM group. A European consensus on outcome measures for psychosocial intervention research in dementia care. *Aging Ment Health*. 2008 Jan;12(1):14-29.
- ³⁰ Wolfson C, Moride Y, Perrault A, Momoli F, Demers L, Oremus M. Drug treatments for Alzheimer's disease. II. A review of outcome measures in clinical trials. Ottawa: Canadian Coordinating Office for Health Technology Assessment (CCOHTA); 2000.
- ³¹ Faul F, Erdfelder E, Lang AG, Buchner A. G*Power 3: A flexible statistical power analysis for the social, behavioral, and biomedical sciences. *Behavior Research Methods*. 2007;39:175-91. G*POWER free software available from <http://www.psych.uni-duesseldorf.de/abteilungen/aap/gpower3/>
- ³² Allison P. Missing data. Thousand Oaks: Sage; 2002.
- ³³ Plassman BL, Williams JW Jr, Burke JR, Holsinger T, Benjamin S. Systematic review: factors associated with risk for and possible prevention of cognitive decline in later life. *Ann Intern Med*. 2010 Aug 3;153(3):182-93.
- ³⁴ Howell, DC (1997). Statistical methods for psychology. Fourth Edition. Wadsworth:Belmont,CA.
- ³⁵ Coley N, Gardette V, Cantet C, Gillette-Guyonnet S, Nourhashemi F, Vellas B, Andrieu S. How should we deal with missing data in clinical trials involving Alzheimer's disease patients? *Curr Alzheimer Res*. 2011 Jan 19. [Epub ahead of print]
- ³⁶ Zwarenstein M, Treweek S, Gagnier JJ, Altman DG, Tunis S, Haynes B, Oxman AD, Moher D; CONSORT group; Pragmatic Trials in Healthcare (Practihc) group. Improving the reporting of pragmatic trials: an extension of the CONSORT statement. *BMJ*. 2008 Nov 11;337:a2390.
- ³⁷ Gitlin LN, Winter L, Dennis MP, Hodgson N, Hauck WW. A biobehavioral home-based intervention and the well-being of patients with dementia and their caregivers: the COPE randomized trial. *JAMA*. 2010 Sep 1;304(9):983-91.
- ³⁸ Smits CH, de Lange J, Dröes RM, Meiland F, Vernooij-Dassen M, Pot AM. Effects of combined intervention programmes for people with dementia living at home and their caregivers: a systematic review. *Int J Geriatr Psychiatry*. 2007 Dec;22(12):1181-93.

- 1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
- ³⁹ Rieckmann N, Schwarzbach C, Nocon M, Roll S, Vauth C, Willich SN, Greiner W. Concepts of care for people with dementia [Internet]. *GMS Health Technol Assess* 2009;5:Doc01. [cited 2010 Oct 26]. Available from: <http://www.egms.de/static/en/journals/hta/2009-5/hta000063.shtml>. German
- ⁴⁰ Gauthier S, Lopez OL, Waldemar G, Jones RW, Cummings J, Zhang R, Schindler R, Schwam E. Effects of donepezil on activities of daily living: integrated analysis of patient data from studies in mild, moderate and severe Alzheimer's disease. *Int Psychogeriatr*. 2010 Sep;22(6):973-83.

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.