ORIGINAL ARTICLE

Long-term Rehabilitation in Patients With Acquired Brain Injury

A Randomized Controlled Trial of an Intensive, Participation-Focused Outpatient Treatment Program

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SUMMARY

Background: Patients with acquired brain injury who have been discharged from inpatient neurological rehabilitation often continue to suffer from limited independence, participation, and quality of life. Participation-focused outpatient treatment (in German: *teilhabeorientierte ambulante Maßnahme*, TEAM) was developed to improve these patients' outcomes.

Methods: In a randomized, controlled trial, 53 patients who had sustained an acquired brain injury approximately four years earlier were allotted to two different sequences of treatment (26 TEAM/control, 27 control/TEAM). The primary endpoint was the achievement of an individual participation goal one month after the start of treatment. The secondary endpoints included independence in everyday activities, health-related quality of life, participation, and need for nursing care. The intervention was four weeks long and was carried out on an outpatient basis (19.4 ± 1.3 hours per week). Patients in the control group were treated in a manner resembling usual current care. All endpoints were evaluated in a per-protocol (PP) analysis of data from 47 patients. For confirmation, an intention-to-treat (ITT) analysis was also carried out for the primary endpoint and for independence in everyday activities.

Results: According to the PP analysis, TEAM patients achieved their individual participation goals at 1 month more frequently than control patients receiving standard treatment (61% vs. 21%; $p = 0.008$) and improved more with respect to independence in everyday activities. The difference between TEAM and standard treatment was +7.3 points on the FIM (Functional Independence Measure) scale (95% confidence interval [2.8; 11.8]; $p = 0.0024$). The superiority of TEAM was confirmed by the ITT analysis (achievement of the participation goal, TEAM vs. standard treatment: 54% vs. 19%, $p = 0.0103$). Moreover, improvements were seen at 12 months in quality of life, participation, and the need for nursing care.

Conclusion: The TEAM rehabilitation program can help patients in the chronic phase of acquired brain injury achieve participation goals that are relevant to everyday life. An adjustment of the care structure in Germany to include such intensive goal-oriented rehabilitation programs would lead to a more effective mobilization of these patients' potential for long-term rehabilitation.

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Acquired brain injury, such as stroke or traumatic brain injury (TBI), is one of the most common causes of long-term disability. It is associated with loss of quality of life and substantial economic costs (1). Annual incidence rates are 262 per 100 000 population per year for TBI and 217 per 100 000 population for ischemic cerebral infarction, giving an estimate of approximately 380 000 new cases per year in Germany. Even ignoring milder cases with complete remission, there are hundreds of thousands of affected individuals living with the resulting disabilities (2, 3).

For moderate and serious injury, the most effective neurological rehabilitation possible is needed to prevent or reduce long-term disability. In Germany, such rehabilitation is established in a multiphase model according to the recommendations of the Federal Rehabilitation Working Group (BAR, Bundesarbeitsgemeinschaft Rehabilitation) (4). However, in recent years the duration of patients' stays in inpatient neurological early rehabilitation (BAR phase B) has shortened, from a mean of 47 days in 2005 to 38 days in 2008. This means that patients are being discharged home or to a facility earlier and earlier (5, 6). After inpatient rehabilitation has ended, participation and quality of life often remain considerably restricted, and assistance and care are required (6). For example, 78% of former early rehabilitation patients are registered disabled, and 51% are allocated a tier of nursing care. Only 8.5% report that their daily lives are not restricted at all (6).

In the multiphase model, neurorehabilitation is coordinated and goal-focused, and is provided by an interdisciplinary rehabilitation team which takes into account factors concerning health, life situation, and context using the WHO International Classification of Functioning, Disability and Health (ICF) (7). In contrast, outpatient care (e.g. physiotherapy, occupational therapy, speech therapy) often fragments into individual, function-focused components that are not united in an overall treatment strategy.

In this article we report on the findings of a randomized controlled clinical trial in which patients with acquired brain injury in a chronic phase underwent treatment for 4 weeks. During the intervention period of the trial, patients were treated in a participation- and goal-focused interdisciplinary outpatient neurorehabilitation

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program while during the control period, patients received current standard outpatient care.

Methods

This was a single-center, randomized, controlled, investigator-blinded trial with 6 trial visits. Although it was planned and conducted as a crossover study, as a result of carryover effects statistical evaluation was performed as for a conventional parallel-group study, using data from the first treatment period (*eMethods*) (8). The first treatment period lasted one month and was followed by a 2-month washout phase. The treatments were then switched, and a final visit was held at 12 months (*eFigure 1*). The trial was approved by the ethics committee of the Faculty of Medicine at Ludwig-Maximilian University Munich. It was entered in the German Clinical Trials Register (DRKS, Deutsches Register Klinischer Studien) after it had begun (trial ID: DRKS00009602).

Patients

Fifty-four chronic-phase patients who had suffered serious acquired brain injury (ischemic cerebral infarction, intracerebral hemorrhage, subarachnoid hemorrhage, TBI) were enrolled in the trial due to persistent disability and participation restriction; 53 were randomized to the 2 treatment orders, at a ratio of 1:1. One patient was excluded between enrolment and randomization as travel could not be arranged (CONSORT flow diagram, *eFigure 2*). The principal inclusion criteria were as follows:

- Cerebral infarction (hemorrhage or ischemia) or TBI 6 months or more ago
- Time from discharge from inpatient rehabilitation treatment to trial enrolment 3 months or more
- Age 18 to 85 years.

Trial intervention

The treatment phase lasted 4 weeks. The aim was for patients and their relatives to learn to deal with specific everyday challenges in the ICF domains self-care, home life, and mobility using a participation-focused outpatient program known as TEAM in line with its initials in German. Before randomization, during the initial visit at home, the patients and their relatives set a specific 4-week rehabilitation goal.

The TEAM intervention was conducted on an outpatient basis for 6 hours every weekday for 4 weeks, at the Burgau Treatment Center (TZB, Therapiezentrum Burgau). The 6 hours consisted of 2.5 hours of individual therapy, 1.5 hours of group therapy, and a one-hour set break. There were 2 meals, with therapeutic supervision, per treatment day. The treatment team was interdisciplinary (nurse and doctor, occupational therapist, physiotherapist, speech therapist, social service provider, technical aid advisor, neuropsychologist). A majority of therapy hours involved the use of Affolter tactical interaction therapy (9, 10). The TEAM intervention also integrated relatives closely, and evaluated patients in their real home environment.

TABLE 1

Demographic and health-related factors at beginning of trial, before randomization, for intention-to-treat population^{*1}

	TEAM group (n = 26)	Control group (n = 27)	p-value
Age (years)	57.3 ± 15.2	58.4 ± 14.3	0.800 ^{*2}
Female/male (number)	9/17	13/14	0.471 ^{*3}
Latency to brain injury (years)	3.9 ± 4.6	4.7 ± 4.7	0.519 ^{*2}
Duration of initial early rehabilitation (days)	105.2 ± 54.4	129.8 ± 90.6	0.279 ^{*2}
mRS	3.2 ± 0.8	3.5 ± 0.6	0.293 ^{*2}
FIM – Missing values, n (%)	88.2 ± 23.0 1	91.3 ± 18.4 3	0.615 ^{*2}
Diagnoses			
Ischemic cerebral infarction, n (%)	15 (57.7)	12 (46.2)	0.802 ^{*4}
Intracerebral hemorrhage, n (%)	4 (15.4)	4 (15.4)	
SAH, n (%)	2 (7.7)	4 (15.4)	
Traumatic brain injury, n (%)	3 (11.5)	4 (15.4)	
– Missing values, n (%)	2 (7.7)	3 (11.5)	
Dwelling-place			
Independent at home, n (%)	2 (7.7)	0 (0)	0.608 ^{*4}
With support at home, n (%)	20 (76.9)	21 (77.8)	
Institutional care, n (%)	1 (3.8)	2 (7.4)	
– Missing values, n (%)	3 (11.5)	4 (14.8)	

^{*1}(n = 53 randomized patients) stratified by treatment group; mean ± standard deviation or absolute frequencies (%) are given; ^{*2}t-test (2-tailed); ^{*3}Chi-square test; ^{*4}Fisher's exact test (2-tailed)
FIM, Functional Independence Measure; mRS, Modified Rankin Scale; SAH, subarachnoid hemorrhage; TEAM: participation-focused outpatient program

In the control group, patients received standard outpatient treatment as they had before the trial. Those providing this treatment were informed of the patients' trial participation and told, in particular, of the patients' specific 4-week rehabilitation goals toward which they were to work.

Assessments and measuring tools

The primary outcome was defined as the extent of individual goal attainment. The tool used to measure this was goal attainment scaling (GAS). This characterizes the extent to which an individual target is attained using 5 levels, ranging from –2 (worse than initially) to +2 (better than planned), and makes it possible to quantify different patient-specific goals so that they can be compared with each other in rehabilitation research (case study in *eBox*) (11, 12).

The following measuring tools were also used:

- The Functional Independence Measure (FIM) (13, 14)
- EuroQol (EQ-5D: health-related quality of life [QoL]) (15)
- Short-Form 36 (SF-36: self-evaluation QoL questionnaire) (16)
- The WHO Disability Assessment Schedule (WHODAS: evaluation of changes in health, participation, and disability) (17)

Changes in various domains and outcomes during the one-year trial period. Significance data according to t-test for matched samples (2-tailed). For FIM, EQ-5D, and SF-36, an increase in score reflects an improvement between the beginning and end of the trial. For WHODAS and NAA, in contrast, a decrease in score reflects an improvement (reduced participation restriction or reduced care needs). EQ-5D, EuroQol Quality of Life questionnaire; FIM, Functional Independence Measure; NAA, New Appraisal Assessment: Nursing Care; SF-36, Short-Form 36 quality of life questionnaire; WHODAS, WHO Disability Assessment Schedule for activity limitation and participation restriction

- The German New Appraisal Assessment: Nursing Care (analyzes patients' resources to determine their care needs)
- The Caregiver Strain Index (CSI) (18).

The modified Rankin Scale (mRS) was used for clinical characterization of the trial population on initial examination. Because this allows for only very rough outcome evaluation, mRS findings were not analyzed later in the trial (details on the measuring tools used can be found in the *eMethods* section).

Statistical evaluation

Both the GAS for the primary outcome and the other measuring tools underwent per-protocol analysis after the 4-week intervention (first treatment period). For GAS and FIM, intention-to-treat evaluation was also performed as a sensitivity analysis. This included drop-outs. The statistical methods used and further information on the trial design are detailed in the *eMethods* section.

Results

Fifty-three patients were randomized to the two treatment orders (26 patients to the trial intervention followed by standard treatment in the control phase, 27 to standard treatment followed by the trial intervention). Forty-seven patients (23 in the TEAM group, 24 in the control group) completed the trial according to the schedule and were defined as the population to be analyzed in the per-protocol analysis. In addition, in-

tention-to-treat analysis was performed for GAS and FIM (*eMethods*). There were no differences between the 2 groups at the beginning of the trial in terms of either demographics or health- and illness-related factors (*Table 1*).

During the TEAM phases patients received 19.4 ± 1.3 (mean [M] $\pm$ standard deviation [SD]) hours of treatment per week. This was split into 6.4 hours of occupational therapy, 4.0 hours of physiotherapy, 1.7 hours of speech therapy, and 7.3 hours of group therapy focusing on everyday activities. During the control phase patients received their standard treatment. This was 2.2 ± 0.9 hours (M $\pm$ SD) of physiotherapy, 1.8 ± 1.0 hours of occupational therapy, and 1.2 ± 1.1 hours of speech therapy.

Results of the randomized controlled trial phase

In the TEAM group, 61% (14/23) of patients had achieved their individual goals by the end of the one-month initial treatment phase, versus only 21% (5/24) in the control group ($p = 0.008$; Fisher's exact test for differences between rates; number needed to treat (NNT) = $1/0.400 = 2.5$ [1.564; 12.827]).

In independence in daily activities, over the same period there was a significant increase in FIM score from 88.25 ± 22.99 (M $\pm$ SD) to 95.86 ± 16.4 in the TEAM group, versus 91.4 ± 18.4 to 92.2 ± 19.5 in the control group ($p = 0.0003$, Mann-Whitney U-test).

Both the significantly higher extent of goal attainment and the improvement in FIM for the TEAM

program were confirmed in sensitivity analyses performed for all 53 randomized patients, i.e. including the 6 dropouts who had not begun the trial intervention: the figure for goal attainment was 54% [35; 72] for TEAM, versus 19% [8; 38] for standard treatment. The mean change in FIM score for TEAM was 7.40 ± 0.55 , versus 0.89 ± 0.29 for standard treatment ($p < 0.0041$, *eMethods*).

At 3 months (at the end of the 2-month washout phase), there were no significant differences between the TEAM program and standard treatment in terms of either the tools used to evaluate quality of life and participation or those used to assess the situation of relatives providing care (*eTable 1*).

Follow-up results

Twelve months after the beginning of the trial 80.9% (38/47) [66.74; 90.85] of all trial participants had achieved their original individual participation and activity goals (*eFigure 3*). Because of the trial's crossover design, all patients had by now undergone the TEAM intervention. Regardless of treatment order, there were significant improvements among the trial population in the domains independence in daily activities, QoL (EQ-5D), participation, and care needs (*Figure 1*, *Table 2*).

Examination of FIM alone shows that independence improved significantly during TEAM treatment with both treatment orders (*Figure 2*).

Complications during TEAM treatment

There were a total of 4 falls during TEAM treatment. The most common reason for medical consultations and treatments during TEAM treatment was adjustment of blood pressure medication, in most cases due to hypertensive values.

Discussion

In this randomized, controlled, investigator-blinded clinical trial, we were able to demonstrate that a participation-focused, intensive rehabilitation program lasting only 4 weeks enabled patient-specific goals highly relevant to everyday life to be attained more frequently than standard outpatient care, even among patients with serious acquired brain injury sustained a mean of 4 years previously. This is important because during such a chronic phase it is normally assumed that there will be a plateau rather than further dynamic improvement (19). However, other studies of rehabilitation interventions have already shown that significant functional or activity-related gains remain possible more than 6 months after brain injury (20, 21). Even the rather crude FIM tool to describe functional independence in daily activities showed small but significant improvements for the TEAM treatment. After the crossover, patients in the group receiving TEAM first and standard treatment second were able to maintain their progress and even build on it over 12 months. In contrast, the patients who received standard treatment first and TEAM second did not improve until they were

TABLE 2

Changes in clinical evaluation scales in parallel-group analysis (first one-month treatment period before crossover only) and at one-year follow-up

Outcome	Parallel-group analysis: 1 st period Effect estimate, 95% CI, p	Total change at 1 year vs. baseline Δ , 95% CI, p
FIM	7.3 [2.81; 11.79] $p = 0.0024$	8.4 [5.2; 11.7] $p < 0.0001$
WHODAS	-3.92 [-11.20; 3.36] $p = 0.2827$	-6.4 [-9.9; -2.8] $p = 0.0009$
EQ-5D (VAS)	8.0 [-1.1; 17.1] $p = 0.082$	9.0 [3.0; 15.0] $p = 0.004$
SF-36 PCS	2.53 [-1.55; 6.61] $p = 0.218$	0.60 [-1.7; 2.9] $p = 0.601$
SF-36 MCS	1.04 [-5.07; 7.14] $p = 0.735$	0.04 [-2.9; 3.0] $p = 0.979$
CSI	-1.69 [-5.43; 2.04] $p = 0.365$	0.11 [-1.23; 1.45] $p = 0.871$
NAA	-4.09 [-11.11; 2.94] $p = 0.2469$	-4 [-7.98; -0.018] $p = 0.049$
GAS	OR = 5.911 [1.622; 21.537] $p = 0.0077$	OR = 7.0 [2.088; 23.468] $p = 0.0005$

CSI, Caregiver Strain Index; EQ-5D, EuroQol Quality of Life questionnaire; FIM, Functional Independence Measure; GAS, Goal Attainment Scale (binary); CI, confidence interval; PCS, SF-36 physical composite summary; NAA, New Appraisal Assessment: Nursing Care; OR, odds ratio; MCS, SF-36 mental composite summary; SF-36, Short-Form 36 quality of life questionnaire; VAS, visual analog scale; WHODAS: WHO Disability Assessment Schedule for activity limitation and participation restriction

undergoing the TEAM treatment, including in independence in daily activities. This can be seen as further evidence of the efficacy of the trial intervention (*Figure 2*).

The special feature of this trial is its focus on attainment of a predefined, participation-related goal relevant to everyday life and its verification of goal attainment in the real home environment. There have already been multiple clinical studies of rehabilitation showing that specific measures can attain functional and activity-related improvements even in chronic patients, such as constraint-induced movement therapy for arm and hand function (22), robotic arm and hand training (23–25), task-specific arm and hand training (26), and intensive speech therapy combined with transcranial magnetic stimulation (27). However, many of these studies were not controlled or used only very small case numbers, and patients' individual living environments were not taken into account when their results were measured. This latter seems to us to be a decisive aspect of patients' post-clinical long-term rehabilitation.

Several of our trial participants had also achieved functional and activity-related gains during standard outpatient treatment, but they were unable to use these gains in their real home environments (see *eBox* for case study). This corresponds to the logic of the ICF, which works on the basis that actual participation in life is governed not only by the severity of the damage sustained and resulting disability but also, and

FIGURE 2

Changes in FIM (ΔFIM) during trial, from initial value at beginning of trial, by treatment group. Significance data are from t-tests for independent samples (2-tailed) at each point in time. TEAM treatment was administered to the TEAM group between T1 and T2 and to the control group between T3 and T4.

FIM, Functional Independence Measure; TEAM, participation-focused outpatient program

substantially, by the resources available to the patient and his/her environment or the hindering factors in these areas (28). Comprehensive rehabilitation programs should attach sufficient importance to all these factors in chronic-phase patients.

Participation-focused treatment has also been performed in other studies of rehabilitation, for example in a smaller, uncontrolled case series of 12 chronically ill stroke patients (29). In this study participation improved steadily over a 5-month observation period. There were similar findings in a nonrandomized trial involving 83 stroke patients, 27 of whom took part in a special outpatient treatment program (30). The participation of patients in the intervention group improved significantly in comparison to untreated patients. This is in line with the results we present here and illustrates that participation-focused intensive treatment programs can be successful even in chronic-phase patients.

After 12 months our trial patients achieved increased participation, reduced care needs, greater independence, and better health-related quality of life than at baseline. However, because this was a crossover trial, all patients received a one-month therapeutic intervention, so the trial could not examine whether the positive changes were due to the TEAM intervention. Nevertheless, the long-term positive improvements in quality of life are significant, as many earlier longitudinal studies had shown that after an improvement within the first 6 months quality of life did not improve further even after years (31, 32).

Whether such long-term rehabilitation programs may also be worthwhile in terms of health economics should be clarified in future pilot projects. Lesser care needs and greater independence in daily life may lead to a lessening of the burden on the social insurance system in multiple sectors in Germany.

The finding that there is long-term potential for rehabilitation following acquired brain injury may sound ominous to those who provide funding, but it may have major implications for care in Germany, where this potential as yet remains almost untapped. Care after acquired brain injury is currently characterized by isolated function-focused, individual treatment components provided too infrequently. There is often no coordination of these individual treatment components, which are undoubtedly performed very skillfully and with the best of intentions; primary care physicians and neurologists in private practice in particular are often unable to cope with the resulting workload through no fault of their own. Specific essentials such as determining which technical aids are required or advice on social services are usually completely absent. In addition, experienced rehabilitation physicians are usually no longer involved at all in this phase of recovery, which often lasts for decades. However, the uncoordinated prescription of treatment and aids, performed with the best of intentions, leads to high costs even though they do not allow patients to achieve as many concrete goals as focused treatment programs (Figure 3a). On the basis of the scientific evidence, it would be far more sensible to treat patients at regular intervals with further intensive rehabilitation programs in order to achieve their next goals which are relevant to their everyday lives (Figure 3b). We have previously been able to show that a similar approach with very seriously affected patients receiving inpatient rehabilitation at intervals can still result in significant improvements even after several years (33). The core features of the post-clinical rehabilitation program for chronic-phase patients presented here correspond in broad terms to the recommendations recently formulated by

FIGURE 3

Attainment of independence and participation goals in daily life following acquired brain injury in relation to therapy and care structure

- Current care structure: in the rehabilitation phase model, there is a very dynamic increase in independence and attainment of individual participation goals in the first weeks and months. After rehabilitation ends, typical therapeutic practice leads to only small improvements, or even to a plateau.
- The addition of intensive therapy phases (e.g. TEAM) can always allow new individual participation goals to be attained, and there is a sustained improvement in independence.

Germany's Federal Rehabilitation Working Group (BAR) for phase E of neurological rehabilitation (34). A comprehensive care structure should be put in place for this area as swiftly as possible.

Limitations

One limitation we must acknowledge is that the design of this trial did not allow us to investigate whether or not the content of the TEAM rehabilitation program was more effective than other therapies; this would have required a control group receiving treatment at the

same frequency but with different content. An apparent contradiction in the findings of our trial is that although the number of individual patient goals achieved using the TEAM treatment was statistically significantly greater, this seems to have had no effect on generic measuring tools for health-related quality of life (EQ-5D, SF-36) or participation (WHODAS) at the end of the first treatment period, at one month. However, measuring quality of life and participation in neurological patients is difficult, particularly when generic and general measuring tools are used (35). Attainment of

specific everyday goals may lie below the sensitivity threshold of the measuring procedure. Intention-to-treat analysis was performed only to confirm the extent of individual goal attainment.

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Conflict of interest statement

Prof. Bender, Luzia Fischer, Dr. Huber, and Kerstin Jawny are staff physicians in a neurological rehabilitation facility that provides a corresponding commercial outpatient rehabilitation program.

Prof. Bender has received reimbursement of travel expenses and event fees from Bayer, and a lecture fee from Covidien. He receives material resources for a research project from Hocoma and Hasomed.

Christine Adrion, Prof. Mansmann, and Prof. Straube declare that no conflict of interest exists.

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KEY MESSAGES

- There is potential for long-term rehabilitation in neurological patients with acquired brain injury.
- Intensive, participation-focused rehabilitation programs enable chronic patients to attain goals relevant to their daily lives and to achieve increased independence in daily activities.
- There is continued, sustained improvement in patients' independence even after the end of the intensive rehabilitation program.
- Participation, quality of life, and independence improve in the long term, with reduced care needs.

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Supplementary material
For eReferences please refer to:
www.aerzteblatt-international.de/ref3816

eMethods, eBoxes, eFigures, eTables:
www.aerzteblatt-international.de/16m0634

CLINICAL SNAPSHOT

Heart of Darkness

Pathology specimen: metastatic melanoma in the myocardium and coronary arteries

A 72-year-old man was taken by ambulance to the emergency room after initially successful out-of-hospital cardiopulmonary resuscitation. On arrival, his vital signs were barely stable. He had no major known cardiovascular risk factors. A 12-lead EKG revealed an acute myocardial infarction, further interventions were unsuccessful, and he went into cardiogenic shock and died 90 minutes after arrival. The autopsy revealed the cause of the extensive myocardial infarction: neither ischemic cardiomyopathy nor a ruptured plaque in a coronary artery, but rather metastatic spread of a malignant, superficially spreading melanoma (Clark level IV) into the coronary circulation, leading to coronary arterial occlusion. The cancer had been diagnosed previously, but not its spread into the coronary vessels.

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Conflict of interest statement

The authors declare that no conflict of interest exists.

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Supplementary material to:

Long-term Rehabilitation in Patients With Acquired Brain Injury

A randomized controlled trial of an intensive, participation-focused outpatient treatment program

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eMETHODS

This was a crossover trial with a total of 6 trial visits, a crossover after 3 months, and 6-month follow-up after the end of the two 1-month treatment phases (*eFigure 1*). A pure parallel-group design proved impracticable, as the trial would not have aroused sufficient interest among patients or their relatives, and there may also have been ethical concerns. When the crossover was planned it was discussed that evaluation as for a crossover trial might be complicated by the fact that the effects of the TEAM treatment could be long-lasting. In fact, after the first TEAM patients had been treated, the improvements attained were shown to be sustained (a carryover effect), and patients' condition did not drop back to initial levels despite the 2-month washout phase. As a result of these considerations and formal statistical criteria (test for sequence effect), we decided to assess the effect of treatment in a 2-arm parallel-group trial from the first trial phase onwards. The carryover effect led to differences in the effect estimates for the two interventions in the single crossover period. A crossover trial requires this not to be the case.

Thus, the trial analysis is divided into the following three sections:

- Results of the randomized controlled crossover trial (TEAM and control groups) using data from the first treatment period (T1 to T2) (*Table 2*)
- Results of the randomized controlled trial phase (TEAM and control groups) using data from the first one-month treatment period followed by a 2-month follow-up (washout) phase (T1 versus T3, *eTable 1*)
- One-year results (T1 to T6) of all trial patients treated using the TEAM method by point T6 (one year) but still in different orders (order A = first TEAM, then control; order B = first control, then TEAM).

Assessments and measuring tools

An overview of the clinical evaluation scales and scores used is provided in *eTable 2*.

The trial employees responsible for recording assessments were trained in how to perform them before the trial began. Without exception, these employees had many years' experience in nursing, case management, therapy, and science and research and had already recorded similar data in previous scientific projects (e1). *eTable 3* provides details of the assessment plan.

The employees who performed all assessments were not involved in the treatment beforehand and were blinded to the groups to which the patients belonged, i.e. they did not know whether patients belonged to the control or TEAM order groups. The assessments were performed in patients' homes and in the Burgau Treatment Center (TZB). Assessment was to focus in particular on the specific status of patients' participation and care in individual post-inpatient everyday home life.

The Goal Attainment Scale (GAS)

The GAS rates the extent of individual goal attainment using 5 categories ranging from -2 (worse than before the beginning of therapy) to +2 (significantly more achieved than planned) (e2). By definition, the baseline condition at the beginning of the trial is -1, and the treatment goal is defined as 0. Values of +1 and +2 therefore indicate that more has been achieved than was initially hoped. On the one hand, this may be evidence of unexpectedly effective therapy or unexpectedly great patient resources, but on the other it may indicate that a goal was unambitious. The GAS makes it possible, in particular, to measure very different patient-specific goals in rehabilitation research in a way that makes them comparable with each other. It has already been used in multiple rehabilitation studies (e3).

The Functional Independence Measure (FIM)

The FIM is a standard evaluation tool in neurological rehabilitation and provides information on functional independence in daily activities (e4, e5). It assesses independence in the domains of self-care, continence, transfer, locomotion, communication, and cognitive abilities, including social behavior. A total of 18 items are assessed using a 7-point Likert scale (ranging from 1 = complete support needed to 7 = patient fully independent), so scores range from 18 (maximum dependence) to 126 (complete independence). In addition to the 6 individual domains, additional subscales can also be calculated, particularly motor FIM and cognitive FIM.

EuroQol (EQ-5D)

EQ-5D is a widely used tool to measure health-related quality of life (e6). EQ-5D consists of 2 components: one for answering 5 different health-related questions (on mobility, self-care, activities, pain, and depression) and one consisting of a 20 cm-long visual analog scale (VAS) for overall evaluation of current health, ranging from 0 (worst imaginable condition) to 100 (best possible health). The latter is frequently used in studies on health-related quality of life and was therefore also used for statistical evaluation in this trial (e7). The TEAM trial involved version EQ-5D-5L, in which each of the 5 areas has 5 levels from which to choose an answer.

Short-Form 36 (SF-36)

SF-36 is a self-evaluation questionnaire that measures health-related quality of life. It has already been used many times in patients with acquired brain injury (e8). It contains questions on health that can be allocated to 8 different domains: vitality, physical function, physical pain, general perception of health, physical functioning, emotional functioning, social functioning, and psychological wellbeing. There is no total score: instead a physical component summary and a mental component

summary are calculated. Scores can range from 0 (poor health) to 100 (best possible health).

The WHO Disability Assessment Schedule (WHODAS)

The WHODAS is a tool developed to evaluate changes in health and disability. It is conceptually based on the International Classification of Functioning, Disability and Health (ICF). It assesses 6 domains: cognition, mobility, self-care, social interaction, life activities, and participation (e9). For this trial, the complex scoring system was used. This ultimately gives a level of disability ranging from 0 (no disability) to 100 (complete disability). The WHODAS seems to be a suitable tool for measuring functional ability and disability in stroke patients (e10).

The New Appraisal Assessment: Nursing Care (NAA)

The NAA, which is currently being tested under the management of Germany's Ministry of Health, was developed to provide a structured summary of patients' care needs by analyzing their resources (e11). It is a very wide-ranging tool and requires both quantitative and qualitative evaluations. Only the quantitatively answered categories and questions were evaluated for the purposes of this trial. These were the following:

- Mobility (questions 1.1 to 1.5)
- Cognitive and communicative abilities (questions 2.1 to 2.11)
- Behavior and psychological problems (questions 3.1 to 3.13)
- Self-care (questions 4.1 to 4.12)
- Organization of daily life and social contact (question 6.1 to 6.6)
- Housework (questions 8.1 to 8.7).

Higher scores indicate greater care needs; lower scores indicate greater independence (0 = complete independence).

The Caregiver Strain Index (CSI)

The CSI is a self-evaluation questionnaire for relatives that quantifies the negative impact of caring for dependent relatives on one's own well-being (e12). Various aspects of daily life are examined, and scores range from 0 (no burden) to 26 (very great burden). Scores of 7 or more indicate a substantial burden (e13).

The modified Rankin Scale (mRS)

The mRS is a crude measure of overall health outcome following stroke. Scores range from 0 (no symptoms) to 6 (death) (e14). In clinical trials, the scale is often evaluated on a binary basis, with a good outcome defined as an mRS score of 2 or less (mild impact, can care for self with no help but restricted in daily life) and a poor outcome defined as a score of 3 or more (moderate impact requiring help in daily life).

Detail of statistical methods

Calculation of case number (based on crossover design)

Extent of individual goal attainment was defined as the primary outcome. The Goal Attainment Scale (GAS)

was used to measure this. This was divided into 2 categories: less than 0 (failure) and 0 or more (success). A success rate of 55% was assumed for the TEAM group, and of 25% for the control group, which received standard treatment. The case number was determined using simulation with a random effects model for the logit of probability of success. The random effect used was taken to have a normal distribution of $N(0;0.2)$. The logit of success using TEAM treatment (standard treatment) was $\alpha_i + 0.2$ ($\alpha_i -1.1$). It was calculated that 27 patients per treatment order were needed in order to determine a difference between the two interventions with a power of 80% at the 5% level.

The principal secondary outcome was change in FIM as a result of the intervention. With 22 patients per treatment order (44 patients in total), a change in FIM for the TEAM intervention that differs by 3.5 points from the change found for standard treatment can be found with a power of 80%, at the 5% significance level (2-tailed) with a simple crossover. A conservative estimate of the crossover standard deviation (SD), $8 \times 2^{0.5}$, was used for this. Eight is the standard deviation of the change in FIM. The estimate of the SD is conservative, assuming that there is a positive correlation between the change in FIM in the two crossover periods.

In view of the findings for the primary outcome, we therefore aimed to enroll 27 patients per treatment order in the trial.

As a result of carryover effects, the planned crossover-design evaluation could not be performed. The first period was evaluated as a parallel-group design. The analysis lost a great deal of power as a result: there is more variation in the outcomes because the trial participants no longer act as their own controls. Significant findings of this analysis are reliable with an α error of 0.05 (protection against false positives is guaranteed as required). However, statistically insignificant findings cannot be interpreted as an absence of important difference (protection against false negatives is no longer guaranteed). Eliminating this type of uncertainty using post-hoc power calculation is not recommended in the literature (e15). Consulting the corresponding confidence intervals provides information on false negatives. These have therefore been included in the results tables.

Methods of statistical analysis

Unless otherwise stated, this report states mean $\pm$ deviation as the descriptive statistic. For normally distributed variables, *t*-tests for independent samples were used to compare the means of the two groups (TEAM versus control).

A linear model with random effects was calculated to analyze the crossover trial. A sequence effect was tested for by evaluating the interaction effect: treatment $\times$ time. A significance level of 0.10 was used for this.

To evaluate treatment effects in the parallel groups, a general linear model with repeat measurements at each of 2 points in time (e.g. T1 for TEAM and T3 after TEAM) or a *t*-test of the differences for unmatched

samples was used. *t*-tests for matched samples were used to evaluate individual long-term progress.

For discrete variables (e.g. sex), 2 x 2 tables were analyzed using the chi-square test (or Fisher's exact test). A significance level of 0.05 was used. All tests were 2-tailed.

All calculations were performed using the statistics package R (version 3.1.2; www.R-project.org) or IBM SPSS Statistics (version 23).

Dropouts, sensitivity analyses

As all 6 patients who dropped out of the trial (3 per treatment order) were excluded shortly after randomization, before the intervention had begun or data had been collected, they were not included in the intention-to-treat statistical analyses (full analysis set: 47 patients).

In sensitivity analyses, the robustness of these findings was investigated for all 53 randomized patients, including the 6 dropouts, for both main outcomes (GAS and FIM). For FIM score, multiple imputation procedures (assuming missing figures were missing at random) were used to deal appropriately with the absence of data from the dropouts. For GAS (on a binary basis), a worst-case analysis was performed analogously to the confirmatory main analysis, assuming nonattainment of individual GAS goals for the 6 dropouts (assumption of 100% treatment failure for dropouts).

The CONSORT flow diagram for details on trial enrolment, randomization to the 2 treatment orders, and patient flow is shown in *eFigure 2*.

Results

eTable 1 contains information on quality of life, participation, care needs, and burdening of relatives.

Extent of goal attainment (as a percentage) in patients' individual participation goals at each visit, for the total trial population, is shown in *eFigure 3*.

Sensitivity analyses for GAS and FIM scores

Outcome goal attainment (GAS) (data from first treatment period): For corresponding ITT analysis including the 6 dropouts, failure (i.e. nonattainment of GAS goal) was assumed conservatively for these patients. This gives 12 treatment failures and 14 successes for treatment order A (TEAM), and 22 failures and 5 successes for treatment order B (control). This worst-case analysis confirms again the superiority of the TEAM intervention over standard treatment: the percentage of goal attainment using TEAM was 53.85% [35.05; 71.61], versus 18.52% [7.92; 37.51] for the control.

Odds ratio (OR) for success: 5.133 [1.486; 17.738]; *p* = 0.0103.

Outcome ability in daily life (FIM) (data from first treatment period): With the assumption of missing at random for the 6 dropouts, there are 1000 imputations in the Mann-Whitney U-test, *p*-value <0.0041.

In multiple imputations the means for the increase in independence in daily activities (end of first treatment phase versus baseline) for the two groups was estimated as follows:

- Group A (TEAM), mean change: 7.399 FIM points, SD = 0.553
- Group B (standard), mean change: 0.893 FIM points, SD = 0.293.

This sensitivity analysis can thus confirm the robustness of the main finding.

eFIGURE 1

TEAM trial design and conduct

TEAM: Participation-focused outpatient program

eFIGURE 2

CONSORT flow diagram showing details on trial enrolment, randomization to the two treatment orders, and patient flow

eFIGURE 3

Goal attainment (%)

for individual participation goals at each visit, as percentages of the total trial population ($n = 47$)

Visits:

- 1 = enrolment
- 2 = 1 month
- 3 = 3 months
- 4 = 4 months
- 5 = 6 months
- 6 = 12 months

eTABLE 1

Quality of life, participation, care needs, and burden on relatives at times T1 (baseline) and T3 (end of first treatment period, including 2-month washout phase)

Measuring tool, domain	TEAM group (n = 23)		Control group (n = 24)		p-value *
	0 months	3 months	0 months	3 months	
WHODAS 2.0, overall	59 ± 17	57 ± 18	66 ± 16	61 ± 17	0.279
– Cognition	43 ± 15	42 ± 21	50 ± 22	43 ± 21	0.093
– Mobility	64 ± 27	61 ± 28	69 ± 24	67 ± 27	0.971
– Self-care	61 ± 26	56 ± 24	60 ± 28	55 ± 34	0.842
– Getting along	42 ± 28	37 ± 26	54 ± 26	51 ± 26	0.974
– Life activities	66 ± 20	65 ± 19	67 ± 16	63 ± 21	0.701
– Participation	62 ± 18	61 ± 20	74 ± 17	66 ± 20	0.256
SF-36 patients PCS	29 ± 8	31 ± 7	29 ± 10	28 ± 8	0.368
SF-36 patients MCS	48 ± 11	49 ± 13	46 ± 12	48 ± 12	0.829
SF-36 relatives PCS	49.7 ± 11.5	47.9 ± 10.2	44.5 ± 10.6	44.8 ± 10.3	0.611
SF-36 relatives MCS	44.1 ± 12.2	44.5 ± 10.3	44.1 ± 10.2	46.3 ± 12	0.179
EQ-5D VAS patients	43 ± 15	50 ± 17	47 ± 22	55 ± 22	0.918
EQ-5D VAS relatives	75.8 ± 19	71.5 ± 18.9	67.3 ± 17.2	69.5 ± 18.8	0.128
NAA, overall	39 ± 27	33 ± 24	35 ± 21	35 ± 20	0.245
– Mobility	2 ± 3	2 ± 3	2 ± 3	2 ± 3	0.605
– Cognition	6 ± 7	5 ± 6	5 ± 4	5 ± 5	0.708
– Conduct	4 ± 5	4 ± 5	3 ± 2	3 ± 3	0.461
– Self-care	8 ± 7	6 ± 6	7 ± 8	6 ± 7	0.697
– Daily activities	5 ± 5	4 ± 5	4 ± 4	4 ± 4	0.392
– Chores	15 ± 6	12 ± 6	15 ± 6	14 ± 5	0.127
CSI relatives	9.8 ± 6.4	9.8 ± 6.0	11.8 ± 6	11.5 ± 6.5	0.751

*general linear model with repeat measurement, 2-tailed

CSI, Caregiver Strain Index; EQ-5D, EuroQol Quality of Life questionnaire; PCS, physical composite summary; NAA, New Appraisal Assessment: Nursing Care; MPS, mental composite summary; SF-36, Short-Form 36 quality of life questionnaire; TEAM, participation-focused outpatient program; VAS, visual analog scale; WHODAS, WHO Disability Assessment Schedule 2.0

eTABLE 2

Assessments/Measuring tools to test hypothesis

No.	Aspect tested	Measuring tool
1.	Extent of individual goal attainment	Goal Attainment Scale (GAS)
2.	Improvement in independence in daily activities	Functional Independence Measure (FIM)
3.	Improvement in participation	WHO Disability Assessment Schedule (WHO-DAS) 2.0
4.	Extent of care needs	New Appraisal Assessment: Nursing Care (NAA)
5.	Improvement in quality of life	EuroQol Quality of Life questionnaire (EQ-5D) Short-Form 36 quality of life questionnaire (SF-36)
6.	Reduction in burden on caregiving relatives	Caregiver Strain Index (CSI)
7.	Global outcome	Modified Rankin Scale (mRS)

eTABLE 3

Trial assessment schedule

Category	Assessment	T1			T2			T3			T4			T5			T6				
Time of assessment		Baseline before randomization			After 1 st TEAM phase (at 1 month)			Before 2 nd TEAM phase (at 3 months)			After 2 nd TEAM phase (at 4 months)			At 6 months			Final visit at 1 year				
		Patient	Relative	Home	BTC	Patient	Relative	Home	BTC	Patient	Relative	Home	BTC	Patient	Relative	Home	BTC	Patient	Relative	Home	BTC
IDA	FIM	+		+	+	+		+		+		+		+			+	+		+	
QoL	SF-36	+	+	+	+	+	+	+	+	+	+	+	+	+	+		+	+	+	+	
	EQ-5D	+	+	+	+	+	+	+		+	+	+		+	+		+	+	+	+	
Participation	WHODAS 2	+	+	+	+	+	+	+	+	+	+	+	+	+	+		+	+	+	+	
	GAS	+		+	+	+		+		+		+		+			+	+		+	
Use of nursing	NAA	+		+		+		+		+		+		+			+				
	CSI		+		+		+	+			+	+			+		+		+	+	
Global outcome	mRS	+		+	+	+		+		+		+		+			+	+		+	

IDA, independence in daily activities; CSI, Caregiver Strain Index; EQ-5D, EuroQol Quality of Life questionnaire; FIM, Functional Independence Measure; GAS, Goal Attainment Scale; mRS, Modified Rankin Scale; NAA, New Appraisal Assessment; Nursing Care; QoL, Quality of life; SF-36, Short-Form 36 quality of life questionnaire; TEAM, participation-focused outpatient program; BTC, Burgau Treatment Center; VAS, visual analog scale; WHODAS 2, WHO Disability Assessment Schedule 2.0

eBOX

Case study

Patient H was encouraged by her physiotherapist to sign up for the TEAM trial two years after her stroke (subarachnoid hemorrhage [SAH] 2012). She and her husband were disappointed and frustrated by the lack of transferability of the activities practiced and learned in therapy to everyday home life.

Following her SAH, patient H spent 4 months in inpatient rehabilitation (2.5 months in phase B, 1.5 months in phase C). From there she was discharged home. The 51-year-old qualified geriatric care nurse lives with her husband in a small, disability-adapted apartment in a high-rise block.

During diagnosis for TEAM participation patient H gave an initial insight into her daily life, which had changed in many ways for her, her husband, and the rest of their family following her SAH. Patient H's mobility was hugely restricted by her right-sided hemiparesis: she could not move her right arm voluntarily, and the only movement in her right leg was bending of her hip and knee, which required a great deal of effort. As a result of a lack of trunk control and resulting balance problems, she required two side armrests in order to sit for long periods without a risk of falling. Patient H could control her wheelchair using her left leg and foot and so move around her apartment without outside help, but this required a great deal of time and effort. Everyday activities posed huge challenges for her. In the mornings it took her more than 1.5 hours to get out of bed, sit in her wheelchair, and wash at the sink. In addition, during such activities her muscle tension increased so much that she experienced pain in her right arm and right foot and her trunk became so rigid that she needed to lie down for one hour afterwards.

Patient H described her greatest burden/participation restriction as follows: "I feel trapped in my wheelchair and the apartment. I constantly need help because I can't get up on my own to get something out of the cupboard or carry a cup to the table." She was therefore continually reliant on her husband or mother to help and assist her; they helped her to go to the toilet, for example.

Before her TEAM treatment patient H left her apartment only to attend physiotherapy. There she had spent two years practicing getting out of her wheelchair alone. Approximately 10 months previously she had been able to take four steps alone, using parallel bars, for the first time. Patient H and her husband were overjoyed at this. Her mother, who drove her to visit the physiotherapist once a week, also hoped that this would result in relief and an easing of the burden for all family members. Unfortunately, patient H was not able to use these newly learned activities—standing up and taking steps—at home. Standing up continued to require so much effort in the right side of her body that she lost contact between her right foot and the floor, so she risked falling when going to the toilet, for example. Patient H's disappointment increased from one physiotherapy session to the next, and she canceled therapy sessions more and more frequently. Her husband, who helped her to get into the bath and with other difficult motor activities, started to suffer back pain and required inpatient treatment. Her mother wondered, "Does my daughter even want to be able to live life independently again?" When we first met patient H, we noticed scarring on her right arm and upper body. Patient H explained, "When I haven't got anything to do, which is often, sometimes I start scratching myself without really wanting to, and I don't notice what I'm doing until I start bleeding."

TEAM participation diagnosis centered on analyzing, together with patient H, why she was not able to integrate the activities of standing up and walking into her individual everyday home life. The conclusion reached was that it seemed to be because when getting up and standing, patient H was not able to determine for herself where her center of gravity was or in which direction she needed to move it in order to place her weight equally on both feet. Her fear on changing position seemed to be absolutely justified therapeutically. At the same time, it emerged that the layout of the countertops in her kitchen was unfavorable, so she was not able to use the abilities she had effectively.

At the case conference, patient H formulated her TEAM trial goal as follows: "In 4 weeks' time I'd like to be able to get about my apartment without my wheelchair and also be able to carry things like a laundry hamper."

Within a real therapeutic living environment (e.g. kitchen) and situation (e.g. breakfast), work was done with patient H on the skill of determining her center of gravity herself in every starting position and correcting it with reference to her leg, foot, and trunk position, in 2.5 hours of individual therapy per day. This successfully laid the groundwork for stable posture, stable standing, and control in the supporting and nonsupporting legs while walking. In 1.5 hours of daily group therapy, strategies were developed, with therapeutic guidance, to use the newly acquired abilities in collaboration with others and with the use of divided attention. To optimize environmental factors at home and ensure that changes were made, for example in washing and dressing, a TEAM therapist made 4 visits to the patient at home.

One week after the end of the TEAM treatment patient H had parked her wheelchair in the study and always walked around her apartment. She reported that she herself was amazed how much else had changed in her everyday life. She no longer needed the nursing bed that had been in the middle of the living room, as she could now get up and walk from her normal bed. In the mornings she had finished bathing after 60 minutes. A quite new discovery for her was that there was barely any increase in tension in her arm and leg, so this no longer caused her pain, and she no longer needed a rest in the mornings. She was very happy that she could once again manage everyday housework without help: she now did all the laundry herself and looked after her cat. Her husband said, "I'd never have thought it possible I'd see my wife so happy without her wheelchair here." Patient H added proudly, "I can do a bit of shopping on my own, on foot with the walking stick, on the first floor, then afterwards I meet my mom for a coffee like I used to." Her mother said, relieved, "My daughter needs much less help from me, and that means we have time to do things together again, like we did before her stroke." When asked by the TEAM therapist how her skin looked, patient H had to check it herself and said, astonished, "No, I don't scratch myself anymore—I don't get bored anymore."