Home-based constraint-induced movement therapy for patients with upper limb dysfunction after stroke (HOMECIMT): a cluster-randomised, controlled trial

Anne Barzel, Gesche Ketels, Anne Stark, Britta Tetzlaff, Anne Daubmann, Karl Wegscheider, Hendrik van den Bussche, Martin Scherer

Summary

Background Constraint-induced movement therapy (CIMT) is recommended for patients with upper limb dysfunction after stroke, yet evidence to support the implementation of CIMT in ambulatory care is insufficient. We assessed the efficacy of home CIMT, a modified form of CIMT that trains arm use in daily activities within the home environment.

Methods In this parallel, cluster-randomised controlled trial, we selected 71 therapy practices in northern Germany that treat adult patients with upper limb dysfunction after stroke. Practices were stratified by region and randomly allocated by an external biometrician (1:1, block size of four) using a computer-generated sequence. 37 practices were randomly assigned to provide 4 weeks of home CIMT and 34 practices to provide 4 weeks of standard therapy. Eligible patients had mild to moderate impairment of arm function at least 6 months after stroke and a friend or family member willing to participate as a non-professional coach. Patients of both groups received 5 h of professional therapist contact in 4 weeks. In the home CIMT group, therapists used the contact time to instruct and supervise patients and coaches in home CIMT. Patients in the standard therapy group received conventional physical or occupational therapy, but additional home training was not obligatory. All assessments were done by masked outcome assessors at baseline, after 4 weeks of intervention, and at 6 month follow-up. The primary outcomes were quality of movement, assessed by the Motor Activity Log (MAL-QOM, assessor-assisted self-reported), and performance time, assessed by the Wolf Motor Function Test (WMFT-PT, assessor-reported). Primary outcomes were tested hierarchically after 4 weeks of intervention and analysed by intention to treat, using mixed linear models. This trial is registered with ClinicalTrials.gov, NCT01343602.

Findings Between July 11, 2011, and June 4, 2013, 85 of 156 enrolled patients were assigned home CIMT and 71 patients were assigned standard therapy. 82 (96%) patients in the home CIMT group and 71 (100%) patients in the standard therapy group completed treatment and were assessed at 4 weeks. Patients in both groups improved in quality of movement (MAL-QOM; change from baseline 0·56, 95% CI 0·41–0·71, p<0·0001 for home CIMT *vs* 0·31, 0·15–0·46, p=0·0003 for standard therapy). Patients in the home CIMT group improved more than patients in the standard therapy group (between-group difference 0·26, 95% CI 0·05–0·46; p=0·0156). Both groups also improved in motor function performance time (WMFT-PT; change from baseline –25·60%, 95% CI –36·75 to –12·49, p=0·0006 for home CIMT *vs* –27·52%, –38·94 to –13·94, p=0·0004 for standard therapy), but the extent of improvement did not differ between groups (2·65%, –17·94 to 28·40; p=0·8152). Nine adverse events (of which six were serious) were reported in the home CIMT group and ten (of which seven were serious) in the standard therapy group; however, none was deemed related to the study intervention.

Interpretation Home-based CIMT can enhance the perceived use of the stroke-affected arm in daily activities more effectively than conventional therapy, but was not superior with respect to motor function. Further research is needed to confirm whether home CIMT leads to clinically significant improvements and if so to identify patients that are most likely to benefit.

Funding German Federal Ministry of Education and Research.

Lancet Neurol 2015

Published Online
July 29, 2015
http://dx.doi.org/10.1016/S1474-4422(15)00147-7

See Online/Comment
http://dx.doi.org/10.1016/S1474-4422(15)00183-0

Department of Primary Medical Care (A Barzel MD, A Stark MSc, B Tetzlaff MSc, Prof H van den Bussche MD, Prof M Scherer MD), **Department of Physiotherapy** (G Ketels BA), **and Department of Medical Biometry and Epidemiology** (A Daubmann MSc, Prof K Wegscheider PhD), **University Medical Center Hamburg-Eppendorf, Hamburg, Germany**

Correspondence to:
Dr Anne Barzel, Department of Primary Medical Care, University Medical Center Hamburg-Eppendorf, D-20246 Hamburg, Germany
a.barzel@uke.de

Introduction

Constraint-induced movement therapy (CIMT) is a promising intervention for the rehabilitation of patients with upper limb dysfunction after stroke.[1,2] Results of the EXCITE trial,[3] the largest CIMT trial to date, showed that patients who receive CIMT have significant and long-term improvements in arm function. Tasks used in CIMT trials relate to activities of daily living,[4] and CIMT was found to be effective with respect to activity and participation components of the International Classification of Functioning, Disability, and Health.[2,5,6] However, this evidence does not necessarily change clinical practice.[7] CIMT has not been established as standard care for ambulatory stroke patients. Because of the large professional resource demand of 60 h one-to-one supervision in the original protocol,[3,8] modified types of CIMT have been developed.[9] In most studies, including a trial by Smania and colleagues,[10] modified CIMT was more effective than conventional therapy, although the strength of these results was limited by small sample size or high dropout rate, or both. Therefore, there is a broad agreement on the need for

Research in context

Evidence before this study

We did a search of interventional studies in PubMed, Cochrane Library, Medline, and Ovid with the terms "stroke", "hemiplegia", "constraint-induced movement therapy", "forced use therapy", "upper limb or upper extremity or arm", and "physical therapy" or "occupational therapy" published up to March 26, 2015. We identified eight systematic reviews and reports of 18 randomised controlled trials of CIMT versus conventional therapy. In a large clinical trial, patients allocated to CIMT for 60 h (6 h per weekday, 5 days per week for 2 weeks) showed significant improvement that persisted for 1 year. Most reported randomised controlled trials used modified CIMT with less professional training (20–30 h) and sample sizes of 16–66 patients, with ten studies having a sample size of 35 patients or fewer. Moreover, only a minority of studies determined a sample size calculation a priori. Loss to follow-up was 0–39% and remained unclear in two studies. At present, little follow-up data of modified CIMT are available and no data from more than 3 months post intervention exist. Thus, the long-term benefits of modified CIMT have been questioned. In line with previous systematic reviews, findings from a Cochrane review concluded that there is a need for adequately powered, high-quality randomised controlled trials to confirm the benefits of modified CIMT interventions. Moreover, in a review, Kwakkel and colleagues demanded innovative, adaptive forms of CIMT to reduce the staff-to-patient ratio.

Added value of this study

We present a sufficiently powered, cluster-randomised trial with a 6 month follow-up to assess the efficacy of home-based CIMT in patients with chronic moderate arm impairment after stroke. Our results suggest that 4 weeks of self-determined training in the home environment, with weekly visits by supervising therapists, can enhance perceived arm use in activities of daily living more effectively than conventional therapy, but is not superior to standard therapy with respect to motor function.

Implications of all the available evidence

Further research could help determine the clinical significance of the perceived enhanced arm use in activities of daily living and how to identify patients that are most likely to benefit from this method of implementing CIMT in ambulatory care.

more randomised trials with larger sample sizes, relevant measures, and sufficient follow-up.[2,4,11,12]

Home CIMT is a modified form of CIMT that reduces the need for professional assistance in ambulatory care, but contains specific elements of the original CIMT protocol,[8] such as repetitive training of the most affected arm following shaping principles, the transfer package, and immobilisation of the unaffected hand (panel). Based on patient participation and enhancement of activities related to daily living, home CIMT trains the increased use of the stroke-affected arm in daily life within the patient's home environment. Patients are involved in treatment planning and delivery by formulating participation-oriented goals (eg, drinking from a cup) and taking personal responsibility for the daily independent practice together with a non-professional coach (eg, family member). We have previously shown in a feasibility study[13] that patients who do home CIMT achieved similar results as patients who received original CIMT.

The aim of the HOMECIMT trial was to test home CIMT against standard therapy for patients with upper limb dysfunction after stroke in ambulatory care. We hypothesised that patients who receive home CIMT will increase use of their stroke-affected arm in daily activities more than patients who receive conventional physical or occupational therapy.

Methods

Study design

We did this parallel, cluster-randomised, single-blind controlled intervention trial of home CIMT versus standard care for patients with stroke-derived upper limb dysfunction receiving treatment in community therapy practices in northern Germany. Because we judged that the same therapist would not be able to practise two different treatments without sharing the aspects of the training between the two groups, we chose a cluster randomisation design to reduce contamination of between groups. The study protocol has been published[14] and ethics approval was granted by the Ethics Committee of the Medical Association of Hamburg, Germany (reference PV3737).

Participants

We used a geographical information system[15] to define a comprehensible recruitment area in northern Germany, in which all identified therapy practices were invited to participate in the study. Based on community numbers, we formed regions in which recruitment was performed consecutively to afford easy access for the study personnel located in Hamburg. All physical and occupational therapy practices treating adult patients with upper limb dysfunction after stroke were eligible, unless they already offered CIMT. Each practice was allowed one participating therapist with a professional qualification or at least 2 years of experience in treatment of chronic impairment caused by stroke. Patient recruitment followed a two-step eligibility screening. First, we identified all potentially eligible patients from each practice, and then we assessed their eligibility in participating practices. Patients were eligible if they had a stroke a minimum of 6 months before study enrolment, with subsequent mild to moderate impairment of arm function and minimal

residual hand function (minimum 10° active wrist extension, 10° active thumb abduction or extension, and 10° extension of two additional fingers),[8,13] had a referral for physical or occupational therapy, were aged 18 years or older, and had a caregiver who was prepared to be a non-professional coach (eg, family member). We

***Panel:* Comparison of home CIMT and standard therapy**

Home CIMT*

Location

The location of home CIMT is in the patient's own home environment.

Professional therapy

Patients have two home visits of 50–60 min in the first week and three home visits of 50–60 min in the next 3 weeks with a physical or occupational therapist. During the first and second home visits, patients receive information and instruction of the basic principles of CIMT, agree on therapy (behavioural contract),† set goals relevant to the patient's participation in everyday activities (Goal Attainment Scale), learn to immobilise the less affected arm with a resting glove,‡ discuss responsibilities of non-professional coach, and try exercises that are relevant to everyday life with special focus on activities of daily living (eg, holding the handle of a cup and bringing it to the mouth, opening and carefully closing kitchen cupboards, hanging up a clothes hanger, opening a drawer with a knob, cutting carrots into pieces); these exercises are adapted to the patient's abilities, and the patient receives two to three additional exercises weekly (10–15 exercises in total).§ The last three home visits focus on supervision and adjustment through problem solving (ie, clarifying patient's or non-professional coachs' questions†) and controlling or adjusting exercises and practice.¶

Non-professional practice

The patient is accompanied by a non-professional coach and is recommended to do exercises with the stroke-affected arm in the home environment for 2 h each weekday, giving 40 h of practice in 20 days. Three to 15 exercises are done repetitively, each in a set of ten, spending 30–60 s per trial. The non-affected hand is immobilised with a resting glove (2 h) and feedback on exercise performance is given by the non-professional coach.||

Documentation

The non-professional coach|| maintains a training diary to document the time per exercise (using a stopwatch), the number of repetitions, and the time of practising.

Additional recommendation

Patients should wear the resting glove during activities of daily living (2–4 h/day)‡ and use the stroke-affected arm as much as possible in everyday activities.†

Standard therapy

Location

The location of standard therapy depends on the prescription and is given either in a patient's home or in a therapeutic practice.

Professional therapy

Patients have ten sessions of 25–30 min or five sessions of 50–60 min sessions in 4 weeks together with a physical or occupational therapist. Techniques are applied during therapy sessions (eg, neurodevelopmental treatment [Bobath], Perfetti, proprioceptive neuromuscular facilitation, Affolter, apparatus therapy, functional training, massage therapy, and soft tissue manipulation). Therapy content is adjusted according to usual care of stroke patients with upper limb impairment (eg, arm, shoulder, and hand mobilisation, isometric training, strengthening of muscles, muscle tonus reduction, training of skills and activities of daily living, perceptual and sensory training, assisted movement, fine motor skills training, trunk mobilisation and stabilisation). The selection of techniques and therapy content is subject to the therapist's assessment of the patient and the prescription and depends on the therapist's individual knowledge and preference.

Non-professional practice

The choice of non-professional practice depends on the therapist's recommendation but is not mandatory. A non-professional coach is not intended. Specific homework is given by the therapist, but is not mandatory.

Documentation

The therapist uses a standardised documentation sheet to record the number and content of therapy sessions with respect to the applied therapy and techniques.

Additional recommendations

Use of a resting glove is not part of standard therapy, and patients should use the stroke-affected arm in everyday life activities dependent on the therapist's recommendation.

Home CIMT=constraint-induced movement therapy at home. *Home CIMT is a modification of original CIMT,[8,22] which contains the three basic components (the transfer package,† immobilisation of the non-affected hand,‡ and repetitive training of the more-affected arm§¶|| following shaping principles). By contrast with original CIMT, professional contact time in home CIMT is low (5 h *vs* 60 h) and practising is not delivered by therapists in a 1:1 ratio but is self-determined by the patient and a non-professional coach. Thus, some CIMT components are done partly by professional therapists and partly by patients together with their non-professional coach. Moreover, a special focus of home CIMT is set on patients' participation in jointly selecting tasks and exercises related to activities of daily living in the home environment. †The transfer package is a set of techniques to incorporate therapeutic gains from the training into daily life,[22] including behavioural contract (therapist and patient, and for home CIMT this includes a non-professional coach), daily home diary (patient and non-professional coach), problem solving (therapists, telephone hotline), home skill assignment (original CIMT, not required in home CIMT since patients perform self-determined practicing in their home environment). ‡Immobilisation of the less affected upper extremity involves wearing a hand splint to prevent use of that arm for a target of 90% of waking hours (original CIMT) or wearing a resting glove for 4–6 h/day (home CIMT). §Selecting tasks that are tailored to address the motor deficits of the individual patient. ¶Modelling, prompting, and cuing of task performance. ||Quantifying (number of repetitions within the 30–60 s trial period or time needed to do a set number of repetitions) and immediate feedback of improvements in the speed and quality of movement (by the non-professional coach in home CIMT).

excluded patients with severely impaired verbal communication, inability to give consent, severe neurocognitive deficits (a score of less than 23 in the mini mental state examination), terminal illness, or life-threatening comorbidities, or who had previously received CIMT. Written informed consent was obtained from all participating therapists and patients, but caregivers were not asked for informed consent.

Randomisation and masking

Of the 231 identified practices, we excluded 160 practices that had no eligible patients, had no interest or time to participate, or met other exclusion criteria. The remaining 71 practices were stratified by region, and block randomisation (blocks of four) was used to allocate the practices to either home CIMT or standard therapy (1:1). Patients were included in the study before randomisation of practices to minimise differential self-selection. The randomisation was done centrally using a computer-generated sequence. A biometrical research assistant, who was otherwise not involved in the study, did the randomisation consecutively for each region as soon as written consent was obtained from all patients of that region. Neither the therapists nor the patients could feasibly be masked. Outcome assessors were masked to the patients' practice affiliation and were responsible for the data collection, including all outcome measurements. To keep assessors masked, patients and coaches were prompted not to reveal their treatment or study experiences to the assessors except for if safety measures were necessary. The statistician (AD) was masked to group allocation.

Procedures

Stroke-related anamnesis and patients' characteristics, such as age, sex, education,[16] handedness (ie, dominant hand affected by stroke), stroke severity,[17] motor impairment,[18] cognition,[19] comorbidity,[20] and muscle power[21] were recorded at baseline. We began the 4 week study intervention, as applied by their local physical or occupational therapist, within 2 weeks of the baseline assessment. Although patients in each group spent the same amount of time with a professional therapist (250–300 min), the therapy content and the therapists' role differed substantially between the two groups (panel).

In the home CIMT group, therapists used the first of five home visits to instruct the patient and the coach in the principles of home CIMT, set individually tailored goals, and work through the first two to three exercises, focusing on everyday practice. During subsequent weekly home visits, therapists supervised the training, set up new exercises, and applied behavioural techniques.[22] Professional therapy time was not used to practise exercises. Rather, patients were instructed to train in their home environment for 2 h each day, accompanied by a coach (figure 1). Additionally, patients were asked to wear a resting glove during exercises and activities of daily living to immobilise their non-affected hand. The therapists guided the coach on how to document the time or repetitions per time for each exercise and to assist the patient in keeping a training diary.

Patients in the standard therapy group received standard therapy, consisting of various therapeutic techniques typical of stroke therapy. The standard therapy group therapists reported details of professional treatment delivery and any agreements (eg, homework) made with patients via a standardised documentation sheet.

Therapists in the home CIMT group received a 5 h training session in home CIMT principles by study personnel experienced in CIMT. An expert telephone hotline was provided for additional support. Therapists in the standard therapy group obtained only written instructions to keep any deviation from standard care to a minimum. However, because informed consent was given before study enrolment, therapists of both groups were aware that the study objective was to enhance use of the stroke-affected arm in everyday life.

For assessment of home CIMT versus standard therapy, we used the Motor Activity Log (MAL) to measure activity[23,24] and the Wolf Motor Function Test (WMFT) to measure stroke-specific functional ability[25,26] as prerequisites for participation in activities of daily living.[14] Both measurements are customarily used in trials of CIMT. The MAL[8] is a written, structured assessor-assisted self-report of use of the stroke-affected arm that assesses quality of movement (MAL-QOM) and amount of arm usage (MAL-AOU) on a scale of 0–5 (where a score of 0 indicates worst performance or no use of arm, and 5 indicates best performance or normal movement) for 30 activities of daily living. In the WMFT, a trained assessor measures the time a patient takes to complete 15 functional tasks with the stroke-affected arm, allowing up to 120 s per task (performance time, WMFT-PT), and the patient's functional ability to do the task (WMFT-FA, where

Figure 1: **Patient and therapist during the initial meeting in the patient's home environment**
The therapist is instructing the patient how to perform daily practising based on the patient's goal (eg, eating with a fork); the patient is wearing a glove to immobilise his non-affected right hand.

0 indicates no attempt and 5 indicates normal movement).

To enable adjustment of the baseline data, we examined cognition, depression,[27] anxiety,[28] pain intensity,[29] and spasticity. All patient outcome measurements were assessed by masked assessors during home visits at baseline, at 4 weeks post intervention, and at 6 month follow-up, with an interim interview at 3 month follow-up (MAL). Assessors were therapists who had received a training session before they started collecting patient data during home visits. The study was monitored by a therapist with no other connections to this study, who regularly contacted therapists and assessors, using a standardised documentation sheet to ensure the trial was done in accordance with the study protocol. Furthermore, patients and assessors were requested to report any adverse events and were repeatedly asked whether they recognised any harms. Compliance was assessed in all participants via a form (standard therapy group) or a training diary (home CIMT group). Adherence to protocol was defined as a minimum of 75% of the agreed exercise time for home CIMT and a minimum of 75% of the required amount of professional standard therapy.

Outcomes

The coprimary outcomes were changes in activity and changes in motor function of the stroke-affected arm 4 weeks post intervention. We prespecified the MAL-QOM as the first of the hierarchically ordered primary outcomes because it is more relevant to daily activities than the WMFT-PT. The two other subscores, MAL-AOU and WMFT-FA, were analysed as secondary outcomes. Other secondary outcomes were hand function (a subdomain of the Stroke Impact Scale [SIS]), finger dexterity (Nine Hole Peg Test [NHPT]), independence in daily life (Barthel Index [BI]), and instrumental activities of daily living (IADL) at 4 weeks postintervention and at 6 month follow-up, as well as MAL-QOM and WMFT-PT at 6 months.

Statistical analysis

For the sample size calculation, effect sizes of 0·50 (MAL-QOM) and 0·55 (WMFT-PT) were assumed based on the reported minimal clinically important improvement.[23–26] Thus, MAL-QOM determined the sample size.[14] To reach a power of 80% with a type I error of 5%, 128 patients (64 patients per group) had to be included if randomisation took place at the patient level. With an assumed intracluster correlation of 0·05 and three patients per cluster, for cluster randomisation the design effect is 1·1, which increased the required sample size to 72 patients and 24 practices per group. Further details of sample size calculation are presented in the appendix. The data were analysed according to CONSORT statement extension for cluster-randomised trials.[30] We assessed baseline descriptive statistics for all randomly assigned patients (the intention-to-treat population) by treatment allocation.

The hypothesis that home CIMT is superior to

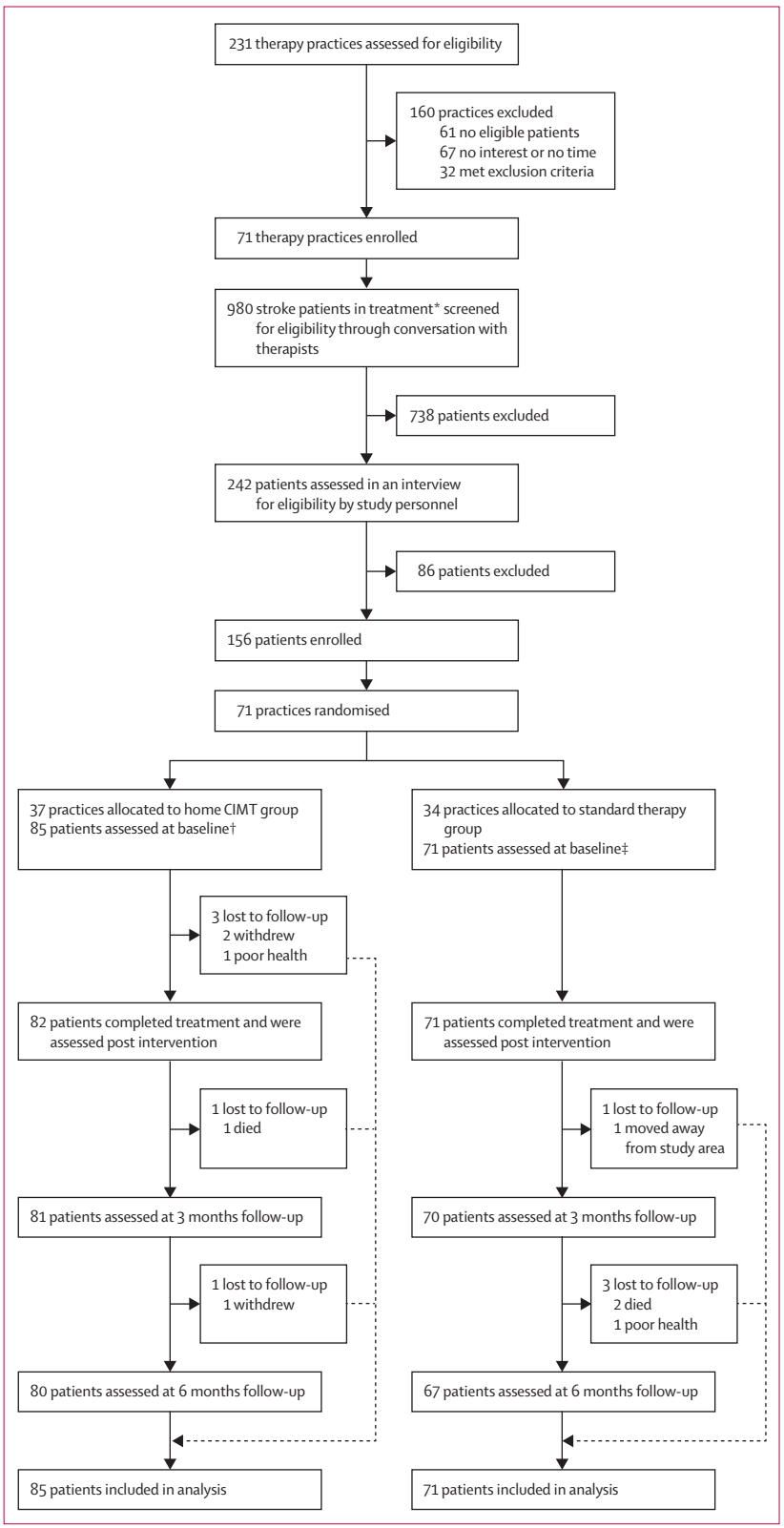

***Figure 2*: Trial profile**

*Median 12 patients (IQR 6–18) per practice. †Median two patients (IQR 1–3) per practice. ‡Median two patients (IQR 1–3) per practice.

See Online for appendix

standard therapy at 4 weeks post intervention was hierarchically tested for the two ordered primary outcomes (first MAL-QOM, then log WMFT-PT) at the two-sided significance level of 0·05. For this purpose, we did a random effect ANCOVA[31] for each endpoint, with practice as a random effect, group and region as fixed factors, and baseline age, sex, educational level, depression, anxiety, comorbidity, cognition, and handedness as covariates. The intraclass correlation coefficient, a measure of the heterogeneity of the average responses between practices, was calculated and tested based on the random terms of the model. For WMFT-PT, we back-transformed the logarithmic values to allow interpretation on the original scale.

As a secondary analysis, we did an analogous random-effects repeated measurement ANCOVA including the 6 month follow-up, for each of the prespecified secondary outcome and the two primary outcomes, allowing heteroscedasticity and autocorrelation. These results were examined exploratorily.

The intention-to-treat population was included in both primary and secondary outcome analyses. In case of missing values, a last observation carried forward imputation was performed. Additionally, we did all primary and secondary analyses with the per-protocol population, which was defined by compliance to treatment standards and group allocation, full 4 week intervention, and complete data collection, to assess the consistency of the results of the primary analyses. We report the number of patients with an adverse event, and we did sensitivity analyses for the primary analysis with different imputations for missing values. For statistical analyses, we used IBM SPSS Statistics version 21.0 and SAS version 9.4.

This trial is registered with ClinicalTrials.gov, number NCT01343602.

	Home CIMT group (n=85)	Standard therapy group (n=71)
Age, years	62·55 (13·73)	65·30 (12·63)
Female	34 (40%)	28 (39%)
Living situation		
Alone	11 (13%)	9 (13%)
With family or friends	72 (85%)	58 (82%)
Institutional care	2 (2%)	4 (6%)
Level of education (CASMIN classification*)[16]		
Low	48 (57%)	33 (47%)
Middle	22 (26%)	26 (37%)
High	15 (18%)	12 (17%)
Employment situation		
Employed	10 (12%)	8 (11%)
Unemployed or retired	75 (88%)	63 (89%)
Type of stroke		
Haemorrhage	25 (30%)†	18 (25%)
Infarct	32 (38%)†	32 (45%)
Other or unknown	27 (32%)†	21 (30%)
Time since stroke, months	56·57 (47·36)†	45·65 (57·69)
Paresis on pre-stroke dominant side	41 (48%)	34 (48%)
Therapy applied in ambulatory care		
Physical therapy	77 (91%)	64 (90%)
Occupational therapy	72 (85%)	61 (86%)
Speech therapy	24 (28%)	20 (28%)
Stroke severity (Orpington Prognostic Scale)[17]		
Minor	68 (80%)	54 (76%)
Moderate	16 (19%)	16 (23%)
Major	1 (1%)	1 (1%)
Motor impairment (Motricity Index,[18] score 0–100)‡	63·06 (17·06)	66·07 (18·82)
Muscle power (upper extremity Medical Research Council Scale,[21] score 0–1)‡¶	0·62 (0·18)	0·67 (0·21)§
Spasticity (Modified Ashworth Spasticity Scale, score 0–5)‖	1·56 (1·15)	1·41 (1·19)
Pain intensity (Grading Chronic Pain Scale, score 0–100)‖	22·27 (25·39)	30·14 (28·08)§
Cognition (mini mental state examination,[19] score 0–30)‡	27·53 (4·01)	27·69 (3·12)
Comorbidity disease index,[20] number of affected domains**		
None	16 (19%)	15 (21%)
One	25 (29%)	19 (27%)
Two	20 (24%)	15 (21%)
Three or more	24 (28%)	22 (31%)

(Table 1 continues on next page)

Role of the funding source

The sponsors of the study had no role in the study design, data collection, analysis or interpretation, or in writing of the report. All authors had full access to all data in the study and agreed with the decision to submit the manuscript for publication. AB and MS had final responsibility for the decision to submit for publication.

Results

Between July 11, 2011, and June 4, 2013, 156 eligible patients were enrolled by the participating practices, of whom 85 (54%) received home CIMT and 71 (46%) received standard therapy (figure 2). 82 (96%) patients in the home CIMT group and 71 (100%) patients in the standard therapy group completed treatment. 81 (95%) patients in the home CIMT group and 70 (99%) patients in the standard therapy group were assessed at 3 months follow-up. 80 (94%) patients in the home CIMT group and 67 (94%) patients in the standard therapy group were assessed at 6 month follow-up. Patient demographic and clinical baseline characteristics are described in table 1. For the prespecified parameters that were used for adjustment of the baseline data, we detected no relevant differences between groups (appendix).

After 4 weeks of intervention, both groups showed an increase in the quality of movement of the stroke-affected arm (MAL-QOM) compared with baseline, when keeping the other variables constant (table 2, figure 3), with a greater improvement in the quality of movement in the home CIMT group than in the standard therapy group. Both groups improved performance time (WMFT-PT) significantly relative to baseline, but there was no

difference in performance time between the home CIMT and standard therapy groups at follow-up.

At 6 month follow-up, our analysis of MAL-QOM showed a greater improvement in quality of movement in the home CIMT group than in the standard therapy group (table 2). The amount of arm use (MAL-AOU) was significantly higher in the home CIMT group than in standard therapy group at all measurements. In the WMFT-PT analysis, patients in both home CIMT and standard therapy groups had improved performance time at the 6 month follow-up relative to baseline, but no difference was found between groups. Also, the WMFT-FA analysis showed no difference in functional ability between groups. We found only minimal changes and no differences between groups for other secondary outcomes, such as hand function, finger dexterity, independence in daily life, and instrumental activities of daily living (table 2).

Patients reported 19 adverse events during the study period, none of which was deemed related to the study interventions. Serious adverse events were reported in both groups. Admission to hospital was reported for five patients in the home CIMT group (one cardiovascular disease, one pneumonia, two falls, and one arm fracture) versus five patients in the standard therapy group (one recurrent stroke, one newly diagnosed cancer, one seizure, one ankle injury, and one lower leg fracture). Death was reported for one patient in the home CIMT group (cardiac event) versus two patients in the standard therapy group (one heart failure, one unknown reason). Other adverse events were lumbago (one patient in the home CIMT group *vs* two patients in the standard therapy group), rheumatism (one *vs* none), and poor health (one *vs* one).

Training diaries from the home CIMT group revealed an averaged exercise time (while wearing the resting glove) of 27·7 h (SD 14·7; median 32 h [IQR 15–40]) within the 4 week intervention. We also noted 12 cases of patients not adhering to the home CIMT protocol because of insufficient exercise time, because the therapy was considered too difficult by patient or caregiver, or because the therapist did not follow the protocol. Additional time wearing the resting glove, which was recommended but not mandatory, in the home CIMT group was documented in 53 (65%) of 81 training diaries, indicating a range of 20–80 h. According to therapists' documentation, no compliance problems occurred in the standard therapy group, but duration of additional exercise was not recorded since it was not mandatory.

In our per-protocol analyses, between-group differences in primary outcomes were larger in favour of the home CIMT group than the corresponding effects in the intention-to-treat analysis (appendix); however, significances of the intention-to-treat analysis were maintained, and the results of WMFT-PT did not differ between treatment groups. Sensitivity analysis confirmed the results of the intention-to-treat primary analysis for the MAL-QOM and WMFT-PT, but differences from baseline were lost for the WMFT-PT results (appendix).

	Home CIMT group (n=85)	Standard therapy group (n=71)
(Continued from previous page)		
Depression (Patient Health Questionnaire, score 0–27)††	6·69 (5·23)	6·40 (5·07)
Anxiety (Generalised Anxiety Disorder Scale-7, score 0–21)‡‡	3·92 (4·46)	3·70 (4·26)
MAL-QOM (score 0–5)	1·19 (1·02)	1·55 (1·27)
WMFT-PT (score 0–120 s)	17·03 (2·20)	13·87 (2·19)
MAL-AOU (score 0–5)	1·02 (0·97)	1·47 (1·35)
WMFT-FA (score 0–5)	2·71 (0·98)	2·82 (1·06)
Nine hole peg test, Pens/s	0·15 (0·20)	0·20 (0·23)
SIS hand function (score 0–100)	28·40 (28·62)	33·96 (28·72)
Barthel index (score 0–100)	79·71 (22·18)	82·82 (20·16)
IADL (score 0–5 or 0–8)	4·13 (2·39)	4·13 (2·30)

Data are n (%) or mean (SD). Home CIMT=home-based constraint-induced movement therapy. MAL-QOM=Motor Activity Log of quality of movement. WMFT-PT=Wolf Motor Function Test of Performance Time. MAL-AOU=Motor Activity Log of Amount Of Arm Usage. WMFT-FA=Wolf Motor Function Test of Functional Ability. SIS=Stroke Impact Scale. IADL=Instrumental Activities of Daily Living. *Education grade according to the international CASMIN classification: inadequately completed general education, general elementary education, or basic vocational qualification (low), intermediate qualification or general maturity certificate (middle), lower or higher tertiary education (high).†n=84. ‡Higher values indicate better function. §n=70. ¶Medical Research Council Scale index is the sum of the upper extremity muscle power assessments (flexion and extension of shoulder, elbow, wrist, fingers; 0–5 points each) in relation to the total score of 40 points. ||High values indicate more spasticity or more pain, respectively. **Includes eight domains (cardiovascular, respiratory, musculoskeletal, neurological [beside stroke], cancer, diabetes, visual, general [insomnia, chronic pain, anxiety, or depression]). ††Depression severity: minimal (0–4), mild (5–9), moderate (10–14), severe (15–27). ‡‡Anxiety severity: minimal (0–4), mild (5–9), moderate (10–14), severe (15–21). §§The number of pegs per s (maximum 18, ie nine pegs in and nine pegs out of the board during a maximum time of 120 s).

Table 1: **Baseline demographic and clinical characteristics**

Discussion

In the HOMECIMT trial, we show that 4 weeks of home CIMT can improve self-reported quality of arm use in activities of daily living in patients with upper limb dysfunction after stroke compared with standard physical or occupational therapy. However, we found no difference in the time needed to perform functional tasks (WMFT-PT) between patients receiving home CIMT and standard therapy. Our analysis of the activity outcome (MAL-QOM and MAL-AOU) showed that at the 6 month follow-up, self-reported arm use was still better in the home CIMT group than in the standard therapy group, but analysis of functional outcome (WMFT-PT and WMFT-FA) showed no difference in performance time and functional ability between groups.

Home CIMT was developed to provide a participation-oriented, therapeutic concept to the treatment of patients with chronic stroke-related dysfunction in long-term care.[13,14] With a mean post stroke time of about 4 years, our study population was representative of the typical patient in ambulatory care. By contrast with other trials of CIMT and modified CIMT,[4] home CIMT is done exclusively in the patient's own home. Within this environment, participation-oriented goals related to the individual's resources and capabilities were set, and patients had to take responsibility for the daily self-determined practice together with a non-professional coach. The therapists' role in home CIMT differed substantially from

	Home CIMT group n=85			Standard therapy group n=71				
	Mean (SD)	Change from baseline		Mean (SD)	Change from baseline		Between-group differences (home CIMT *vs* standard therapy)*	
		Adjusted mean (95% CI)	p value		Adjusted mean (95% CI)	p value	Adjusted mean (95% CI)	p value
Primary outcomes†								
MAL-QOM (score 0–5) after 4 weeks of intervention	1·78 (1·13)	0·56 (0·41–0·71)	<0·0001	1·81 (1·23)	0·31 (0·15; 0·46)	0·0003	0·26 (0·05–0·46)	0·0156
WMFT-PT after 4 weeks of intervention (0–120 s)‡	12·71 (1·62)	–25·60% (–36·75 to –12·49)	0·0006	10·98 (1·64)	–27·52% (–38·94 to –13·94)	0·0004	2·65% (–17·94–28·40)	0·8152
Secondary outcomes§ ¶								
MAL-QOM (score 0–5)								
4 weeks intervention	1·78 (1·13)	0·58 (0·44–0·72)	<0·0001	1·81 (1·23)	0·37 (0·22–0·51)	<0·0001	0·21 (0·04–0·38)	0·0154
3 months follow-up	1·80 (1·13)	0·52 (0·39–0·66)	<0·0001	1·78 (1·23)	0·32 (0·17– 0·46)	<0·0001		
6 months follow-up	1·73 (1·28)	0·58 (0·44–0·72)	<0·0001	1·87 (1·44)	0·37 (0·23–0·52)	<0·0001		
MAL-AOU (score 0–5)								
4 weeks intervention	1·58 (1·18)	0·53 (0·37–0·69)	<0·0001	1·65 (1·31)	0·25 (0·08–0·42)	0·0045	0·28 (0·07–0·49)	0·0105
3 months follow-up	1·53 (1·20)	0·49 (0·31–0·66)	<0·0001	1·61 (1·24)	0·20 (0·02–0·39)	0·0315		
6 months follow-up	1·57 (1·31)	0·57 (0·41–0·74)	<0·0001	1·75 (1·47)	0·29 (0·12–0·47)	0·0012		
WMFT-PT (0–120 s)‡								
4 weeks intervention	12·71 (1·62)	–25·57% (–36·64 to –12·57)	0·0005	10·98 (1·64)	–28·08% (–39·33 to –14·75)	0·0003	3·48% (–17·09–29·16)	0·7573
6 months follow-up	13·37 (1·95)	–23·73% (–36·43 to –8·49)	0·0040	10·90 (1·73)	–26·30% (–39·06 to –10·87)	0·0020		
WMFT-FA (score 0–5)								
4 weeks intervention	2·88 (0·96)	0·15 (0·05–0·26)	0·0033	3·10 (1·11)	0·28 (0·18–0·39)	<0·0001	–0·13 (–0·27–0·01)	0·0678
6 months follow-up	2·88 (1·11)	0·12 (–0·00–0·25)	0·0547	3·04 (1·24)	0·25 (0·13–0·38)	0·0002		
Finger dexterity (nine hole peg test, Pens/s ‖)								
4 weeks intervention	0·17 (0·21)	–0·01 (–0·01–0·03)	0·3259	0·21 (0·23)	0·01 (–0·01–0·03)	0·1900	–0·00 (–0·03–0·02)	0·7595
6 months follow-up	0·16 (0·21)	0·00 (–0·02–0·02)	0·8412	0·21 (0·24)	0·01 (–0·02–0·03)	0·5847		
Hand function (SIS, score 0–100)								
4 weeks intervention	39·09 (31·03)	9·89 (5·83–13·96)	<0·0001	36·83 (28·97)	4·42 (0·09–8·74)	0·0453	5·47 (–0·00– 10·95)	0·0501
6 months follow-up	38·35 (30·93)	11·09 (6·76–15·43)	<0·0001	40·55 (33·84)	5·62 (1·04–10·20)	0·0167		
Independence in daily life (Barthel Index, score 0–100)								
4 weeks intervention	82·65 (20·74)	2·32 (0·86–3·79)	0·0021	83·52 (20·20)	1·25 (–0·27–2·77)	0·1074	1·07 (–0·82–2·97)	0·2653
6 months follow-up	80·71 (22·30)	0·98 (–0·72–2·67)	0·2572	82·89 (19·78)	–0·10 (–1·84–1·65)	0·9132		
IADL (score 0–5 or 0–8)								
4 weeks intervention	4·05 (2·45)	–0·09 (–0·35–0·17)	0·5091	4·03 (2·24)	–0·07 (–0·35–0·20)	0·5991	–0·01 (–0·35–0·33)	0·9372
6 months follow-up	4·27 (2·57)	0·14 (–0·14–0·41)	0·3205	4·25 (2·46)	0·15 (–0·14–0·44)	0·3005		

CIMT=constraint-induced movement therapy. MAL-QOM=Motor Activity Log of Quality of Movement. WMFT-PT=Wolf Motor Function Test of Performance Time. MAL-AOU=Motor Activity Log of Amount of Arm Usage. WMFT-FA=Wolf Motor Function Test of Functional Ability. SIS=Stroke Impact Scale. IADL=Instrumental Activities of Daily Living. *Interpretation of between-group differences depends on the scale of the outcome variable: positive values are in favour of the home CIMT group and negative values are in favour of the standard therapy group, except for WMFT-PT. †Random effects analysis of covariance. ‡Geometric mean and SE because of the log-normal distribution, which is caused the change to multiplicative model. §Random effects repeated measurement ANCOVA. ¶For the primary analysis, only data from baseline and 4 weeks were used; in secondary analyses, repeated measurements up to 6 months were used, including the 4 week measurements. Minimal differences occur between adjusted means and p values since adjustment changed slightly. ‖The number of pegs per s (maximum 18 ie, nine pegs in and nine pegs out of the board during a maximum time of 120 s).

Table 2: **Effects of home-based constraint-induced movement therapy and standard therapy on primary and secondary outcomes**

conventional physical or occupational therapy since the therapeutic contact time is mainly used for instruction and supervision of the patients and the coach.

Other CIMT trial protocols have applied a minimum of 30 h[32] and up to 60 h[3,6] of professional therapy in a 1:1 ratio of therapist to patient. However, resource intensity and therapy dosage have been repeatedly described as limiting factors to the implementation of CIMT or modified forms of CIMT in standard care.[9,12,33]

Retention in our study was excellent, with dropout of three patients from the home CIMT group and no patients from the standard therapy group. Our results of enhanced quality of arm use (MAL-QOM) of home CIMT over standard therapy are in agreement with results of other studies of CIMT and modified CIMT.[3,8,9,32,34] Although MAL baseline values are comparable to those of other CIMT trials,[3,9] improvements in arm use are somewhat smaller in our trial. However, considering the difference in post-stroke time (3–9 months in the EXCITE trial[3]), our findings show that improvements in real-world arm use are still achievable even years after a stroke. Furthermore, a

long-lasting effect on arm use has only been shown in a few studies[3,35] and is remarkable in view of the relatively low dose and intensity of professional training in our study. In line with other trials,[3,10] participants receiving standard therapy in the standard therapy group also showed improvements, indicating the benefit of standard therapy for care of patients with chronic impairment caused by stroke. However, the difference in the extent of improvement between groups was small. With respect to the functional outcome (WMFT-PT), other trials have also shown no significant benefit of CIMT over standard therapy.[10,36] Few studies that apply higher doses of professional therapy found beneficial effects in the WMFT.[3,37] A potential dose effect has been discussed previously.[2,6,12] In our study, the patients and non-professional coaches might not have emphasised speed in the same way as professional therapists. Additionally, how fast everyday activities are performed might be of secondary importance for patients, as long as they can use their stroke-affected arm.

By contrast with the results of the EXCITE trial,[3] we found no difference in hand function (Stroke Impact Scale) between groups. With respect to disability (Barthel Index and instrumental activities of daily living), patients showed only small changes. This can be explained by the fact that these measurements include features not particularly targeted by home CIMT. The medical literature is inconclusive about the effect of CIMT or modified CIMT on these outcomes.[4,9,34]

Most upper limb function measurements assess function in the sense of capacity (eg, WMFT, Arm Research Arm Test), whereas only a few measurements assess perceived performance (eg, MAL) or actual performance (eg, accelerometry) in daily life.[38] Thus, accelerometry seems to be an appropriately objective measurement but is not yet sufficiently standardised.[39] In our study, we used MAL-QOM and WMFT-PT as primary outcomes and were able to compare our results to other CIMT studies. However, further research is necessary to develop a more appropriate measurement to quantify arm use in activities in daily living relevant to patients with chronic stroke-related impairments.

Our study has several limitations. First, standard therapy can imply some uncertainty with respect to the therapy applied. However, we monitored standard therapy thoroughly and asked therapists in the standard therapy group to document the performed therapy sessions. Second, the self-determined practising accompanied by a non-professional coach was mandatory only in the home CIMT group, leading to a potential bias with regard to practising time. Third, motivation and study participation might have affected our results, and we cannot exclude the possibility that therapists, patients, or coaches were particularly motivated to achieve improvements. Fourth, our first primary outcome (MAL-QOM) is based on the patients' perceived performance and is therefore a subjective estimate. However, the reliability and the validity of the MAL-QOM have been shown.[23] An increased self-efficacy and motivation, which is intended in home CIMT, might have triggered positive responses in the home CIMT group, but that might be true for patients in the real world as well as in our study. Fifth, we did not collect any personal data from the participating coaches; we are doing a separate qualitative study to gather information on the experiences of patients and coaches with home CIMT to gain a deeper insight into the strategies of coping with the new therapeutic concept in everyday life. Finally, our study design permitted only practices without previous experience in CIMT. Thus, we do not know whether the difference between groups in MAL-QOM would have been larger if therapists with advanced CIMT expertise had applied home CIMT. In summary, home CIMT combined the therapists' professional guidance and the patients' self-determined training together with a coach in the home environment. Yet, in view of the small clinical improvement, we suggest that future studies explore whether the effect of home CIMT can be increased through an intensified support in daily practise, for example via electronic devices with videos or apps.

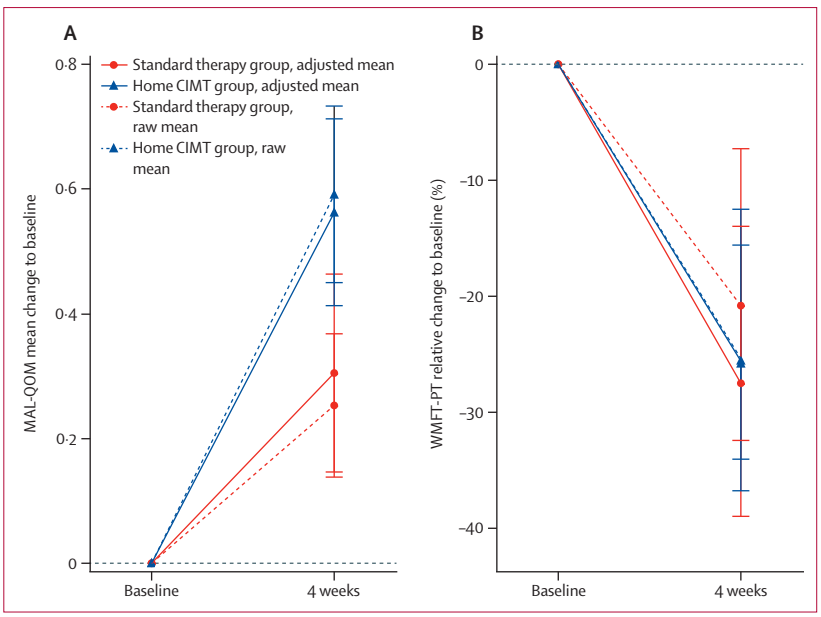

***Figure 3*: Mean changes from baseline to 4 weeks for the two primary outcomes**
(A) Motor Activity Log-Quality of Movement (MAL-QOM) is expressed as absolute change from baseline, with 0 indicating no change. (B) Wolf Motor Function Test of Performance Time (WMFT-PT) is expressed as change relative to baseline, with decrease indicating improvement. Means are shown as raw means and adjusted for age, sex, handedness, depression, anxiety, cognition, comorbidity, and education.

Contributors
AB, GK, and HvdB had the idea for the study. AB, GK, and KW initiated the study. AB, AS and BT participated in implementing the study. AS prepared the data for analysis, and AD and KW performed the data analysis. AB wrote the first draft of the manuscript, and AS, BT, GK, AD, KW, and MS revised it. All authors commented on the draft and approved the final manuscript.

Declaration of interests
We declare no competing interests.

Acknowledgments
The study was funded by the German Federal Ministry of Education and Research (grant number BMBF-01-GX-1003). We thank Heike Krüger and Kerstin Haevernick, who conducted and monitored the recruitment, training of therapists, and monitoring as first contact persons for therapists and patients. We also thank Daniela Koller, who advised us on the geographical recruitment method and composed straight line buffer regions around cities to define included communities. We thank the members of the scientific advisory board: Joachim Liepert and Christian Gerloff. Finally, we thank Thomas Heitzer for the profound reading and support in the final correction of the paper.

References

1 Langhorne P, Coupar F, Pollock A. Motor recovery after stroke: a systematic review. *Lancet Neurol* 2009; **8:** 741–54.
2 Kwakkel G, Veerbeek JM, van Wegen EEH, Wolf SL. Constraint-induced movement therapy after stroke. *Lancet Neurol* 2015; **14:** 224–34.
3 Wolf SL, Winstein CJ, Miller JP, et al. Effect of constraint-induced movement therapy on upper extremity function 3 to 9 months after stroke: the EXCITE randomized clinical trial. *JAMA* 2006; **296:** 2095–104.
4 Sirtori V, Corbetta D, Moja L, Gatti R. Constraint-induced movement therapy for upper extremities in stroke patients. *Cochrane Database Syst Rev* 2009; **4:** CD004433.
5 WHO. International classification of functioning, disability and health. http://www.who.int/classifications/icf/en (accessed Dec 1, 2014).
6 Peurala SH, Kantanen MP, Sjögren T, Paltamaa J, Karhula M, Heinonen A. Effectiveness of constraint-induced movement therapy on activity and participation after stroke: a systematic review and meta-analysis of randomized controlled trials. *Clin Rehabil* 2012; **26:** 209–23.
7 Langhorne P, Bernhardt J, Kwakkel G. Stroke rehabilitation. *Lancet* 2011; **377:** 1693–702.
8 Taub E, Uswatte G, King DK, Morris D, Crago JE, Chatterjee A. A placebo-controlled trial of constraint-induced movement therapy for upper extremity after stroke. *Stroke* 2006; **37:** 1045–49.
9 Shi YX, Tian JH, Yang KH, Zhao Y. Modified constraint-induced movement therapy versus traditional rehabilitation in patients with upper-extremity dysfunction after stroke: a systematic review and meta-analysis. *Arch Phys Med Rehabil* 2011; **92:** 972–82.
10 Smania N, Gandolfi M, Paolucci S, et al. Reduced-intensity modified constraint-induced movement therapy versus conventional therapy for upper extremity rehabilitation after stroke: a multicenter trial. *Neurorehabil Neural Repair* 2012; **26:** 1035–45.
11 Corbetta D, Sirtori V, Moja L, Gatti R. Constraint-induced movement therapy in stroke patients: systematic review and meta-analysis. *Eur J Phys Rehabil Med* 2010; **46:** 537–44.
12 Pollock A, Farmer SE, Brady MC, et al. Interventions for improving upper limb function after stroke. *Cochrane Database Syst Rev* 2014; **11:** CD010820.
13 Barzel A, Liepert J, Haevernick K, et al. Comparison of two types of constraint-induced movement therapy in chronic stroke patients: a pilot study. *Restor Neurol Neurosci* 2009; **27:** 673–80.
14 Barzel A, Ketels G, Tetzlaff B, et al. Enhancing activities of daily living of chronic stroke patients in primary health care by modified constraint-induced movement therapy (HOMECIMT): study protocol for a cluster randomized controlled trial. *Trials* 2013; **14:** 334.
15 Kurland KS, Gorr WL. GIS tutorial for health, 4th edn. Redlands, California: Esri Press, 2012.
16 Brauns H, Steinmann S. Educational reform in France, West-Germany, the United Kingdom and Hungary. Updating the CASMIN educational classification. *ZUMA-Nachrichten* 1999; **23:** 7–44.
17 Rieck M, Moreland J. The Orpington Prognostic Scale for patients with stroke: reliability and pilot predictive data for discharge destination and therapeutic services. *Disabil Rehabil* 2005; **27:** 1425–33.
18 Collin C, Wade D. Assessing motor impairment after stroke: a pilot reliability study. *J Neurol Neurosurg Psychiatry* 1990; **53:** 576–79.
19 Folstein MF, Folstein SE, McHugh PR. Mini-mental state. A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res* 1975; **12:** 189–98.
20 Rigler SK, Studenski S, Wallace D, Reker DM, Duncan PW. Co-morbidity adjustment for functional outcomes in community-dwelling older adults. *Clin Rehabil* 2002; **16:** 420–28.
21 Gregson JM, Leathley MJ, Moore AP, Smith TL, Sharma AK, Watkins CL. Reliability of measurements of muscle tone and muscle power in stroke patients. *Age Ageing* 2000; **29:** 223–28.
22 Taub E, Uswatte G, Mark VW, et al. Method for enhancing real-world use of a more-affected arm in chronic stroke: the transfer package of CI therapy. *Stroke* 2013; **44:** 1383–88.
23 Uswatte G, Taub E, Morris D, Vignolo M, McCulloch K. Reliability and validity of the upper-extremity Motor Activity Log-14 for measuring real-world arm use. *Stroke* 2005; **36:** 2493–96.
24 Lang CE, Edwards DF, Birkenmeier RL, Dromerick AW. Estimating minimal clinically important differences of upper-extremity measures early after stroke. *Arch Phys Med Rehabil* 2008; **89:** 1693–1700.
25 Morris DM, Uswatte G, Crago JE, Cook EW 3rd, Taub E. The reliability of the wolf motor function test for assessing upper-extremity function after stroke. *Arch Phys Med Rehabil* 2001; **82:** 750–55.
26 Lin K, Hsieh Y, Wu C, Chen C, Jang Y, Liu J. Minimal detectable change and clinically important difference of the Wolf motor function test in stroke patients. *Neurorehabil Neural Repair* 2009; **23:** 429–34.
27 Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med* 2001; **16:** 606–13.
28 Spitzer RL, Kroenke R, Williams JB, Lowe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. *Arch Intern Med* 2006; **166:** 1092–97.
29 Klasen BW, Hallner D, Schaub C, Willburger R, Hasenbring M. Validation and reliability of the German version of the Chronic Pain Grade questionnaire in primary care back pain patients. *Psychosoc Med* 2004; **1:** Doc07.
30 Campbell MK, Elbourne DR, Altman DG. CONSORT statement: extension to cluster randomised trials. *BMJ* 2004; **328:** 702–08.
31 Senn S, Stevens L, Chaturvedi N. Repeated measures in clinical trials: simple strategies for analysis using summary measures. *Stat Med* 2000; **19:** 861–77.
32 Lin K, Chang Y, Wu C, Chen Y. Effects of constraint-induced therapy versus bilateral arm training on motor performance, daily functions, and quality of life in stroke survivors. *Neurorehabil Neural Repair* 2009; **23:** 441–48.
33 Viana R, Teasell R. Barriers to the implementation of constraint-induced movement therapy into practice. *Top Stroke Rehabil* 2012; **19:** 104–14.
34 Brunner IC, Skouen JS, Strand LI. Is modified constraint-induced movement therapy more effective than bimanual training in improving arm motor function in the subacute phase post stroke? A randomized controlled trial. *Clin Rehabil* 2012; **26:** 1078–86.
35 Sawaki L, Butler AJ, Leng X, et al. Constraint-induced movement therapy results in increased motor map area in subjects 3 to 9 months after stroke. *Neurorehabil Neural Repair* 2008; **22:** 505–13.
36 McIntyre A, Viana R, Janzen S, Mehta S, Pereira S, Teasell R. Systematic review and meta-analysis of constraint-induced movement therapy in the hemiparetic upper extremity more than six months post stroke. *Top Stroke Rehabil* 2012; **19:** 499–513.
37 Dahl AE, Askim T, Stock R, Langørgen E, Lydersen S, Indredavik B. Short- and long-term outcome of constraint-induced movement therapy after stroke: a randomized controlled feasibility trial. *Clin Rehabil* 2008; **22:** 436–47.
38 Lemmens RJ, Timmermans AA, Janssen-Potten YJ, Smeets RJ, Seelen HA. Valid and reliable instruments for arm-hand assessment at ICF activity level in persons with hemiplegia: a systematic review. *BMC Neurol* 2012; **12:** 21.
39 Noorkõiv M, Rodgers H, Price CI. Accelerometer measurement of upper extremity movement after stroke: a systematic review of clinical studies. *J Neuroeng Rehabil* 2014; **11:** 144.