Sirtori V, Corbetta D, et al. Constraint-induced movement therapy for upper extremities in stroke patients. Cochrane Database of Systematic Reviews 2009, Issue 4, Art No. CD004433.

Design: Meta-analysis of clinical trials

PICOS:

- Patients: Adults with a clinical diagnosis of stroke and paresis of one arm
- Interventions: Rehabilitation with Constraint-Induced Movement Therapy (CIMT), modified CIMT (mCIMT), or Forced Use (FU) therapy:
    - CIMT is restraint of the unaffected upper limb with more than three hours per day of active therapy
    - mCIMT is restraint of the unaffected upper limb, with three hours or less of active therapy per day
    - FU is restraint of the unaffected upper limb, but without specific treatment of the affected upper limb
- Comparison: Other rehabilitative techniques (physical or occupational therapy), or no intervention
    - Four post-hoc subgroup comparisons were made:
        - "Dosage" of CIMT, defined as more than 30 hours of training of the affected limb versus 30 hours or less of such training
        - Anatomical region constraint: whether the unaffected arm was constrained only at the hand by use of a mitt, or whether both hand and arm were constrained by a sling and a mitt
        - Constraint effect: Studies in which the groups differed only in the presence or absence of unaffected limb constraint (i.e., the amount of active therapy of the affected limb was the same in both groups)
        - Time since stroke: classified as beginning CIMT zero to three months after stroke, three to six months, or more than nine months after stroke
- Outcomes: Primary outcome was disability, as measured by the Functional Independence Measure (FIM) or Barthel Index (BI)
    - Secondary outcomes were considered to be tests of arm motor function and motor impairment, grip strength, and dexterity, and quality of life
- Study types: Randomized or quasi-randomized trials

Study selection:

- Electronic databases included the Cochrane Stroke Group register, MEDLINE, EMBASE, and CINAHL through June 2008
- Two authors independently rated quality using the Cochrane Handbook, which emphasizes control of bias through randomization, allocation concealment, complete follow-up, blinded assessment of outcome, and validity + reliability of scales used to measure outcomes
- Most of the articles in the initial search were excluded because of not being randomized, or for not considering CIMT or mCIMT

Pertinent results:

- 19 trials with 619 patients met the authors' inclusion criteria
- There was some variation in the inclusion criteria for the individual trials, but most trials required some movement of extension in the interphalangeal and M-P joints, absence of cognitive impairments, no balance problems in walking, absence of excessive pain and of joint limitation in the affected limb, and no excessive spasticity in any joint
- Although the Cochrane reviewers emphasized disability as their primary outcome, many of the included studies reported secondary outcomes such as motor function and impairment
- For disability measured immediately post-intervention, there were 6 studies with 184 patients, in which CIMT had a significant effect (0.36 standard deviations of difference between CIMT and control interventions); however, 69 of the patients contributing to this pooled effect size were recruited from studies with more than 10% loss to follow-up
    - When disability was measured 3 to 6 months after treatment, the effect of CIMT on disability was not significant; the difference between CIMT and control was only 0.07 standard deviations (2 studies with 73 patients)
- For arm motor function, 14 studies with 436 patients provided data on 373 patients; the effect of CIMT was significant (0.72 SD of difference between CIMT and control intervention)
    - Arm motor impairment was measured in11 studies with 192 patients, and the effect of CIMT was significant (0.59 SD in favor of CIMT over control intervention)
- Additional analyses of perceived arm motor function (amount of use of the limb and quality of use) were measured as well; CIMT also had significant advantages in these analyses; measures of dexterity were poorly reported and not interpretable
- Quality of life was estimated in 3 studies with 278 patients, but the effect of CIMT was not significantly different from control interventions

Authors' conclusions:

- CIMT has moderately positive effects on disability at the end of treatment, but there was no evidence of a benefit at 6 months; it is not clear whether CIMT maintains its benefits in the long run
- Many studies had methodological problems, with poor reporting of randomization methods and small sample sizes
- Publication bias was considered a possibility; many authors of trials have a cultural and professional interest in disseminating positive results of the rehabilitation techniques they propose
- Additional studies would need to measure disability as a primary outcome, and would need to explore benefits for longer periods of time (one year) and to have at least 74 patients for arm motor function measures

Comments:

- Although a risk of bias was noted for several included studies, other studies appear to have had better control of bias, and one of these (Wolf 2006) was the basis for later study with a longer follow-up (Wolf 2008), which was not yet published for the meta-analysis
    - Because the reviewers converted the outcomes from their original scales into standardized mean scores, the numbers in the meta-analyses do not correspond to the numbers in the original articles
        - For example, Analysis 4.1 reports that Wolf 2006 had a mean arm motor function of 0.29 in the CIMT group, but this number does not appear in Table 2 of Wolf 2006, where the post-treatment scores are reported
    - Wolf 2008 remedies one of the problems noted by the authors for the motor function outcomes; it measured the effects of CIMT 12 months after treatment and then 12 months subsequently (2 year follow-up time)
    - Wolf 2006 had 12 month data, but this was not used in the meta-analyses, since other studies had measured only the post-treatment motor outcomes
    - For Wolf 2006, CIMT had a significant treatment effect at 12 months for the motor function outcomes in comparison with the control group
    - Wolf 2008 did have some attrition between 12 months and 24 months, bu reported that the motor function scores were maintained (had not deteriorated) at the later follow-up
        - Wolf 2008 recruited 105 patients into the CIMT group, and had 98 patients post-treatment, 86 patients at month 12, and 68 patients at month 24
        - The potential biases arising from this attrition are not discussed by the authors and are a matter of speculation to predict, but the authors do report that the attrition of 33.9% at trial's end would be 23.6% at trials end "if drop outs caused by death or deteriorating medical status are not included"
        - The attrition of 28 patients between 12 and 24 months in Wolf 2008 is displayed in Figure 1 as "8 withdrew consent, 7 changed condition, 4 died, 1 lost to followup, 8 other or unknown"
        - If the attrition occurred largely for medical reasons which were superimposed on the arm function, the measurement of retention of motor function with CIMT gains some plausibility

Assessment: High quality meta-analysis which provides good evidence for the favorable effect of CIMT on arm motor function at the end of treatment. Wolf 2008, which was still in progress when the Cochrane review was being written, supports some evidence that the motor function associated with CIMT is maintained at 24 months after treatment

References:

Wolf SI, Winstein CJ, et al. Effect of Constraint-Induced Movement Therapy on Upper Extremity Function 3 to 9 Months After Stroke. JAMA 2006;296:2095-2104.

Wolf SI, Winstein CJ, et al. The EXCITE Tria;: Retention of Improved Upper Extremity Function Among Stroke Survivors Receiving CI Movement Therapy. Lancet Neurol 2008;7(1)33-40.